GEORGIA DEPARTMENT OF COMMUNITY HEALTH

Georgia Department of Community Health

DRUG UTILIZATION REVIEW BOARD MEETING

Department of Community Health
2 Peachtree Street – 5th Floor Board Room
Atlanta, Georgia 30303

March 26, 2015

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GEORGIA DEPARTMENT OF COMMUNITY HEALTH

DRUG UTILIZATION REVIEW BOARD MEETING
AGENDA
2 Peachtree Street - 5th Floor DCH Board Room
Atlanta, Georgia 30303
Thursday, March 26, 2015
9:00 a.m. to 4:00 p.m.

CALL TO ORDER	*Drew Miller, RPh, Chair*
COMMENTS FROM THE DEPARTMENT	*Linda Wiant, PharmD, Chief*
MINUTES FROM PREVIOUS MEETING	*Chair*
EXTERNAL COMMENTS SESSION	*Chair*
ADJOURNMENT OF OPEN SESSION	*Chair*
EXECUTIVE SESSION	*Steve Liles, PharmD, Senior Director, Goold*
LUNCH	
RECONVENING OF OPEN SESSION	*Chair*
CLINICAL REVIEWS AND DURB VOTES	*Tara R. Cockerham, PharmD, NorthStar*
➢ **Manufacturers' Forum**	*Afzal Mistry, PharmD, NorthStar* *Emily Baker, PharmD, BCPS, NorthStar*

- **Therapeutic Class** – Anticonvulsants, including new drug Aptiom
- **New Drugs**
  - Cycloset, Jardiance, Tanzeum, Trulicity
  - Anoro Ellipta, Incruse Ellipta, Striverdi Respimat
  - Otezla, Stelara
  - Zontivity
  - Harvoni, Viekira
  - Plegridy
  - Uceris
- **Supplemental Rebate Classes**
- **Utilization Trends**
- **Drug Information**
  - Drug Update Newsletter
  - Horizon Watch Report
  - Patent Expiration Report
  - Clinical Compass Newsletter

FUTURE AGENDA ITEMS	*Chair*
ADJOURNMENT	*Chair*

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Department of Community Health
Drug Utilization Review Board (DURB)
MINUTES
Thursday, December 4, 2014

MEMBERS PRESENT

Joseph R. Bona, M.D., MBA, Chair
Osgood (Drew) A. Miller, R.Ph., Vice-Chair
Mia Avery, Pharm.D.
Gurinder J.S. Doad, M.D.
Deborah W. Fincher, M.S., R.Ph.
M. Celeste Fowler, Pharm.D.
Thomas B. Gore, M.D.
John Greeson, M.D., MBA
John Johnson, M.D., MBA
Robyn Lorys, Pharm.D.
J. Russell (Rusty) May, Pharm.D.
Brent L. Rollins, R.Ph., Ph.D.
Robert E. Shervette III, M.D.
Mary Virginia "Ginny" Yates, Pharm.D.

MEMBERS ABSENT

Ann R. Damon, Pharm.D.
Edwina L. Jones, Pharm.D., MBA
Donald A. Paul, M.D.

Staff

Linda Wiant, Pharm.D., Pharmacy Director, Pharmacy Services
Turkesia Robertson-Jones, Pharm.D., Pharmacy Operations Manager, Pharmacy Services
Gilletta Gray, R.Ph., Clinical Manager, Pharmacy Services
Lori Garner, MHS, MBA, R.Ph., Pharmacist, Pharmacy Services
Rose Marie Duncan, MBA, Program Associate, Pharmacy Services

NorthStar HealthCare Consulting

Emily Baker, Pharm.D., BCPS, MHA, MBA, President
Tara R. Cockerham, Pharm.D., Clinical Programs Director
Afzal “Fez” Mistry, Pharm.D., Clinical Pharmacist

Catamaran

Susan McCreight, Sr. Director, Public Sector Account Management
Mark Hall, MBA, PMP, Account Manager
Talmahjia “Tami” Sweat, Pharm.D., Clinical Systems Product Manager

Goold Health Services

Steve Liles, Pharm.D., Sr. Director, Pharmacy Services
Doug Martin, Pharm.D., Pharmacy Project Manager

Call to Order

The Drug Utilization Review Board (DURB/DUR Board/Board) held its fourth meeting for the calendar year on December 4, 2014. The Chair, Joseph R. Bona, M.D., MBA, called the meeting to order at 9:35am. Members of the Board introduced themselves.

Comments from the Department

Linda Wiant, Pharm.D., Pharmacy Director, Pharmacy Services, commented on the following items:

1. Industry News – Handouts were provided of recent industry news and claims information from DCH's quarterly reports.
2. New Members – A welcome was extended to new and returning members: John Johnson, M.D., MBA and J. Russell (Rusty) May, Pharm.D., and to guest, Diane May, Pharm.D.
3. Jerry Dubberly, Pharm.D., MBA, Chief Medical Assistance Plans – It was announced his last day at DCH will be early January.
4. Board Transitions – Gurinder J.S. Doad, M.D. will be Vice-Chair; Osgood (Drew) A. Miller, R.Ph., will be Chair. Joseph R. Bona, M.D., MBA, was thanked for his service as Chair.

Minutes from the Previous Meeting

Dr. Bona asked for corrections or changes to the minutes from the September 18, 2014 meeting. There were no corrections. A motion was made (Thomas B. Gore, M.D.), seconded (J. Russell (Rusty) May, Pharm.D.), and carried to approve the minutes as written.

Advocate Comments Session

There were no advocate comments.

Adjournment of Open Session

The DUR Board voted to close the open meeting pursuant to the Open Meeting Act of Georgia Section 50-14-1 – 50-14-6 and pursuant to Federal Law Section 1396R-8B3D. The individuals recorded in attendance with the Board members were from the Department of Community Health, Goold Health Services, NorthStar HealthCare Consulting, and Catamaran. A motion was made by Osgood (Drew) A. Miller, R.Ph., Vice-Chair, and seconded by Robert E. Shervette III, M.D., to adjourn the open session and approve the closed session. There was a unanimous vote approving the closed session. The Chairman, Dr. Joseph R. Bona, adjourned the open session at approximately 9:43 am, at which time members took a break then reconvened for the executive (closed) session.

Executive Session

The Executive Session was held from 9:46am to 10:25am.

Reconvening of Open Session

The DUR Board reconvened for the open session at 10:29am.

Manufacturers' Forum

Tara Cockerham, Pharm.D., reviewed information regarding the Manufacturers' Forum that was provided in the Manufacturer Information section in the DUR Board binder. A total of five (5) manufacturers participated and provided information regarding the following drugs discussed at the December 2014 DURB meeting:

Manufacturers	Drugs
Merck	Grastek, Ragwitek
Greer	Oralair
Amgen	Neupogen, Neulasta
AstraZeneca	Myalept
Novartis	Zykadia

Questions and comments were received from the Board on the following:

- Ragwitek – Pediatric indication not pursued due to most children not having Ragweed allergies.

The next forum will be held on Thursday, February 5, 2015 and Tuesday, February 10, 2015 from 9am-5pm at the NorthStar Healthcare Consulting office: 1121 Alderman Drive, Suite 112, Alpharetta, GA 30005.

New Drug Reviews

Clinical information for the following new drugs, in the market six months or more, was presented for discussion and recommendations. The complete detailed drug summary is in the New Drugs for Review section of the DUR Board binder.

Therapeutic Class	Drugs	Presenter
Antihemophilic	*Eloctate*	Emily Baker, Pharm.D., BCPS
Allergen Immunotherapy	*Grastek, Oralair, Ragwitek*	Emily Baker, Pharm.D., BCPS
Lysosomal Storage Disorder	*Myalept*	Emily Baker, Pharm.D., BCPS
Antineoplastic	*Zykadia*	Afzal Mistry, Pharm.D.
Sedative Hypnotic	*Hetlioz*	Afzal Mistry, Pharm.D.

Guest Expert Speaker

Nathan Segall, M.D., Certified Principal Investigator, founder of Clinical Research Atlanta, discussed patient cases and the three oral formulations indicated as immunotherapy for the treatment of grass pollens. He addressed questions and comments from the Board on the following:

- Determination of which patients will benefit from these medications – look at history, skin tests, in vitro tests
- Restrict prescribing to Allergists – some Primary Care physicians could do well with prescribing and some Allergists may never prescribe; Some Otolaryngologists-red flag.
- Patients needing immunotherapy vs. being controlled with corticosteroids, etc. – look at calculation of costs; injections and sublingual therapy help more than other medications; don't put on if not going to stay on it
- 30 minutes in physician office – only applies to first dose, not every season

- EpiPens – only need to have 1 on hand
- Oral pruritis – may happen every season
- Only have grass allergy taking oral med and still on immunotherapy – probably won't happen
- Kids referred to allergist that have behavioral problems
- Concern of breaks in dental mucosa and dental hygiene in Medicaid patients

The Board discussed the drug information, provided comments, and raised questions on the following from the New Drugs Reviews:

- Myalept – novel agent; restrictive program
- Hetlioz – both Phase 3 studies and comparison with melatonin not published; significant cost; driving restrictions (not given within 4 hours)

The Board voted and made recommendations for all new drug reviews noted in the Board's Recommendations to the Department.

Therapeutic Class Reviews

Clinical information for the following therapeutic classes was presented for discussion by Dr. Tara Cockerham. The complete detailed therapeutic class reviews were provided in the Therapeutic Class Reviews section of the DUR Board binder.

Therapeutic Class Name
Sedative Hypnotics
Granulocyte Colony Stimulating Factors

The Board commented on the following:

- Granulocyte Colony Stimulating Factors – use of agents for primary and secondary prophylaxis; product selection is patient specific, look at comorbidities; contraindications-hypersensitivity to *E. coli*.

The Board voted and made recommendations noted in the Board's Recommendations to the Department.

Utilization Trend Review

Utilization trends for Georgia Medicaid Fee-for-Service were provided in detail in the Utilization Trends section of the DUR Board binder.

Drug Information

Information from the following was provided in detail in the Drug Information section of the DUR Board binder used for this meeting:

- Drug Update Newsletter
- Horizon Watch Report
- Patent Expiration Report
- Clinical Compass Newsletter

Future Agenda Items

The following future agenda items were noted:

- Feasibility of applying a MAC on hemophilia products

Upcoming Meetings

The following upcoming meetings were published in the DURB binder:

- Drug Utilization Review Board
  2 Peachtree Street NW
  5th Floor Board Room
  Atlanta, Georgia 30303

  Thursday, March 26, 2015
  Thursday, June 4, 2015
  Thursday, September 24, 2015
  Tuesday, December 15, 2015

- Manufacturers' Forum
  NorthStar Healthcare Consulting
  1121 Alderman Drive
  Suite 112
  Alpharetta, Georgia 30005

  Thursday, February 5, 2015
  Tuesday, February 10, 2015 (if needed)
  Thursday, April 30, 2015
  Thursday, August 6, 2015
  Thursday, November 5, 2015

Disclosure Forms

Disclosure forms were received and reviewed by the Department for completeness for all Board members attending the meeting.

Board's Recommendations to the Department

After all clinical and financial evaluations and discussions, the DUR Board voted and presented the Department with the following recommendations for changes to the Preferred Drug List (PDL). All motions and votes are noted in Attachment A.

New Drug Reviews

Antihemophilic

The DUR Board recommended ***Non-Preferred*** status with ***Prior Authorization*** for ***Eloctate® (Intravenous) Vial***.

Allergen Immunotherapy

The DUR Board recommended ***Non-Preferred*** status with ***Prior Authorization*** for ***Grastek® (Sublingual) Tablet***, ***Oralair® (Sublingual) Tablet*** and ***Ragwitek®***

(Sublingual) Tablet.

Lysosomal Storage Disorder

The DUR Board recommended ***Preferred*** status with ***Prior Authorization*** for ***Myalept®*** ***(Subcutaneous) Vial***.

Antineoplastic

The DUR Board recommended ***Preferred*** status with ***Prior Authorization*** for ***Zykadia® (Oral) Capsule***.

Sedative Hypnotic

The DUR Board recommended ***Non-Preferred*** status with ***Prior Authorization*** for ***Hetlioz® (Oral) Capsule***.

Class Reviews

Sedative Hypnotics

The DUR Board recommended ***No Changes***.

Granulocyte Colony Stimulating Factors

The DUR Board recommended ***No Changes***.

Conclusion

At the conclusion of the reconvened open session and no other business for discussion, there was a unanimous decision to adjourn the meeting. Chair Bona adjourned the meeting at 12:16pm.

THESE MINUTES ARE HEREBY APPROVED AND ADOPTED, THIS THE _____ DAY OF _____, 2015.

_____

Joseph R. Bona, M.D., MBA, Chair

Drug Utilization Review Board

Motions - Votes - New Drugs

December 4, 2014

New Drug	Drug	PDL Status	Motion - Recommendations	Additional Comments
ANTIHEMOPHILIC PRODUCTS-FACTOR VIII	ADVATE (INTRAVEN) VIAL	P	P	
	ELOCTATE (INTRAVEN) VIAL	NPPA	NPPA	
	HELIXATE FS (INTRAVEN) VIAL	P	P	
	KOGENATE FS (INTRAVEN) KIT	P	P	
	KOGENATE FS (INTRAVEN) VIAL	P	P	
	RECOMBINATE (INTRAVEN) VIAL	P	P	
	XYNTHA (INTRAVEN) KIT	P	P	
	XYNTHA SOLOFUSE (INTRAVEN) SYRINGEKIT	P	P	

	Board Members - Present (Strike out, when absent)	Motion Maker (√)	Seconded By (√)	VOTES YES (√)	NO (√)	ABSTAIN (√)
1	Avery, Mia, Pharm.D.			√		
2	Bona, Joseph R. M.D. - Chair			√		
3	Doad, Gurinder J.S., M.D.			√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Fowler, M. Celeste, Pharm.D.			√		
6	Gore, Thomas B., M.D.	√		√		
7	Greeson, John D., M.D., MBA		√	√		
8	Johnson, John, M.D., MBA			√		
9	Lorys, Robyn Pharm.D.			√		
10	May, J. Russell (Rusty)			√		
11	Miller, Osgood (Drew) A. R.Ph. - **Vice**			√		
12	Rollins, Brent L., R.Ph., Ph.D.			√		
13	Shervette III, Robert E., M.D.			√		
14	Yates, Mary Virginia "Ginny", Pharm.D.			√		
			TOTAL	14	0	0

	Board Members - Absent
1	Damon, Ann R., Pharm.D.
2	Jones, Edwina L., Pharm.D., MBA
3	Paul, Donald A., M.D.

Drug Utilization Review Board

Motions - Votes - **New Drugs**

December 4, 2014

New Drug	Drug	PDL Status	Motion - Recommendations	Additional Comments
ALLERGEN IMMUNOTHERAP Y	RAGWITEK (SUBLINGUAL) TAB SUBL	NPPA	NPPA	
	GRASTEK (SUBLINGUAL) TAB SUBL	NPPA	NPPA	
	ORALAIR (ORAL) TAB SUBL	NPPA	NPPA	

	Board Members - Present (Strike out, when absent)	Motion Maker (√)	Seconded By (√)	VOTES YES (√)	NO (√)	ABSTAIN (√)
1	Avery, Mia, Pharm.D.		√	√		
2	Bona, Joseph R. M.D. - Chair			√		
3	Doad, Gurinder J.S., M.D.			√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Fowler, M. Celeste, Pharm.D.			√		
6	Gore, Thomas B., M.D.			√		
7	Greeson, John D., M.D., MBA			√		
8	Johnson, John, M.D., MBA			√		
9	Lorys, Robyn Pharm.D.	√		√		
10	May, J. Russell (Rusty)			√		
11	Miller, Osgood (Drew) A. R.Ph. - **Vice**			√		
12	Rollins, Brent L., R.Ph., Ph.D.			√		
13	Shervette III, Robert E., M.D.			√		
14	Yates, Mary Virginia "Ginny", Pharm.D.			√		
			TOTAL	14	0	0

	Board Members - Absent
1	Damon, Ann R., Pharm.D.
2	Jones, Edwina L., Pharm.D., MBA
3	Paul, Donald A., M.D.

Drug Utilization Review Board

Motions - Votes - New Drugs

December 4, 2014

New Drug	Drug	PDL Status	Motion - Recommendations	Additional Comments	
LYSOSOMAL STORAGE DISORDER TX	MYALEPT (SUB-Q) VIAL	NPPA	PPA		
Board Members - Present (Strike out, when absent)	Motion Maker (√)	Seconded By (√)	VOTES YES (√)	NO (√)	ABSTAIN (√)
1 Avery, Mia, Pharm.D.			√		
2 Bona, Joseph R. M.D. - Chair			√		
3 Doad, Gurinder J.S., M.D.	√		√		
4 Fincher, Deborah W., M.S., R.Ph.			√		
5 Fowler, M. Celeste, Pharm.D.			√		
6 Gore, Thomas B., M.D.			√		
7 Greeson, John D., M.D., MBA			√		
8 Johnson, John, M.D., MBA			√		
9 Lorys, Robyn Pharm.D.		√	√		
10 May, J. Russell (Rusty)			√		
11 Miller, Osgood (Drew) A. R.Ph. - **Vice**			√		
12 Rollins, Brent L., R.Ph., Ph.D.			√		
13 Shervette III, Robert E., M.D.			√		
14 Yates, Mary Virginia "Ginny", Pharm.D.			√		
		TOTAL	14	0	0

Board Members - Absent	
1 Damon, Ann R., Pharm.D.	
2 Jones, Edwina L., Pharm.D., MBA	
3 Paul, Donald A., M.D.	13

Drug Utilization Review Board

Motions - Votes - New Drugs

December 4, 2014

New Drug	Drug	PDL Status	Motion - Recommendations	Additional Comments
ANTINEOPLASTICS	XALKORI (ORAL) CAPSULE	PPA	PPA	
	ZYKADIA (ORAL) CAPSULE	PPA	PPA	

	Board Members - Present (Strike out, when absent)	Motion Maker (√)	Seconded By (√)	VOTES YES (√)	NO (√)	ABSTAIN (√)
1	Avery, Mia, Pharm.D.			√		
2	Bona, Joseph R. M.D. - Chair			√		
3	Doad, Gurinder J.S., M.D.			√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Fowler, M. Celeste, Pharm.D.			√		
6	Gore, Thomas B., M.D.			√		
7	Greeson, John D., M.D., MBA			√		
8	Johnson, John, M.D., MBA		√	√		
9	Lorys, Robyn Pharm.D.			√		
10	May, J. Russell (Rusty)	√		√		
11	Miller, Osgood (Drew) A. R.Ph. - **Vice**			√		
12	Rollins, Brent L., R.Ph., Ph.D.			√		
13	Shervette III, Robert E., M.D.			√		
14	Yates, Mary Virginia "Ginny", Pharm.D.			√		
			TOTAL	14	0	0

	Board Members - Absent
1	Damon, Ann R., Pharm.D.
2	Jones, Edwina L., Pharm.D., MBA
3	Paul, Donald A., M.D.

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Drug Utilization Review Board

Motions - Votes - New Drugs

December 4, 2014

New Drug	Drug	PDL Status	Motion - Recommendations	Additional Comments	
SEDATIVE-HYPNOTICS	HETLIOZ (ORAL) CAPSULE	NPPA	NPPA		
Board Members - Present (Strike out, when absent)	Motion Maker (√)	Seconded By (√)	VOTES YES (√)	NO (√)	ABSTAIN (√)
1 Avery, Mia, Pharm.D.			√		
2 Bona, Joseph R. M.D. - Chair			√		
3 Doad, Gurinder J.S., M.D.			√		
4 Fincher, Deborah W., M.S., R.Ph.			√		
5 Fowler, M. Celeste, Pharm.D.			√		
6 Gore, Thomas B., M.D.		√	√		
7 Greeson, John D., M.D., MBA			√		
8 Johnson, John, M.D., MBA			√		
9 Lorys, Robyn Pharm.D.			√		
10 May, J. Russell (Rusty)	√		√		
11 Miller, Osgood (Drew) A. R.Ph. - **Vice**			√		
12 Rollins, Brent L., R.Ph., Ph.D.			√		
13 Shervette III, Robert E., M.D.			√		
14 Yates, Mary Virginia "Ginny", Pharm.D.			√		
		TOTAL	14	0	0

Board Members - Absent
1 Damon, Ann R., Pharm.D.
2 Jones, Edwina L., Pharm.D., MBA
3 Paul, Donald A., M.D.

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Drug Utilization Review Board

Motions - Votes - **New Drugs**

December 4, 2014

Class Review

SEDATIVE HYPNOTICS

RECOMMENDATION: No changes to the Sedative Hypnotics class.

	Board Members - Present (Strike out, when absent)	Motion Maker (√)	Seconded By (√)	VOTES YES (√)	NO (√)	ABSTAIN (√)
1	Avery, Mia, Pharm.D.			√		
2	Bona, Joseph R. M.D. - Chair			√		
3	Doad, Gurinder J.S., M.D.			√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Fowler, M. Celeste, Pharm.D.			√		
6	Gore, Thomas B., M.D.			√		
7	Greeson, John D., M.D., MBA			√		
8	Johnson, John, M.D., MBA			√		
9	Lorys, Robyn Pharm.D.			√		
10	May, J. Russell (Rusty)	√		√		
11	Miller, Osgood (Drew) A. R.Ph. - **Vice**		√	√		
12	Rollins, Brent L., R.Ph., Ph.D.			√		
13	Shervette III, Robert E., M.D.			√		
14	Yates, Mary Virginia "Ginny", Pharm.D.			√		
			TOTAL	14	0	0

	Board Members - Absent
1	Damon, Ann R., Pharm.D.
2	Jones, Edwina L., Pharm.D., MBA
3	Paul, Donald A., M.D.

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Class Review

GRANULOCYTE COLONY STIMULATING FACTORS

RECOMMENDATION: No changes to the Granulocyte Colony Stimulating Factors class.

	Board Members - Present (Strike out, when absent)	Motion Maker (√)	Seconded By (√)	VOTES YES (√)	NO (√)	ABSTAIN (√)
1	Avery, Mia, Pharm.D.	√		√		
2	Bona, Joseph R. M.D. - Chair			√		
3	Doad, Gurinder J.S., M.D.			√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Fowler, M. Celeste, Pharm.D.			√		
6	Gore, Thomas B., M.D.			√		
7	Greeson, John D., M.D., MBA			√		
8	Johnson, John, M.D., MBA		√	√		
9	Lorys, Robyn Pharm.D.					√
10	May, J. Russell (Rusty)			√		
11	Miller, Osgood (Drew) A. R.Ph. - **Vice**			√		
12	Rollins, Brent L., R.Ph., Ph.D.			√		
13	Shervette III, Robert E., M.D.			√		
14	Yates, Mary Virginia "Ginny", Pharm.D.			√		
			TOTAL	13	0	1

	Board Members - Absent
1	Damon, Ann R., Pharm.D.
2	Jones, Edwina L., Pharm.D., MBA
3	Paul, Donald A., M.D.

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Drug Utilization Review Board Meeting			
December 4, 2014			
Therapeutic Class	Drug Name	Current PDL Status	DCH Decisions
New Drug Reviews			
Antihemophillic			
	Eloctate (Intravenous) Vial	NP/PA	NP/PA
Allergen Immunotherapy			
	Grastek (Sublingual) Tablet	NP/PA	NP/PA
	Oralair (Sublingual) Tablet	NP/PA	NP/PA
	Ragwitek (Sublingual) Tablet	NP/PA	NP/PA
Lysosomal Storage Disorder			
	Myalept (Subcutaneous) Vial	NP/PA	P/PA
Antineoplastic			
	Zykadia (Oral) Capsule	P/PA	P/PA
Sedative Hypnotic			
	Hetlioz (Oral) Capsule	NP/PA	NP/PA

PDL=Preferred Drug List; P=preferred; NP=non-preferred; PA=prior authorization

Class Reviews

Sedative Hypnotics

The DUR Board recommended No Changes.

Granulocyte Colony Stimulating Factors

The DUR Board recommended No Changes.

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Manufacturers' Forum
Manufacturer Presentations

Dates: February 5, 2015 and February 10, 2015

Location: NorthStar HealthCare Consulting
1121 Alderman Drive
Suite 112
Alpharetta, Georgia 30005

Attendees
Department of Community Health
Linda Wiant, PharmD, Director, Pharmacy Services

NorthStar HealthCare Consulting
Tara R. Cockerham, PharmD, Clinical Programs Director
Emily Baker, PharmD, BCPS, MBA, MHA, President
Afzal Mistry, PharmD, Clinical Pharmacist

Catamaran
Talmahjia "Tami" Sweat, PharmD, Director, Clinical Management-Public Sector

Drug Summary Documents
Please note that relevant, electronic materials that were provided by manufacturers were forwarded to the Drug Utilization Review Board (DURB). The manufacturers presenting at the Forum referred the audience and the readers of the materials to the prescribing information for additional information on the drug, especially in regards to safety.

Drug Presentations

I. Otsuka
Walter Lawhorn, PharmD, Medical Science Liaison
Rod Teat, PharmD, Medical Science Liaison
Dianna Sedgwick, CMR, Senior Account Executive

Abilify® Maintena® (aripiprazole extended-release)
Cost Effectiveness of Aripiprazole Once Monthly Compared to Paliperidone Palmitate Long-acting
In response to a request from NorthStar HealthCare Consulting, this presentation is a medical summary of a peer reviewed journal article (Citrome et al 2014) as well as information on the ABILIFY MAINTENA® (aripiprazole) pre-filled dual chamber syringe and the pivotal study in acutely relapsed adults with schizophrenia.

Introduction
- Abilify Maintena is indicated for the treatment of schizophrenia.
- Boxed Warning: Increased mortality in elderly patients with dementia-related psychosis

Summary of Citrome et al 2014
- **Citrome et al (2014)** developed a 1-year decision-analytic model to compare the cost-effectiveness between two long-acting antipsychotic injectables.
  - Abilify Maintena (AOM) and paliperidone palmitate (PLAI) were analyzed when initiating maintenance therapy in adult schizophrenia patients.
  - Relapse rates, adverse events, and direct medical costs were estimated for a one year time horizon.
  - Data from AOM and PLAI placebo-controlled pivotal clinical trials and from product prescribing information were utilized to estimate the incidence of adverse events (akathisia, weight gain, hyperlipidemia, hyperprolactinemia and extrapyramidal symptoms) and relapse rates.
  - Cost effectiveness of AOM compared to PLAI calculated the additional costs per relapse averted with the following:
    - Costs and number of relapses for those starting on each index therapy

- Incremental costs and the decrease in number of relapses when using AOM compared with PLAI.
- In order to reflect the variation in dosing based on practice setting, four dosing strategies were utilized.
  - Dosing used during the pivotal clinical trials of AOM and PLAI
  - Real-world dosing based on observed dosing patterns
  - Dosing based on prescribing information
  - Highest dose available with equivalent treatment efficacy
- Patients entering into the model either remained on initial treatment during the course of 1 year or discontinued after 6 months due to adverse events, lack of efficacy, or for other reasons including non-compliance.
  - Patients that discontinued due to adverse events or lack of efficacy were switched to a different standard-of-care long-acting injectable therapy which included fluphenazine, haloperidol, or risperidone.
  - Patients that discontinued due to any other reasons did not receive additional therapy.
  - The model assumed one office visit per month for actively treated patients and an additional three office visits for any patient that switched therapies in order to reflect the increase in patient monitoring during the conversion of medications.
- When real-world dosing and the highest available dosing/equivalent treatment efficacy was assumed, the analyses showed AOM was dominant (defined as more efficacious, less costly) strategy based on ICER (incremental cost-effectiveness ratio) compared with PLAI.
- AOM remained a cost-effective treatment option compared with PLAI for the clinical trial and PI-based dosing strategies.

ABILIFY MAINTENA Pivotal Studies
The efficacy of ABILIFY MAINTENA for treatment of schizophrenia was established in:
- One short-term (12-week), randomized, double-blind, placebo-controlled trial in acutely relapsed adults, Protocol 31-12-291 (Study 1)
- One longer-term, double-blind, placebo-controlled, randomized-withdrawal (maintenance) trial in adults, Protocol 31-07-246 (Study 2).

Short-Term Efficacy
In the short-term (12-week), randomized, double-blind, placebo-controlled trial in acutely relapsed adults (Study 1), the primary measure used for assessing psychiatric signs and symptoms was the Positive and Negative Syndrome Scale (PANSS). The primary endpoint was the change from baseline in PANSS total score to week 10. ABILIFY MAINTENA was superior to placebo in improving the PANSS total score at the end of week 10. Based on the placebo-controlled trial of ABILIFY MAINTENA in schizophrenia, the most commonly observed adverse reactions associated with the use of aripiprazole in patients (incidence of 5% or greater and aripiprazole incidence at least twice that for placebo) were increased weight (16.8% vs 7.0%), Akathisia (11.4% vs 3.5%), injection site pain (5.4% vs 0.6%) and sedation (5.4% vs 1.2%).

Aripiprazole Kits
ABILIFY MAINTENA is a long-acting aripiprazole formulation with 4 week dosing intervals indicated for the treatment of schizophrenia. ABILIFY MAINTENA comes in two types of kits. 1) Pre-filled Dual Chamber Syringe available in 300 mg or 400 mg strength syringes and 2) Single-use vials available in 300 mg or 400 mg strength vials.

Questions and Answers
There were no additional questions and answers.

II. AbbVie
Andrea R Hume, MD, Medical Outcomes Science Liaison
Phil Hecht, MBA, Managed Care Area Manager

Viekira Pak® (ombitasvir, paritaprevir, and ritonavir tablets; dasabuvir tablets)
BACKGROUND
• Chronic hepatitis C is a serious viral infection that can result in liver damage or hepatocellular carcinoma in some patients.
• AASLD/IDSA/IAS-USA guidelines recommend highest priority be given to treating HCV patients with advanced hepatic fibrosis or compensated cirrhosis (METAVIR F3 or F4), organ transplant, or type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (e.g., vasculitis), proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis and high priority to HCV patients with hepatic fibrosis (METAVIR F2), HIV or

HBV coinfection, other coexisting liver disease (e.g., NASH), debilitating fatigue, type 2 diabetes mellitus, or porphyria cutanea tarda.
• In the U.S., deaths due to hepatitis C virus have surpassed HIV in recent years.
• Successful HCV treatment results in sustained virologic response (SVR), which is equivalent to virologic cure; virologic cure is expected to benefit chronically infected persons.

INDICATIONS AND USAGE
VIEKIRA PAK with or without ribavirin is indicated for the treatment of patients with genotype 1 chronic hepatitis C virus (HCV) infection including those with compensated cirrhosis. Limitation of Use: VIEKIRA PAK is not recommended for use in patients with decompensated liver disease.

MECHANSIM OF ACTION
• VIEKIRA PAK includes ombitasvir, a hepatitis C virus NS5A inhibitor, paritaprevir, a hepatitis C virus NS3/4A protease inhibitor, ritonavir, a CYP3A inhibitor and dasabuvir, a hepatitis C virus non-nucleoside NS5B palm polymerase inhibitor.

DOSAGE AND ADMINISTRATION
• The recommended oral dose of VIEKIRA PAK is two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets once daily (in the morning) and one dasabuvir 250 mg tablet twice daily (morning and evening) with a meal without regard to fat or calorie content.
• The treatment duration for most genotype 1 patient populations is 12 weeks, including HCV/HIV-1 co-infection patients. The treatment duration for genotype 1a patients with cirrhosis is 24 weeks, although VIEKIRA PAK administered with ribavirin for 12 weeks may be considered for some patients based on prior treatment history. Additionally, in liver transplant recipients with normal hepatic function and mild fibrosis (Metavir fibrosis score ≤2), the recommended duration of VIEKIRA PAK with ribavirin is 24 weeks.

KEY CLINICAL TRIAL SUMMARY
• The efficacy and safety of VIEKIRA PAK was evaluated in six randomized, multicenter, clinical trials in 2,308 subjects with genotype 1 (GT1) chronic hepatitis C virus (HCV) infection, including one trial exclusively in subjects with cirrhosis with mild hepatic impairment (Child-Pugh A).

Clinical Trial Results in Adults with Chronic HCV Genotype 1a and 1b Infection without Cirrhosis
• SVR12 rate of 96% was seen in GT1a treatment-naïve subjects without cirrhosis treated with VIEKIRA PAK in combination with ribavirin in the placebo-controlled trial, SAPPHIRE-I (GT1a treatment-naïve, n=322) and an SVR12 rate of 97% was seen in GT1a treatment-naïve subjects without cirrhosis receiving ribavirin in PEARL-IV (GT1a treatment-naïve, n=100) for 422 GT1a subjects without cirrhosis treated with VIEKIRA PAK in combination with ribavirin. SVR12 rate of 96% was seen in GT1a treatment-experienced subjects in the placebo-controlled trial, SAPPHIRE-II (GT1a treatment-experienced, n=173). In SAPPHIRE-I and SAPPHIRE-II, no placebo subject achieved a HCV RNA <25 IU/mL during treatment.
• Treatment-naïve, HCV GT1a-infected subjects without cirrhosis treated with VIEKIRA PAK in combination with RBV for 12 weeks in PEARL-IV had a significantly higher SVR12 rate than subjects treated with VIEKIRA PAK alone (97% and 90% respectively; difference +7% with 95% confidence interval, +1% to +12%). VIEKIRA PAK alone was not studied in treatment-experienced subjects with GT1a infection.
• The SVR rate for HCV GT1b-infected subjects without cirrhosis treated with VIEKIRA PAK without RBV for 12 weeks in PEARL-II (treatment-experienced: null responder, n=32; partial responder, n=26; relapser, n=33) and PEARL-III (treatment-naïve, n=209) was 100%.

Clinical Trial Results in Adults with Chronic HCV Genotype 1a and 1b Infection and Compensated Cirrhosis
• TURQUOISE-II was an open-label trial that enrolled 380 HCV GT1a and 1b-infected subjects with cirrhosis and mild hepatic impairment (Child-Pugh A) who were either treatment-naïve or did not achieve SVR with prior treatment with pegylated interferon (pegIFN)/RBV.
• SVR12 rate of 95% was seen in GT1a subjects treated with VIEKIRA PAK with ribavirin for 24 weeks in TURQUOISE II.
• In GT1a infected subjects, the overall SVR12 rate difference between 24 and 12 weeks of treatment with VIEKIRA PAK with RBV was +6% with 95% confidence interval, -0.1% to +13% with differences varying by pretreatment history.
• SVR12 rates of 99% were seen in Genotype 1b-infected subjects when treated with VIEKIRA PAK plus ribavirin for 12 weeks.

Effect of Ribavirin Dose Reductions on SVR12
• Seven percent of subjects (101/1551) treated with VIEKIRA PAK with RBV had a RBV dose adjustment due to a decrease in hemoglobin level; of these, 98% (98/100) achieved an SVR12.

Clinical Trial of Selected Liver Transplant Recipients (CORAL-I)
• Of the 34 subjects (29 with HCV GT1a infection and 5 with HCV GT1b infection) enrolled, (97%) achieved SVR12 (97% in subjects with GT1a infection and 100% of subjects with GT1b infection). One subject with HCV GT1a infection relapsed post-treatment.

Clinical Trial in Subjects with HCV/HIV-1 Co-infection (TURQUOISE-I)
• In an open-label clinical trial 63 subjects with HCV GT1 infection co-infected with HIV-1 (19% of subjects had compensated cirrhosis; 67% of subjects were HCV treatment-naïve; 33% of subjects had failed prior treatment with pegIFN/RBV; 89% of subjects had HCV genotype 1a infection) were treated for 12 or 24 weeks with VIEKIRA PAK in combination with RBV.
• The SVR12 rates were 91% (51/56) for subjects with HCV GT1a infection and 100% (7/7) for those with HCV GT1b infection.

Durability of Response
• In an open-label clinical trial, 92% of subjects (526/571) who received various combinations of the direct acting antivirals included in VIEKIRA PAK with or without RBV achieved SVR12, and 99% of those who achieved SVR12 maintained their response through 48 weeks post-treatment (SVR48).

IMPORTANT SAFETY INFORMATION
• The safety assessment was based on data from six Phase 3 clinical trials in more than 2,000 subjects who received VIEKIRA PAK with or without ribavirin for 12 or 24 weeks.
• During clinical trials with VIEKIRA PAK with or without ribavirin, elevations of ALT to greater than 5 times the upper limit of normal (ULN) occurred in approximately 1% of all subjects. ALT elevations were typically asymptomatic, occurred during the first 4 weeks of treatment, and declined within two to eight weeks of onset with continued dosing of VIEKIRA PAK with or without ribavirin.
• Ethinyl estradiol-containing medications must be discontinued prior to starting therapy with VIEKIRA PAK. Alternative methods of contraception (e.g., progestin only contraception or non-hormonal methods) are recommended during VIEKIRA PAK therapy.

Questions and Answers
Q: Does patient need to have compensated disease?
A: Yes, the patient should have compensated cirrhosis for treatment.

Q: How has physician response been to dosing?
A: Physician concern has subsided due to packaging to assist patients.

Q: Has treatment after failure with Viekira been studied?
A: 1.8% of study patients have been enrolled to determine how to treat.

III. Sunovion

Janet Pitner, PharmD, MBA, Director Medical Science Liaison
Jim Shepherd, Account Director

Aptiom® (eslicarbazepine acetate)
Aptiom® (eslicarbazepine acetate, ESL) is a new molecular entity approved by the Food Drug and Administration on November 8, 2013. The precise mechanism(s) by which eslicarbazepine, the primary metabolite of eslicarbazepine acetate, exerts anticonvulsant activity is unknown but is thought to involve inhibition of voltage-gated sodium channels (VGSC). In-vitro electrophysiological studies have shown that eslicarbazepine inhibits sodium currents in a voltage-dependent manner by preferentially binding to and stabilizing the inactivated form of the VGSC and slowing its return to a resting state. The clinical significance of this is unknown; however, *in vivo*, inhibition of VGSC activity would be expected to inhibit repetitive neuronal firing.

The safety and efficacy of ESL as adjunctive treatment in patients with partial-onset seizures were established in three randomized, double-blind, placebo-controlled, multicenter trials in adult patients whose partial-onset seizures were not adequately controlled with 1–3 antiepileptic drugs (AEDs) [Studies 2093-301, 2093-302 and 2093-304]. The standardized seizure frequency during the maintenance phase over 28 days was the primary endpoint. Differences in seizure frequency over the 12-week maintenance period between placebo and the ESL 800 mg and 1200 mg treatment groups were statistically significant in all studies with the exception of placebo versus ESL 800 mg in Study 2093-304 (p=0.058). The proportion of patients with a ≥50% reduction in standardized seizure frequency (secondary endpoint) in the maintenance period relative to baseline was higher with ESL 800 mg and 1200 mg than placebo in all 3 controlled studies. In the pooled analysis, the proportions of 50% responders were 20.9% with placebo and 22.2%, 32.3% and 40.9% in the ESL 400 mg, 800 mg and 1200 mg groups, respectively. ESL 800 mg and 1200 mg were associated with reductions in standardized seizure frequency (secondary endpoint) during the maintenance period of the 3 controlled studies, relative to the baseline period. In the pooled analysis, the relative change from baseline in standardized seizure frequency was -16.7% with placebo and -22.6%, -31.2% and -33.3% in the ESL 400 mg, 800 mg and 1200 mg groups, respectively. ESL was shown to be generally well-tolerated with treatment-emergent adverse events (TEAEs) usually mild to moderate in intensity and occurring most frequently during the first weeks of treatment with ESL. The most common TEAEs in patients receiving ESL (≥4% and ≥2% greater than placebo) were dizziness, somnolence, nausea, headache, diplopia, vomiting, fatigue, vertigo, ataxia, blurred vision, and tremor.

The safety and efficacy of ESL as a monotherapy treatment in patients with partial-onset seizures were evaluated in two double-blind, randomized, historical control, multi-center, conversion to monotherapy studies (Studies 093-045 and 093-046). Patients included in the two studies were aged 16-70 years with partial-onset seizures not adequately controlled with 1-2 AEDs. These studies compared doses of ESL 1200 mg and 1600 mg once daily with a historical control. The primary endpoint was defined as the percent of patients meeting one of five predefined exit criteria signifying worsening seizure control. In both studies ESL monotherapy was shown to be superior to historical controls. The upper confidence intervals of the Kaplan-Meier (KM) estimated exit rates for both ESL 1200 mg and ESL 1600 mg doses were both below the lower limit of the pre-specified threshold of 65.3%, based on the historical controls. In Study 093-045, 171 patients (88.6%) reported ≥ 1 TEAE during the study. In Study 093-046, 116 patients (67.4%) reported ≥ 1 TEAE during the study. The proportions of patients who experienced TEAEs appeared to be dose-related (Study 093-045: 84.6% in the ESL 1200 mg group vs. 90.6% in the ESL 1600 mg group and Study 093-046: 60.3% in the ESL 1200 mg group vs. 71.1% in the ESL 1600 mg group). Consistent with the findings from the adjunct studies, the most common TEAEs in Study 093-045 were dizziness, headache, fatigue, somnolence and nausea, while the most common TEAEs in Study 093-046 were headache, dizziness, nasopharyngitis, nausea and somnolence.

Questions and Answers
Q: Approximately how many were patients having at baseline?
A: 8 or more seizures over 8 weeks.

Q: Are physicians provided with samples of the 400 mg strength?
A: Yes, physicians are provided samples with the 400 mg strength as well as the 800 mg strength.

Q: Can the 800 mg strength tablet be cut in half?
A: Yes, the 800 mg strength tablet can be cut in half but not the 400 mg strength tablet since not scored.

IV. GlaxoSmithKline

Vivian Lee Ryan, Regional Account Manager

Anoro® Ellipta® (umeclidinium bromide and vilanterol trifenatate powder)

PRODUCT DESCRIPTION
Anoro Ellipta is a new, once-daily, combination anticholinergic/long-acting beta agonist (LABA) delivered from a dry powder breath-actuated device. The dry powder inhaler contains two double-foil blister strips of powder formulation for oral inhalation, one strip containing umeclidinium 62.5 mcg per blister and the other containing vilanterol 25 mcg per blister.

INDICATION
Anoro Ellipta is a combination anticholinergic/LABA indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).

IMPORTANT LIMITATIONS OF USE: *Anoro Ellipta* is NOT indicated for the relief of acute bronchospasm or for the treatment of asthma.

BOXED WARNING
WARNING: ASTHMA-RELATED DEATH: Long-acting beta2-adrenergic agonists (LABA) increase the risk of asthma-related death. Data from a large placebo-controlled US trial that compared the safety with another LABA (salmeterol) with placebo added to usual asthma therapy showed an increase in asthma-related deaths in subjects receiving salmeterol. This finding with salmeterol is considered a class effect of LABA, including vilanterol, one of the active ingredients in *Anoro Ellipta* [see Prescribing Information for complete information on Warnings and Precautions]. The safety and efficacy of *Anoro Ellipta* in patients with asthma has not been established. *Anoro Ellipta* is not indicated for the treatment of asthma.

EFFICACY
In a placebo-controlled primary efficacy study, treatment with *Anoro Ellipta* resulted in a statistically significant improvement in the primary lung function endpoint of trough forced expiratory volume in 1 second (FEV1) compared with the individual components and placebo.2 In 2 of the three active-controlled studies, treatment with *Anoro Ellipta* resulted in a statistically significant improvement in trough FEV1 compared with tiotropium (treatment differences : study 1 = 90 mL, *P* <0.001; study 2 = 60 mL, *P* =0.018 but significance cannot be inferred due to the statistical testing hierarchy; study 3 =112mL, P <0.001).3,4 The median time to onset on Day 1, defined as a 100 mL increase from baseline in FEV1 was 27 minutes in subjects receiving *Anoro Ellipta*.

ADVERSE EVENTS
The most common adverse reactions (≥1% and more common than placebo) reported in four 6 month clinical trials with *Anoro Ellipta* (and placebo) were pharyngitis, 2% (<1%); sinusitis 1% (<1%); lower respiratory tract infection 1% (<1%); constipation 1% (<1%); diarrhea 2% (1%); pain in extremity 2% (1%); muscle spasms 1%(<1%); neck pain 1%(<1%); chest pain 1% (<1%).

Questions and Answers
Q: What is the difference in the Ellipta inhaler?
A: The inhaler counts and turns red when patient needs to refill.

Incruse® Ellipta® (umeclidinium inhalation powder)
PRODUCT DESCRIPTION
Incruse Ellipta is a new, once-daily, anticholinergic delivered from a dry powder breath-actuated device. The dry powder inhaler contains a double-foil blister strip with each blister containing *Incruse Ellipta* 62.5 mcg.

INDICATION
Incruse Ellipta is an anticholinergic indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema.

EFFICACY
In the 2 primary efficacy studies, treatment with *Incruse Ellipta* resulted in statistically significant improvements in the primary lung function endpoint of trough FEV1 compared with placebo (treatment difference: study 1 = 115 mL and study 2 = 127 mL; *P* < 0.001 for both studies) at the end of the study period.2,6 In both studies treatment with *Incruse Ellipta* resulted in statistically and clinically significant improvements in mean St. George's Respiratory Questionnaire total score compared to placebo at the end of the study period (treatment difference: study 1 = -4.69 and study 2 = -7.9; *P*<0.001).

ADVERSE EVENTS
The most common adverse reactions (≥1% and more common than placebo) reported with *Incruse Ellipta* (and placebo) were nasopharyngitis 8% (7%); upper respiratory tract infection 5% (4%); pharyngitis 1% (< 1%); viral upper respiratory tract infection 1% (<1%); cough 3% (2%); arthralgia 2% (1%); myalgia 1% (<1%); abdominal pain upper 1% (< 1%); toothache 1% (<1%); contusion 1% (< 1%); tachycardia 1% (<1%).

Questions and Answers
Q: What are considered the advantages of umeclidinium?
A: Dosed once daily and improvement in trough FEV1.

Tanzeum™ (albiglutide)

DESCRIPTION

Tanzeum is a once weekly glucagon-like peptide-1 (GLP-1) receptor agonist delivered from a single-dose pen injection device for the treatment of type 2 diabetes mellitus (T2DM) in adults.8 It is available as 30 mg or 50 mg.

INDICATION

Tanzeum is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

IMPORTANT LIMITATIONS OF USE

Tanzeum is not recommended as first-line therapy for patients inadequately controlled on diet and exercise. *Tanzeum* has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. *Tanzeum* is not indicated in the treatment of patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis and is not a substitute for insulin in these patients. *Tanzeum* has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis and use of *Tanzeum* is not recommended in patients with pre-existing severe gastrointestinal disease. *Tanzeum* has not been studied in combination with prandial insulin.

EFFICACY

In the 8 Phase III studies, (HARMONY Clinical Development Program), the enrolled population spanned newly diagnosed patients treated with diet and exercise alone to patients on background oral monotherapy, oral dual therapy, oral triple therapy and insulin, and the studies evaluated a range of clinically relevant active comparators (metformin, pioglitazone, sitagliptin, glimepiride, insulin glargine, insulin lispro, and liraglutide) together with a placebo comparator. Patients treated with *Tanzeum* demonstrated clinically relevant reductions in glycosylated hemoglobin (HbA1c) of 0.55%-0.89%. When compared with other injectable therapy, *Tanzeum* demonstrated similar reductions in HbA1c in comparison to insulin glargine (+ oral antidiabetic drugs) and insulin lispro (+ insulin glargine ± oral antidiabetic drugs). In comparison to another GLP-1ra, *Tanzeum* showed a reduction in HbA1c of 0.78% compared to a reduction of 0.99% achieved with once daily (QD) liraglutide, which was statistically greater. *Tanzeum* has been evaluated in patients with renal impairment and shown to significantly reduce HbA1c compared to sitagliptin in this patient population. In comparison to oral anti-diabetic drugs, treatment with *Tanzeum* resulted in significant reductions in A1c compared with sitagliptin, glimepiride, and placebo, but the treatment difference between *Tanzeum* and pioglitazone was statistically significant in favor of pioglitazone.

BOXED WARNING

WARNING: RISK OF THYROID C-CELL TUMORS: Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide-1 (GLP-1) receptor agonists at clinically relevant exposures. It is unknown whether *Tanzeum* causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans. *Tanzeum* is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Routine serum calcitonin or thyroid ultrasound monitoring is of uncertain value in patients treated with *Tanzeum*. Patients should be counseled regarding the risk and symptoms of thyroid tumors.

ADVERSE EVENTS

Adverse reactions, reported in ≥5% of patients treated with *Tanzeum* and more frequently than in patients on placebo, were upper respiratory tract infection (14.2%), diarrhea (13.1%), nausea (11.1%), injection site reaction (10.5%), cough (6.9%), back pain (6.7%), arthralgia (6.6%), sinusitis (6.2%), and influenza (5.2%).7 Pancreatitis adjudicated as likely related to therapy occurred more frequently in patients receiving *Tanzeum* (6 of 2,365 [0.3%]) than in patients receiving placebo (0 of 468 [0%]) or active comparators (2 of 2,065 [0.1%]). The incidence of patients treated with *Tanzeum* who experienced documented symptomatic hypoglycemia (plasma glucose concentration ≤70 mg/dL and presence of hypoglycemic symptoms) ranged from 3% to 17%, with a higher incidence occurring in studies where patients were also receiving insulin or sulfonylurea.

Questions and Answers

Q: How are other Medicaid plans covering?
A: Until DURB/P&T reviews, most are non-preferred with prior authorization but some have as non-preferred with no restrictions for all GLP-1s and some have a preferred.
Q: What are considered the advantages of albiglutide?
A: Once weekly dosing and favorable efficacy.

V. Pfizer

Tom Heard, PharmD, CGP, Associate Director, Medical Outcomes
Richard Vissing, PharmD, Senior Director, Medical Affairs
Brian K. Gillespie, Account Manager
Cathy Preiser, Specialty Account Manager

Chantix® (varenicline)
Pronunciation: CHANT-iks

There is boxed warning in the Chantix USPI regarding serious neuropsychiatric events that have been reported in patients treated with Chantix.

INDICATIONS & USAGE
Chantix is indicated as an aid to smoking cessation treatment in adults 18 and over. Patients may benefit from behavioral modification and support during their quit attempt. Patients should be encouraged to continue to attempt to quit if they have lapses after quit day.
****The recommended dose of Chantix** is 1.0 mg twice daily following a 1-week titration as follows:
• Days 1 - 3: 0.5 mg once daily; Days 4 - 7: 0.5 mg twice daily; Day 8 – end of treatment: 1.0 mg twice daily.

SUMMARY OF CHANTIX LABEL UPDATE AS OF OCTOBER 2014
Safety Updates: Since the initial signal of neuropsychiatric symptoms and suicidality emerged, additional analyses and studies have been conducted to further evaluate this association.
A meta-analysis of 5 randomized, double-blind, placebo-controlled trials, including 1907 patients (1130 Chantix, 777 placebo) was conducted to assess suicidal ideation & behavior as reported on the Columbia Suicide Severity Rating Scale (C-SSRS). This meta-analysis included one trial (N=127) in patients with a history of schizophrenia or schizoaffective disorder and another trial (N=525) in patients with a history of depression. The results showed no increase in the incidence of suicidal ideation and/or behavior in patients treated with Chantix (28/1130; 2.5%) compared to patients treated with placebo (27/777; 3.5%), with a Risk Ratio (RR) of 0.79 (95% Confidence Interval [CI]: 0.46, 1.36). Forty-eight (48) of the 55 patients who reported suicidal ideation or behavior (24 Chantix, 24 placebo) were observed in the two trials that enrolled patients with a history of schizophrenia, schizoaffective disorder, or depression. Few events were observed in the other three trials (4 Chantix, 3 placebo).
A pooled analysis of 18 double-blind, randomized, placebo-controlled clinical trials, which includes the 5 trials that collected C-SSRS described above, was conducted to assess the psychiatric safety of Chantix. This pooled analysis included 8521 patients (5072 Chantix, 3449 placebo), some of whom had psychiatric conditions at baseline. The results showed a similar incidence of common psychiatric events in patients treated with Chantix compared to patients treated with placebo.
4 observational studies, each including 10,000 to 30,000 users of Chantix in the adjusted analyses, compared the risk of selected serious neuropsychiatric events (neuropsychiatric hospitalizations, fatal and non-fatal self-harm), between Chantix users &prescription nicotine replacement therapy (NRT) or bupropion users. All studies were retrospective cohort studies & included patients with & without a psychiatric history.
-Two of the studies found no difference in risk of neuropsychiatric hospitalizations between Chantix users and nicotine patch users (Hazard Ratio [HR] 1.14; 95% CI: 0.56-2.34 in the first study, and 0.76; 95% CI: 0.40-1.46 in the second study). However neither study validated the diagnostic codes used to the identify outcomes against medical records.
-A third study reported no difference in risk of psychiatric adverse events diagnosed during an emergency department visit or in-patient admission between Chantix users and bupropion users (HR 0.85; 95% CI: 0.55-1.30). Bupropion has also been associated with neuropsychiatric adverse events
-A fourth study examined risk of fatal and non-fatal self-harm in users of Chantix compared to users of NRT. Although the occurrence of detected suicide was rare during the three months after patients initiated any drug treatment (two cases in 31,260 Chantix users and six cases in 81,545 NRT users), this study has important limitations. Most importantly, these data were captured following public awareness of reports of neuropsychiatric adverse events in Chantix users. Chantix users had fewer comorbid conditions that could put them at risk for neuropsychiatric adverse events, suggesting that patients with a history of neuropsychiatric illness were preferentially prescribed NRT and healthier patients were preferentially prescribed Chantix.
***Reports of Seizures*:** New or worsening seizures have been observed in patients taking Chantix. Chantix should be used cautiously in patients with a history of seizures or other factors that can lower the seizure threshold.
Interaction with alcohol: Increased effects of alcohol have been reported. Instruct patients to reduce the amount of alcohol they consume until they know whether Chantix affects them.
NEW CLINICAL STUDIES

Depression study: Chantix was evaluated in a randomized, double-blind, placebo-controlled study of subjects aged 18 to 75 years with major depressive disorder without psychotic features (DSM-IV TR). If on medication, subjects were to be on a stable antidepressant regimen for at least two months. If not on medication, subjects were to have experienced a major depressive episode in the past 2 years, which was successfully treated. Subjects were randomized to Chantix 1 mg twice daily (n=256) or placebo (n=269) for a treatment of 12 weeks and then followed for 40 weeks post-treatment. Subjects treated with Chantix had a superior rate of CO-confirmed abstinence during weeks 9 through 12 (36%) compared to subjects treated with placebo (16%) and from week 9 through 52 (20%) compared to subjects treated with placebo (10%). The most common adverse events (≥ 10%) in subjects taking varenicline were nausea (27% vs. 10% on placebo), headache (17 vs 11%), abnormal dreams (11% vs 8%), insomnia (11% vs 5%) and irritability (11% vs. 8%). Psychiatric scales showed no differences between the varenicline and placebo groups and no overall worsening of depression during the study in either treatment group. The percentage of subjects with suicidal ideation and/or behavior was similar between the varenicline and placebo groups during treatment (6% and 8%, respectively) and the non-treatment follow-up (6% and 6%, respectively). There was one event of intentional self-injury/possible suicide attempt during treatment (Day 73) in a subject in the placebo group. Suicide could not be ruled out in one subject who died by an overdose of illicit drugs 76 days after last dose of study drug in the varenicline group.

Retreatment Study: Chantix was evaluated in a double-blind, placebo-controlled trial of patients who had made a previous attempt to quit smoking with Chantix, and either did not succeed in quitting or relapsed after treatment. Subjects were randomized 1:1 to Chantix 1 mg twice daily (n=249) or placebo (n=245) for 12 weeks of treatment and followed for 40 weeks post-treatment. Patients included in this study had taken Chantix for a smoking-cessation attempt in the past (for a total treatment duration of a minimum of two weeks), at least three months prior to study entry, and had been smoking for at least four weeks. Patients treated with Chantix had a superior rate of CO-confirmed abstinence during weeks 9 through 12 (45%) compared to patients treated with placebo (12%) and from weeks 9 through 52 (20%) compared to subjects treated with placebo (3%).

Questions and Answers
There were no additional questions and answers.

Lyrica® (pregabalin, C-V
Pronunciation: “LEER-i-kah” (“pre GAB a lin”)

Painful Diabetic Peripheral Neuropathy (pDPN) and Neuropathic Pain Due to Postherpetic Neuralgia (PHN)
Efficacy and safety of pregabalin in the treatment of patients with pDPN and pain on walking. In a randomized, double-blind, placebo-controlled, 2-period (each 6 week period was separated by a 2 week washout interval), cross-over trial (N=203), no statistical differences were observed between treatment groups in the pre-specified analysis (considering Periods 1 and 2 combined) for the co-primary endpoint parameters, which were mean weekly DPN pain diary score at endpoint and mean DPN pain on walking score. Based on a non-pre-specified analysis, Period 1 results for both co-primary parameters indicated improvement (reduction) of mean DPN pain scores and mean DPN pain on walking in patients treated with pregabalin 150-300 mg/day which was statistically significant (Huffman C, Stacey BR, Tuchman M, et al. Clin J Pain 2014 [published online ahead of print])

The efficacy of pregabalin in patients with moderate and severe pain due to DPN/Shifts in pain severity categories among patients with pDPN or PHN treated with pregabalin. In a post-hoc pooled analysis of 11 pDPN trials, pregabalin 300 mg/day provided significant pain relief for patients with moderate or severe pDPN. (Parsons B and Emir B. Poster presented at the 65th American Academy of Neurology Annual Meeting: March 16-23, 2013; San Diego, CA.) In an additional post-hoc analysis of 16 pDPN and PHN trials, patients categorized with pain as mild, moderate, or severe significantly shifted to a less severe pain category, from baseline to endpoint, when treated with pregabalin at doses of 150, 300, and 600 mg/day relative to placebo. The mean endpoint pain score was significantly different from baseline in patients with both moderate and severe pain receiving pregabalin 300 mg/day and 600 mg/day. (Parsons B and Emir B. Poster presented at the 66th Annual Meeting of the American Academy of Neurology: April 26-May 3, 2014; Philadelphia, PA; Data on file.) Please note that the maximum approved dose of pregabalin for treatment of pDPN is 300 mg/day.

Neuropathic Pain Associated with Spinal Cord Injury (SCI)
Shifts in pain severity categories among patients with neuropathic pain (NeP) due to SCI treated with pregabalin. In a post-hoc analysis of the 2 pivotal NeP associated with SCI trials, patients categorized with pain as mild, moderate, or

severe significantly shifted to a less severe pain category, from baseline to endpoint, when treated with pregabalin relative to placebo. (Parsons B and Emir B. Poster presented at the 33rd Annual Scientific Meeting of the American Pain Society: April 30-May 3, 2014: Tampa, FL.)

Health care utilization and expenditures among Medicaid beneficiaries with NeP following SCI: This retrospective longitudinal cohort study used Medicaid beneficiary claims with SCI and evidence of NeP (SCI-NeP cohort) matched with a cohort without NeP (SCI-only cohort) to evaluate health care resource utilization (HRU) and costs for NeP secondary to SCI. Postindex percentages of patients with physician office visits, emergency department visits, SCI- and pain-related procedures, and outpatient prescription utilization were all significantly higher for SCI-NeP compared to the SCI-only cohort (*P*<0.001). Using regression models to account for covariates, adjusted mean expenditures were US$47,518 for SCI-NeP and US$30,150 for SCI only, yielding incremental costs of US$17,369 (95% confidence interval US$9,753 to US$26,555) for SCI-NeP. (Margolis JM, Juneau P, Sadosky A, et al. J Pain Res. 2014)

Fibromyalgia (FM)

Time to improvement of pain and sleep quality in clinical trials of pregabalin for the treatment of FM. In a post-hoc analysis of four 8-14 week FM clinical trials, time-to-onset of improvement in pain (first of 2 consecutive days the mean score was statistically significantly lower for pregabalin versus placebo) occurred at day 1 of treatment for 7 dose arms (average reduction in mean pain score versus placebo, -0.36 for 300 mg/day, -0.55 for 450 mg/day, and -0.41 for 600 mg/d) and at day 2 for 1 arm (-0.59 for 300 mg/day). (Arnold LM, Emir B, Pauer L et al. Pain Med 2014 [epub ahead of print].) Please note that the maximum approved dose of pregabalin for treatment of FM is 450 mg/day.

The efficacy of pregabalin for treating FM pain in patients with moderate or severe baseline widespread pain. In a post-hoc pooled analysis of 4 FM trials, pregabalin provided significant pain relief for patients with moderate (450 mg) or severe (300 and 450 mg) pain. (Clair A. Emir B. Presented at the American College of Rheumatology/Association of Rheumatology Health Professionals (ACR/ARHP) 2014 Annual Scientific Meeting; Boston, MA. November 14–19, 2014.)

Impact of potential pregabalin or duloxetine drug-drug interactions (DDIs) on health care costs and utilization among Medicare members with FM: This study examined the impact of newly initiated pregabalin or duloxetine treatment on FM patients' encounters with potential DDIs, the health care cost and utilization consequences of those interactions, and the impact of treatment on opioid utilization within the Humana population. No significant differences in baseline characteristics were found between matched pregabalin (n=794) and duloxetine cohorts (n=794). Potential DDI prevalence was significantly greater (*P*<0.0001) among duloxetine subjects (71.9%) than among pregabalin subjects (4.0%). The significantly higher prevalence of potential DDIs and potential cost impact found in FM duloxetine subjects, relative to pregabalin subjects, underscore the importance of considering DDIs when selecting a treatment. (Ellis JJ, Sadosky AB, Ten Eyck LL, et al. ClinicoEconomics and Outcomes Research 2014)

Adjunctive Treatment of Partial\Onset Seizures

Efficacy and safety of pregabalin versus levetiracetam as adjunctive therapy in patients with partial seizures: A randomized, double-blind, noninferiority trial. In a randomized, double-blind, noninferiority trial (6-week baseline phase, 4-week dose-escalation phase and a 12-week maintenance phase) to assess the efficacy and safety of pregabalin versus levetiracetam as adjunctive therapy in 509 patients with refractory partial seizures, the number of responders were 97 (59.1%) and 104 (58.8%) in the pregabalin and levetiracetam groups, respectively. The lower bound of the 95% confidence interval for the treatment difference between pregabalin and levetiracetam was -8.0%, which was greater than the prespecified noninferiority margin of -12%, and thus pregabalin was not inferior to levetiracetam.(Zaccara G, Almas M, Pitman V, et al. Epilepsia 2014;55(7):1048-1057.)

Payer Prior Authorization (PA) Analysis

Prior authorization in the treatment of patients with pDPN and FM. The health-care utilization/costs among FM (n=29,746) or pDPN patients (n=14,233) (diagnosed via claims-based algorithm) with and without PA within the benefit structure of a large geographically diverse US commercial health insurance plan were examined from 07/01/2007 to 12/31/2011. For all-cause costs in the FM cohort, the mean differences in difference (DiD) between no PA and PA cohorts was $-197 (*p*=0.6673); for disease-related costs, the mean DiD was $-72 (*p*=0.4186). For all-cause costs in the pDPN cohort, the mean DiD between no PA and PA cohorts was $1,155 (*p*=0.6248); for disease-related costs, the mean DiD was $-2,809 (*p*=0.4312). The results indicated that implementation of a PA may not reduce cost. (Placzek H, Masters ET, Gu T, et al. Accepted to Pain Practice; 2014.)

Questions and Answers

There were no additional questions and answers.

Quillivant™ XR (methylphenidate HCl) for Extended-Release Oral Suspension, CII
Pronunciations: Brand: Quillivant XR (kwil-ə-vant) Generic: methylphenidate (METH il FEN i date**)**

PRODUCT INDICATION
Quillivant XR is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The efficacy of Quillivant XR was established in a 2-week, placebo-controlled trial in children aged 6 to 12 years with a diagnosis of ADHD. Accumulated efficacy data from other methylphenidate products were also considered.

DOSE
Quillivant XR allows healthcare professionals to fine tune the dose and significantly improve attention and behavior from morning through homework time. The recommended starting dose is 20 mg once daily and may be titrated weekly in increments of 10 mg to 20 mg. Daily doses above 60 mg have not been studied and are not recommended. Prior to dispensing, a pharmacist must reconstitute Quillivant XR with water and insert the bottle adapter into the neck of the bottle. Included with each prescription is an oral dosing dispenser which fits into the hole in the adapter and is used to measure the dose of Quillivant XR.

CLINICAL EFFICACY
During the Quillivant XR efficacy study in 45 children ages 6 to 12 years with ADHD, the Permanent Product Measure of Performance (PERMP) was administered, which is a skill-adjusted math test designed to measure each child's ability to attend to, initiate and complete written seat work. Results showed at each post-dose time point measured (0.75, 2, 4, 8, 10, and 12 hours), the number of problems attempted and the number of problems answered correctly were significantly higher during treatment with Quillivant XR than with placebo ($p<0.0001$ for the mean of post-dose measurements).

MECHANISM OF RELEASE
The delivery system of Quillivant XR uses LiquiXR technology to provide a combination of 20% immediate-release and 80% extended-release methylphenidate (MPH). During the manufacturing process, drug/polymer complexes are created by mixing positively-charged MPH with a negatively-charged polymer called polistirex. Eighty-percent of the complexes are coated with an extended-release coating, while the other 20% remain uncoated. The uncoated complexes immediately release MPH into the small intestine where it is absorbed. The coated complexes release MPH at varying rates, depending on the thickness of the coating. The thicker the coating, the slower the release.

ISI and BLACK BOX
Quillivant XR package insert discusses Important Safety Information including a **boxed warning for Abuse and Dependence**.

CONCLUSION
For a child with ADHD experiencing hyperactivity, impulsiveness or inattention, Quillivant XR allows healthcare professionals the ability to individually optimize the dose to help balance efficacy and side effects. Quillivant XR is the only liquid extended-release ADHD treatment for ages 6 years and above. Having an extended- release liquid formulation of methylphenidate available offers an important treatment option to clinicians and their patients with ADHD.

Questions and Answers
Q: What are considered the advantages of Quillivant XR?
A: Only extended-release oral liquid for ADHD for patients 6 years of age and older, starts acting within 45 minutes and lasts for approximately 12 hours.

Toviaz® (fesoterodine fumarate)
Pronunciation: TOH-vee-as

The EIGHT study1 was a 12-week, randomized, double-blind, placebo-controlled, parallel-group, multicenter study. The study consisted of a 2-week single-blind placebo run-in period and a 12-week double-blind treatment. The objective was to demonstrate superior efficacy of 8 mg fesoterodine versus 4 mg of fesoterodine in reducing urgency urinary incontinence (UUI) in patients with overactive bladder (OAB) after 12 weeks of treatment. Eligible patients

included those who were aged ≥18 years with overactive bladder (OAB) symptoms for ≥6 months, ≥8 micturitions and ≥2 and ≤15 urgency urinary incontinence (UUI) episodes/24 hours on baseline diary, and at least moderate bladder-related problems on the Patient Perception of Bladder Condition (PPBC). Demographics were well balanced for all treatment groups.

A total of 4326 subjects were screened and 2012 were randomized of which 1955 received at least one dose of double-blind study drug (386 in placebo group, 790 in fesoterodine 4mg group, and 779 in fesoterodine 8mg group). Those randomized to fesoterodine 8 mg began initial treatment with fesoterodine 4 mg for 1 week, then increased to 8 mg for 11 weeks. At baseline and at Week 12, all patients completed bladder diaries, PPBC, Urgency Perception Scale (UPS), and the Overactive Bladder Questionnaire (OAB-q).

The primary efficacy comparison was the change in the mean number of UUI episodes at week 12 versus baseline with the primary comparison between fesoterodine 8mg and fesoterodine 4mg. The comparison of fesoterodine 8mg and fesoterodine 4mg only occurred after a closed-testing procedure where fesoterodine 8mg was compared to placebo. If the treatment effect of fesoterodine 8 mg versus placebo was significant ($p<0.0001$) then the treatment difference of fesoterodine 8 mg and 4 mg was assessed ($p<0.0109$). In addition, there was a statistically significant decrease in the mean number of UUI episodes/24 hours at Week 12 relative to baseline for the fesoterodine 4 mg group versus placebo group ($p<0.0001$). The LS mean decrease from baseline was -3.12 episodes in the fesoterodine 8 mg group, -2.85 episodes in the fesoterodine 4 mg group, and -2.22 episodes in the placebo group (LS Mean Difference = -0.91 between the fesoterodine 8 mg and placebo groups and -0.27 between the fesoterodine 8 mg and 4 mg groups.) Additionally, statistically significant improvements were seen in the fesoterodine 8 mg group compared to fesoterodine 4 mg or placebo in secondary endpoints of micturitions, urgency episodes, and in scores on the PPBC, UPS, and all OAB-q total and all sub-domains (concern, coping, sleep and social interaction), and significantly higher diary dry rates in the fesoterodine 8 mg group versus the fesoterodine 4mg and placebo groups (all $P<0.05$).

Fesoterodine was generally well tolerated with an acceptable safety profile consistent with previous fesoterodine clinical trials. The most commonly reported adverse events included dry mouth and constipation in the placebo (3% and 2%), fesoterodine 4 mg (13% and 2%), and fesoterodine 8 mg (26% and 4%), respectively and were of mild to moderate severity.

In conclusion, both fesoterodine 4 and 8 mg were effective in improving OAB symptoms compared with placebo. Fesoterodine 8 mg showed significantly superior efficacy vs. fesoterodine 4mg in reducing the mean number of UUI episodes/24 hours from baseline to week 12. The authors of the study publication noted that “clear evidence of dose-dependent efficacy is unique to fesoterodine among antimuscarinics and other oral agents for the treatment of OAB”. These data support the benefit of the availability of two doses of fesoterodine in clinical practice, with the recommended starting dose of 4 mg for all patients and escalation to 8mg dose for patients who require a higher dose to achieve optimal symptom relief.

Questions and Answers
There were no additional questions and answers.

Xeljanz® (tofacitinib)
Pronunciation: ZEL’ JANS’ (TOE fa SIT in ib)

XELJANZ® (tofacitinib) is a novel, orally administered, small molecule, Janus kinase (JAK) inhibitor approved for the treatment of moderate to severe rheumatoid arthritis (RA) in adults who have an inadequate response or intolerance to methotrexate. Xeljanz may be administered as monotherapy or in combination with methotrexate or other non-biologic disease-modifying anti-rheumatic drugs (DMARDs). Xeljanz should not be used in combination with biologic DMARDs or potent immunosuppressants, such as azathioprine and cyclosporine. The recommended dose of Xeljanz is 5 mg twice daily. Dose adjustments may be warranted in specific situations.

Disease Background and Burden of Illness
RA is a chronic, systemic autoimmune disease that affects an estimated 1.5 million patients in the US. Treatment of RA is typically initiated with NSAIDs and/or low-dose glucocorticoids, with the introduction of non-biologic DMARDs (typically methotrexate) as quickly as possible after diagnosis and subsequently initiation of a biologic agent (usually a TNF inhibitor) if further treatment is necessary. Despite the availability of multiple therapeutic options, many patients fail to adequately respond to treatment or stop responding over time. There is no reliable way to predict which patients will respond to a given agent. This limited rate of treatment success, and the fact that many patients discontinue or

switch their therapies (whether non-biologic or biologic), demonstrates the need for additional therapeutic options in RA.

Clinical Pharmacology
Xeljanz is a JAK inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Following oral administration of Xeljanz, peak plasma concentrations are reached within 0.5 to 1 hour, the elimination half-life is about 3 hours, and a dose-proportional increase in systemic exposure was observed in the therapeutic dose range. Steady state concentrations are achieved in 24 to 48 hours with negligible accumulation after twice daily administration. Xeljanz is primarily eliminated via hepatic metabolism (70%) with only 30% attributed to renal excretion. The metabolism of Xeljanz is primarily mediated by CYP3A4 with minor contribution from CYP2C19.

Recent Data
• **Additional patient-reported outcome data.** The previous Xeljanz label included data on physical function measured by changes in the HAQ-DI from five Phase 3 studies (ORAL Scan, ORAL Sync, ORAL Standard, ORAL Step and ORAL Solo). The new data from ORAL Solo, Scan and Step come from the SF-36. In those studies, patients receiving Xeljanz 5 mg twice daily or Xeljanz 10 mg twice daily demonstrated greater improvement from baseline compared to placebo in physical component summary (PCS) and mental component summary (MCS) scores and in all eight domains of the SF-36 at Month 3.
• **Radiographic data.** Radiographic response data from ORAL Scan (Study IV) at 6 months and ORAL Start (Study VI) at 6 and 12 months was added to the label. ORAL Start showed that Xeljanz 5 mg twice daily, as a single agent, was statistically significantly superior to methotrexate (MTX), providing a greater inhibition of progression of structural joint damage, as measured by mean change from baseline in modified Total Sharp Score (mTSS) at Month 6 (primary endpoint), and sustained at 12 months. Xeljanz is not indicated for use in MTX-naïve patients. ORAL Scan demonstrated that Xeljanz 10 mg twice daily provided statistically significantly greater reduction of progression of structural joint damage as measured by mean change from baseline in mTSS compared to placebo at 6 months (primary endpoint). Results for the 5 mg twice daily dose exhibited similar effects on mean progression of structural damage but were not statistically significant. The 10 mg twice daily dose is not approved.

Additionally, among the tofacitinib posters and presentations presented at the American College of Rheumatology Annual Scientific Meeting in November 2014, Wollenhaupt et al presented safety and efficacy data from the long-term extension studies, which included safety information up to 84 months of therapy and efficacy information up to 72 months of therapy. The authors concluded that tofacitinib as monotherapy or in combination with nonbiologic DMARDs in patients with rheumatoid arthritis demonstrated a consistent safety profile and sustained efficacy in the open-label long-term extension studies.

Questions and Answers
Q: What are considered the advantages of Xeljanz?
A: 50% of RA patients discontinue methotrexate after 2 years and Xeljanz has significant efficacy as monotherapy in START and SOLO studies unlike some biologic DMARDs that have better efficacy when used in combination with methotrexate, available as an oral agent, less discontinuation rates unlike injectable biologic DMARDs where discontinuation rates can increase over time, and provides a new mechanism of action.

VI. Indivior

Gregg Wilson, RN, PhD, Medical Science Treatment Advisor
William Mullen, PA-C, MPH, Medical Science Treatment Advisor
Nick Casale, PharmD, MS, Strategic Account Manager

Suboxone® (buprenorphine and naloxone)
SUBOXONE® (buprenorphine and naloxone) Sublingual Film (CIII) is approved for use in both induction and maintenance treatment of opioid dependence in appropriate patients.* SUBOXONE® (buprenorphine and naloxone) Sublingual Film (CIII} is a prescription medicine indicated for treatment of opioid dependence and should be used as part of a complete treatment plan to include counseling and psychosocial support.

Treatment should be initiated under the direction of physicians qualified under the Drug Addiction Treatment Act.

Do not take SUBOXONE® (buprenorphine and naloxone) Sublingual Film (CIII} if you are allergic to buprenorphine or naloxone as serious negative effects, including anaphylactic shock, have been reported. Buprenorphine/naloxone products are not recommended in patients with severe hepatic impairment and may not be appropriate for patients with moderate hepatic impairment. Buprenorphine/naloxone drug products are not recommended for induction in patients with moderate hepatic impairment due to the increased risk of precipitated withdrawal. However, buprenorphine/naloxone products may be used with caution for maintenance treatment in patients with moderate hepatic impairment who have initiated treatment on a buprenorphine product without naloxone.

Data from 2000-2010 show a more than 5-fold increase in non-heroin opioid-abuse treatment admissions in ages 12 and older. Introduced in 2010 by Reckitt Benckiser Pharmaceuticals Inc., SUBOXONE Film delivers buprenorphine and naloxone through a film formulation. Buprenorphine has been shown to be effective for treating opioid dependence in double-blind clinical trials. The buprenorphine component of SUBOXONE Film may reduce subjective opioid cravings. The naloxone component has no clinical effect when administered by the sublingual route because of low sublingual bioavailability, and may help mitigate misuse or abuse by deterring intravenous use of the medication in individuals dependent on full opioid agonists.

In addition, SUBOXONE Film:
• May help with continuity of treatment for appropriate patients*- Prior to induction, consideration should be given to the type of opioid dependence (long- or short-acting opioid products), the time of the last opioid use, and the degree or level of opioid dependence. With its approval for both induction and maintenance phases of treatment in appropriate patients,* SUBOXONE Film may allow patients dependent on short-acting opioids to transition between opioid dependence treatment phases (induction through maintenance) with no changes in medication form or formulation. (For patients taking long-acting opioids, induction with buprenorphine monotherapy is recommended when used according to approved administration instructions. When the long-acting opioid is used, dosage adjustments may be necessary when transitioning from induction with buprenorphine to maintenance treatment with a buprenorphine and naloxone combination product.) Patients being switched between buprenorphine and naloxone or buprenorphine only sublingual tablets and SUBOXONE Sublingual Film should be started on the corresponding dosage of the previously administered product. However, dosage adjustments may be necessary when switching between products. Not all strengths and combinations of the SUBOXONE Sublingual Films are bioequivalent to the SUBOXONE® buprenorphine and naloxone) sublingual tablets as observed in pharmacokinetic studies. Therefore, systemic exposures of buprenorphine and naloxone may be different when patients are switched from tablets to film or vice versa. Patients should be monitored for symptoms related to overdosing or underdosing.
• Provides flexible dosing options - SUBOXONE Film is available in a variety of dosage strengths: 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, and 12 mg/3 mg of buprenorphine and naloxone. On Day 1 of induction, a total daily dosage of up to 8 mg/2 mg SUBOXONE Film is recommended. Clinicians should start the induction phase of treatment with an initial dose of 2 mg/0.5 mg or 4 mg/1 mg buprenorphine/naloxone and may titrate upward in 2- or 4-mg increments of buprenorphine, at approximately 2-hour intervals, under supervision, to 8 mg/2 mg buprenorphine/naloxone based on the control of acute withdrawal symptoms. On Day 2 of induction, a single daily dose target of up to 16 mg/4 mg SUBOXONE Film is recommended. It is recommended that an adequate maintenance dose, titrated to clinical effectiveness, be achieved as rapidly as possible.
• Features child-resistant packaging - Each SUBOXONE Film comes in a unit-dose child-resistant pouch.

Reckitt Benckiser Pharmaceuticals has been offering opioid-dependence treatment options since 2003. Its ongoing commitment to multiple stakeholders is reflected in the informational support it provides to patients, healthcare professionals, and health plans.

*For patients taking long-acting opioids, induction with buprenorphine monotherapy is recommended when used according to approved administration instructions.

Questions and Answers
Q: What are considered the advantages of Suboxone Films?
A: RADARS data shows decreased abuse with films and increased abuse with tablets, film packaging is rated F1, film decreases misuse and pediatric exposure compared to the tablets and can be used for induction as well as maintenance.

VII. AstraZeneca

Tim A. Briscoe, PharmD, CDE, Senior Regional Scientific Manager
Julie Huber, Regional Clinical Account Director
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Brilinta® (ticagrelor)

Pronunciation: BRILINTA® (brih-LIN-tah); Ticagrelor (tye-KA-grel-or)

Overview of BRILINTA

The clinical evidence for the efficacy and safety of BRILINTA is derived from the PLATO (PLATelet inhibition and patient Outcomes) trial. BRILINTA, as compared to clopidogrel, reduced the rate of the combined endpoint of cardiovascular (CV) death, myocardial infarction (MI), or stroke in patients with acute coronary syndrome (ACS) by 16% (relative risk reduction [RRR]; p<0.001), with an absolute risk reduction (ARR) of 1.9%. The difference between treatments was driven by CV death and MI, with no difference in stroke. BRILINTA is the first and only oral antiplatelet agent Food Drug Administration (FDA) approved to demonstrate significant reductions in CV death versus clopidogrel (1.1% ARR; 21% RRR; p=0.001). Maintenance doses of aspirin (ASA) above 100 mg reduce the effectiveness of BRILINTA and should be avoided. The overall rate of PLATO-defined total major bleeding was similar between the BRILINTA and clopidogrel groups; there was a higher rate of non-coronary artery bypass graft (CABG)-related bleeding with BRILINTA.

Indications: BRILINTA is a $P2Y_{12}$ platelet inhibitor indicated to reduce the rate of thrombotic CV events in patients with ACS (unstable angina [UA], nonST elevation myocardial infarction [NSTEMI], or ST elevation myocardial infarction [STEMI]). BRILINTA has been shown to reduce the rate of a combined endpoint of CV death, MI or stroke compared to clopidogrel. The difference between treatments was driven by CV death and MI with no difference in stroke. In patients treated with percutaneous coronary intervention (PCI), it also reduces the rate of stent thrombosis. BRILINTA has been studied in ACS in combination with ASA. Maintenance doses of ASA above 100 mg decreased the effectiveness of BRILINTA. Avoid maintenance doses of ASA above 100 mg daily.
Boxed Warnings: Please refer to the BRILINTA Prescribing Information for Boxed Warnings related to increased risk of bleeding and reduced effectiveness with maintenance doses of ASA greater than 100 mg per day.
Contraindications: BRILINTA is contraindicated in patients with a history of intracranial hemorrhage, active pathological bleeding, severe hepatic impairment, and hypersensitivity to ticagrelor or any component of the product.

Select Subgroup Publications

- Non-ST-elevation (NSTE)-ACS: In a prespecified subgroup analysis, the effects of ticagrelor versus clopidogrel in patients diagnosed with NSTE-ACS (n=11,080) at admission were evaluated. The incidence of the composite of CV death, MI, and stroke was reduced with ticagrelor vs. clopidogrel (10.0% vs. 12.3%; hazard ratio [HR] 0.83; 95% CI 0.74–0.93; p=0.0013). The incidence of CV death (3.7% vs. 4.9%; p=0.0070), MI (6.6% vs. 7.7%; p=0.0419) and all-cause death (4.3% vs. 5.8%; p=0.002) occurred less often with ticagrelor vs clopidogrel. The incidence of stroke did not differ between treatment arms. There was no significant difference in PLATO defined major bleeding with ticagrelor vs. clopidogrel (13.4% vs. 12.6%), but a higher rate of nonCABG-related major bleeding occurred (4.8% vs. 3.8%).
- Stent Thrombosis: In PLATO, 11,289 (60.6%) patients either had a previous stent implanted (n=1404) or underwent stent implantation during the study (n=9885). There was a lower risk of stent thrombosis with ticagrelor (1.3% for adjudicated “definite”) than with clopidogrel (1.9% [HR, 0.67; 95% CI 0.50-0.91; p=0.009]). In a subgroup analysis, when time to stent thrombosis was evaluated, the reduction in definite stent thrombosis with ticagrelor was numerically greater for late stent thrombosis (>30 days: HR, 0.48 [CI 0.24-0.96]), and subacute stent thrombosis (24 hours-30 days post PCI: HR, 0.60 [CI 0.39 – 0.93]) versus acute stent thrombosis (≤24 hours: HR, 0.94 [CI 0.43-2.05]). When major bleeding events were analyzed after any stent thrombosis event, there were 7 events in 128 ticagrelor-treated patients and 16 events in 179 clopidogrel-treated patients.

The PLATO trial was not designed or powered to demonstrate the efficacy or safety of ticagrelor compared with clopidogrel in specific subgroups. Subgroup analyses were performed to confirm consistency of results in different cohorts.

US Clinical Guidelines for the Management of ACS (2011-2014)

- Four major cardiology associations (ACCF, AHA, ACC and SCAI) updated ACS clinical guidelines to include BRILINTA as a Class I recommendation for the management of patients with ACS undergoing PCI with stenting. The 2014 AHA/ACC NSTE-ACS guideline states that it is reasonable to choose ticagrelor over clopidogrel in patients

treated with an ischemia-guided strategy, early invasive strategy, and/or coronary stenting (Class IIa; Level of Evidence B).

Adverse Reactions: The most common adverse reactions are bleeding and dyspnea.

Questions and Answers
There were no additional questions and answers.

Bydureon (exenatide extended-release)
Pronunciation: BYDUREON® [by-DUR-ee-on] (exenatide [ex-EN-a-tide] extended-release for injectable suspension)

Indication and Important Limitations of Use for BYDUREON
• BYDUREON is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise.
• Should not be used to treat type 1 diabetes or diabetic ketoacidosis
• Use with insulin has not been studied and is not recommended
• Has not been studied in patients with history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis

BOXED WARNING: RISK OF THYROID C-CELL TUMORS Exenatide extended-release causes an increased incidence in thyroid C-cell tumors at clinically relevant exposures in rats compared to controls. It is unknown whether BYDUREON causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be determined by clinical or nonclinical studies. BYDUREON is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Routine serum calcitonin or thyroid ultrasound monitoring is of uncertain value in patients treated with BYDUREON. Patients should be counseled regarding the risk and symptoms of thyroid tumors.

Dosing
Administer 2 mg by subcutaneous injection once every seven days (weekly), at any time of the day with or without meals. Bydureon 2 mg has two dosage forms on the market: Bydureon single-dose tray containing a 2 mg vial and the Bydureon single-dose 2 mg pen. The Bydureon® single dose 2 mg pen was approved by the Food and Drug Administration (FDA) in February 2014 and is a pre-filled, single-use pen injector, eliminating the need for the patient to transfer the medication between a vial and syringe during the self-injection process. The Bydureon® Pen provides the same formulation and dose as the Bydureon single-dose tray, and can be administered at any time of the day, with or without meals. No new clinical data was required for the Bydureon Pen.

Clinical Trial Efficacy
The clinical effectiveness of BYDUREON has been demonstrated in 6 head-to-head randomized controlled clinical trials (N = 3223) in which A1C reductions ranged from 1.3% to 1.9% in patient with baseline A1C values of 8.3% to 8.6%. Direct comparative trials showed that A1C reductions with BYDUREON were significantly greater than A1C reductions with BYETTA, sitagliptin, pioglitazone or insulin glargine, but significantly less than with liraglutide in T2DM patients on 1 or more other glucose-lowering therapies. In a head to head comparator study with Byetta, Bydureon had a significantly greater reduction in fasting plasma glucose compared to Byetta at the end of the study, -35mg/dl vs -12mg/dl respectively. Although Bydureon did not provide a greater reduction in 2 hour post prandial plasma glucose compared to Byetta, Bydureon showed significant improvement from baseline to endpoint (-95.4 mg/dl p =0.0124). The risk of hypoglycemia was increased when Bydureon was used in combination with a sulfonylurea. The incidence of minor hypoglycemia without concomitant sulfonylurea was 0.0% for Bydureon and Byetta. Overall, 52% to 77% of patients treated with BYDUREON achieved an A1C of 7% and no major hypoglycemia events were observed. In extension trials, patients treated with BYDUREON for 6 years achieved A1C reductions of -1.6%. Patients on BYDUREON saw a greater A1C reduction at 3years than patients taking insulin glargine (-1.0 + 0.07 for Bydureon vs -0.8 + 0.07 for insulin glargine).

Clinical Trial Safety
A safety analysis of BYDUREON (N=4328) demonstrated that BYDUREON was generally well-tolerated; head-to-head trials provided information on the adverse events observed with BYDUREON and comparators (BYETTA, insulin, liraglutide, metformin, pioglitazone, sitagliptin). The most frequent adverse event observed with BYDUREON was mild-

to-moderate nausea, with an incidence lower than BYETTA or liraglutide. Most nausea events with BYDUREON were transient and occurred within the first 2 weeks of treatment then decreased over time, with only 1.4% of patients discontinuing treatment due to gastrointestinal AEs.10 Injection-site reactions were observed more frequently with BYDUREON than with BYETTA (7.1% vs 2.6%).10 BYDUREON is renally excreted, so BYDUREON is contraindicated in patients with severe renal impairment. EXSCEL, a randomized, double-blinded, placebo controlled trial, has been planned to enroll 14000 patients and study them over 7.5 years to provide data on cardiovascular outcomes and mortality in patients treated with BYDUREON.

Real-world Adherence
Adherence to GLP-1 therapies (ExQW, ExBID, and liraglutide) were measured in adult patients with type 2 diabetes in a retrospective cohort study, using administrative claims data from the Truven Health MarketScan databases. Adherence was measured by the proportion of days covered (PDC) measure, calculated as the total number of days covered with GLP-1 supply during the post-index period divided by 180 days. Patients with a PDC ≥ 80% were classified as adherent. A significantly higher proportion of patients initiating ExQW achieved a PDC ≥80% during the 6-month follow-up compared with ExBID (48.6% vs 30.3%, P<0.0001) and liraglutide (48.6% vs 44.2%, P<0.0001), respectively. After adjusting for potential confounders, adherence was significantly higher among patients initiating ExQW than patients initiating ExBID (OR=0.41, 95% CI=0.34, 0.45) and among patients initiating liraglutide (OR=0.80, 95% CI=0.75, 0.86) during the 6-month follow-up period.

Real-world A1C Outcome
Similar treatment effects were observed in a retrospective cohort study using ambulatory electronic medical record (EMR) data to evaluate A1c outcome at six-month in adult patients with type 2 diabetes initiating either ExQW or liraglutide. After adjusting for potential confounders (e.g., baseline patient and clinical characteristics), the least-squares mean change in A1C from baseline were -0.68% for ExQW compared with -0.61% for liraglutide (P=0.2751). Similarly, among the subgroup of patients with suboptimum glycemic control (A1C ≥7.0%) and no prescription for insulin during the 12-month pre-index period, the adjusted mean change in A1C at 6-month did not differ between ExQW and liraglutide (-0.94% vs -0.85%, respectively, P=0.3728).

Questions and Answers
There were no additional questions and answers.

Byetta® (exenatide)
Pronunciation: BYETTA [bye-A-tuh] (exenatide) [ex-EN-a-tide] injection

Overview of BYETTA
- BYETTA is a GLP-1 receptor agonist that enhances glucose-dependent insulin secretion by the pancreatic beta-cell, suppresses inappropriately elevated glucagon secretion, and slows gastric emptying.
- BYETTA is approved for use as an adjunct (add-on) to insulin glargine. Patients receiving BYETTA and insulin glargine may require adjustment of the insulin dose to reduce the risk of hypoglycemia.
- Studies that assessed the efficacy and safety of the concomitant use of BYETTA and insulin glargine in patients with type 2 diabetes (T2DM) showed reductions in A1C.
- In a 30 week phase 3 randomized study comparing safety and efficacy of BYETTA plus basal insulin to prandial insulin plus basal insulin in 510 patients with T2DM, there was a similar noninferior mean change in A1C from baseline to study end: -1.13% vs -1.10% (*P* =0.627). The most common adverse events in patients taking BYETTA vs insulin lispro were nausea (32.4% vs. 1.6%), vomiting (12.4% vs. 1.0%), and diarrhea (10.8% vs. 5.1%).

Indication
BYETTA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

Important Limitations of Use
- Not a substitute for insulin. BYETTA should not be used for the treatment of type 1 diabetes or diabetic ketoacidosis.
- Concurrent use with prandial insulin has not been studied and cannot be recommended.
- Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Dosing

BYETTA should be initiated at 5 mcg administered BID at any time within the 60-minute period before the morning and evening meals (or before the two main meals of the day, approximately 6 hours or more apart). BYETTA should not be administered after a meal. Based on clinical response, the dose of BYETTA can be increased to 10 mcg BID after 1 month. Initiation with 5 mcg reduces the incidence and severity of gastrointestinal side effects. Each dose should be given as a subcutaneous (SC) injection in the thigh, abdomen, or upper arm.

Renal Impairment
BYETTA is not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance < 30 mL/min) and should be used with caution in patients with renal transplantation. No dosage adjustment of BYETTA is required in patients with mild renal impairment (creatinine clearance 50 to 80 mL/min). Caution should be applied when initiating or escalating doses of BYETTA from 5 mcg to 10 mcg in patients with moderate renal impairment (creatinine clearance 30 to 50 mL/min).

Clinical Data
Hemoglobin A1c (HbA1c) Control Across Clinical Program
The clinical efficacy of BYETTA is supported by data available from over 70 studies that enrolled more than 6500 subjects. The BYETTA clinical trial program enrolled patients requiring glucose-lowering therapies ranging from lifestyle modification to oral therapies, insulin glargine, and combinations of these therapies. The trials showed changes in A1C from baseline of -0.7 to -1.7% with BYETTA 10 mcg in patients with baseline A1C values of 7.8 to 8.7%.1 BYETTA has shown superior efficacy in reducing postprandial glucose excursions. In a 2 week double blind randomized cross over study evaluating the effects of titrated exenatide versus sitagliptin on 2-hr post prandial glucose in sixty-one patients with T2DM, exenatide provided a significantly greater reduction in post prandial glucose compared with sitagliptin (133 +/- 6 mg/dL versus 208 +/- 6 mg/dL respectively, p < 0.0001).
BYETTA as add on to insulin glargine
In a 30 week phase 3 randomized study comparing safety and efficacy of BYETTA plus basal insulin to basal insulin plus prandial insulin in 510 patients with T2DM, there was a similar mean change in A1C from baseline to study end: -1.3% vs -1.10% (*P* =0.627). Noninferiority was assessed using an HbA1c margin of 0.4%. In a 30-week phase 3 study involving 259 patients using insulin glargine (± metformin, pioglitazone, or both), mean changes in A1C in the BYETTA versus placebo groups were – 1.7% versus – 1.0% (*P* < .001). Since biguanides, thiazolidinediones, sulfonylureas, and basal insulin primarily affect fasting glucose concentrations, the action of BYETTA complements the actions of these medications to improve glucose control.

Safety
The most frequent adverse event observed with BYETTA was mild to moderate nausea that decreased over time, with 3% of patients in clinical trials discontinuing treatment due to nausea. Gradual titration of exenatide or use of a lower dose has been shown to reduce the incidence of nausea. BYETTA is renally excreted, so BYETTA should not be used in patients with severe renal impairment. The safety of BYETTA is continuously monitored in the Adverse Event Response System (AERS) and specific concerns are investigated in large patient databases. Postmarketing data has included some reports of acute pancreatitis in patients using BYETTA. However, retrospective database studies have not identified a higher pancreatitis risk with BYETTA than with other glucose-lowering therapies. BYETTA should not be used in patients with a previous history of pancreatitis and should be discontinued in patients diagnosed with pancreatitis.

Questions and Answers
There were no additional questions and answers.

Farxiga® (dapagliflozin)
Pronunciation: FarxigaTM [far-SEE-guh] (dapagliflozin) [DAP a gli FLOE zin] tablets

Overview of FARXIGA
- FARXIGA is an oral sodium-glucose cotransporter 2 (SGLT2) inhibitor that works in the kidney to remove glucose via the urine.
- Clinical studies have demonstrated that FARXIGA is effective in reducing HbA1c with the additional benefits of weight and blood pressure reduction.

Indication
- FARXIGA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM).

Limitation of Use & Dosing

- FARXIGA should not be used to treat patients with type 1 diabetes or diabetic ketoacidosis.
- The recommended starting dose of FARXIGA is 5 mg once daily, taken in the morning, with or without food. In patients tolerating FARXIGA 5 mg who require additional glycemic control, the dose can be increased to 10 mg once daily.
- In patients with volume depletion, correcting this condition prior to initiation of FARXIGA is recommended.
- Assess renal function before initiating FARXIGA and periodically thereafter. Do not initiate FARXIGA if eGFR is < 60 mL/min/1.73 m2, and discontinue FARXIGA if eGFR falls persistently < 60 mL/min/1.73 m2. No dose adjustment is needed in patients with mild renal impairment (eGFR > 60 mL/min/1.73 m2).

Clinical Data

- FARXIGA demonstrated significant reductions in HbA1c when used as monotherapy and in combination with other antidiabetic agents. In a monotherapy study, HbA1c reductions from baseline were -0.9% for FARXIGA 10 mg QAM, -0.8% for FARXIGA 5 mg QAM and -0.2% for the placebo group. FARXIGA 5 mg demonstrated an HbA1c reduction at week 24 from baseline of -0.7% in a placebo-controlled add-on combination study with metformin (MET) and a -2.1% HbA1c reduction from baseline in an active-controlled initial combination therapy study with MET XR. In placebo-controlled trials of FARXIGA 10 mg as an add-on to MET, sitagliptin (± MET), glimepiride, pioglitazone, or insulin (± up to 2 oral antidiabetic therapies), FARXIGA 10 mg demonstrated numerically greater HbA1c reductions versus the 5 mg dose and also consistently resulted in clinically meaningful placebo-corrected HbA1c reductions at week 24 from baseline that ranged from -0.48% to -0.7%. In a 52-week add-on to MET active-comparator study of FARXIGA versus glipizide, HbA1c values were reduced by -0.5% from baseline in both groups.
- Exploratory efficacy analyses of long-term extension treatment data were conducted to assess the durability of treatment effects on HbA1c and other glycemic endpoints. All of the studies within the clinical program that assessed long term data, ranging from 48 weeks to 4 years, showed that the effects of FARXIGA were sustained.
- In placebo-controlled phase 3 studies that evaluated change in mean weight at 24 weeks as a secondary endpoint, placebo-corrected weight reduction in FARXIGA groups ranged from -0.8 kg to -2.2 kg; and with the exception of one monotherapy study, the reductions were statistically significant for the 5 and 10 mg doses of FARXIGA.
- In the FARXIGA 10 mg groups of all of the phase 3 monotherapy and placebo-controlled add-on combination studies where systolic blood pressure (SBP) was evaluated as an additional analysis, there were mean numerical reductions at week 24 versus placebo that ranged from -1.3 mmHg to -5.3 mmHg, placebo-corrected. Two additional studies were designed to evaluate the effect of FARXIGA on BP and HbA1c in patients with T2DM with inadequately controlled hypertension on an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) or an ACEi or ARB plus an additional antihypertensive medication such as a thiazide diuretic, beta blocker or calcium channel blocker. At week 12 in both studies, FARXIGA 10 mg provided significant improvement in seated SBP and significant reduction in 24-hour mean ambulatory SBP.
- More than 11,000 patients with T2DM participated in 24 phase 2b and 3 studies, including both placebo-controlled and active comparator designs with durations ranging from 12 weeks to 4 years. Over 6,000 patients received FARXIGA in these trials. Patient populations examined covered the range of T2DM progression: drug-naïve patients, patients unable to achieve glycemic control on oral therapies, and patients on insulin-based regimens. The program also provided significant experience in elderly patients, patients with a history of cardiovascular (CV) disease, overweight and obese patients, patients with poorly controlled hypertension, and patients with mild to moderate renal impairment. FARXIGA is not indicated for weight loss, the treatment of hypertension, or to reduce CV outcomes.
- **Network Meta Analysis (NMA):** A systematic literature review and Bayesian NMA of eight randomized controlled trials (RCTs) involving anti-diabetes treatments added to metformin demonstrated that FARXIGA when compared with glucagon-like peptide-1 receptor agonists (GLP-1RAs), dipeptidyl peptidase-4 inhibitors (DPP-4is), thiazolidinediones (TZDs), and sulfonylureas (SUs), offers similar HbA1c control after 1 year, with comparable or reduced risk (vs SU) of hypoglycemia, and the additional benefit of weight loss (vs DPP-4i and SU). Results and 95% confidence intervals are below.

	HbA1c (%)	**Weight** (kg)	**Hypoglycemia** (Odds Ratio)
FARXIGA vs GLP-1 RA	0.41 (-0.01, 0.84)	-0.53 (-3.05, 2.00)	NT
FARXIGA vs DPP-4i	-0.11 (-0.42, 0.22)	-2.59 (-4.53, -0.66)	0.57 (0.14, 2.56)
FARXIGA vs TZD	-0.02 (-0.45, 0.40)	-4.76 (-7.28, -2.24)	0.57 (0.08, 4.81)

FARXIGA vs SU	0.00 (-0.29, 0.29)	-4.66 (-6.43, -2.90)	0.05 (0.01, 0.19)

Health Economic and Outcomes Research Data

- A cost effectiveness analysis was conducted to evaluate the clinical and economic consequences associated with the use of FARXIGA as add-on therapy in T2DM. The Cardiff Model, a validated fixed-time stochastic simulation cost-utility, model was adapted to the U.S. payer perspective. Estimated costs and benefits were discounted at a rate of 3% annually over a 40-year time frame. FARXIGA was evaluated as add-on to MET treatment compared to commonly used classes of agents. FARXIGA is cost effective compared to an SU (Incremental Cost Effectiveness Ratio [ICER]: $35,633), TZD (ICER: $32,955), and DPP-4i (ICER: $32,955).

Questions and Answers

There were no additional questions and answers.

VIII. Actavis

Carla McSpadden, RPh, CGP, Senior Medical & Health Outcomes Liaison
Stacie Potter, Associate Director

Fetzima® (levomilnacipran)

INDICATION AND USAGE

FETZIMA (levomilnacipran) extended-release capsules are indicated for the treatment of major depressive disorder (MDD) in adults. Limitation of Use: FETZIMA is not approved for the management of fibromyalgia. Efficacy and safety for the management of fibromyalgia have not been established.

MECHANISM OF ACTION AND PHARMACODYNAMICS

The exact mechanism of the antidepressant action of FETZIMA is unknown, but is thought to be related to the potentiation of serotonin (5-HT) and norepinephrine (NE) in the central nervous system. Non-clinical studies have shown that levomilnacipran is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI). It binds with high affinity to the human 5-HT and NE transporters (Ki = 11 and 91 nM, respectively) and potently inhibits 5-HT and NE reuptake (IC50 = 16-19 and 11 nM, respectively).

PHARMACOKINETICS AND DRUG INTERACTIONS

The relative bioavailability of levomilnacipran after administration of FETZIMA was 92% when compared to oral solution. Levomilnacipran concentration was not significantly affected by food. The Tmax of levomilnacipran is 6-8 hours after oral administration, and the apparent terminal elimination half-life is approximately 12 hours. Plasma protein binding is approximately 22%. Levomilnacipran and its inactive metabolites are eliminated primarily by renal excretion. The dose of FETZIMA should not exceed 80 mg once daily when used with strong CYP3A4 inhibitors. An *in vivo* study showed a clinically meaningful increase in levomilnacipran exposure when FETZIMA was coadministered with the CYP3A4 inhibitor ketoconazole. FETZIMA is predicted to have a low potential to be involved in other clinically significant pharmacokinetic drug interactions.

EFFICACY

The efficacy of FETZIMA for the treatment of MDD was established in three 8-week randomized, double-blind, placebo-controlled studies (at doses 40 to 120 mg once daily) in adult (18 - 78 years of age) outpatients who met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria for MDD. Two of the studies were fixed dose (Study 1 and Study 2) and one study was flexible dose (Study 3). In all three studies, FETZIMA demonstrated superiority over placebo in the improvement of depressive symptoms as measured by the Montgomery-Äsberg Depression Rating Scale (MADRS) total score (primary endpoint). FETZIMA also demonstrated superiority over placebo as measured by improvement in the Sheehan Disability Scale (SDS) functional impairment total score (secondary endpoint).

ADVERSE REACTIONS

In the short-term placebo-controlled studies for MDD, 9% of the 1,583 patients who received FETZIMA (40 to 120 mg) discontinued treatment due to an adverse event (AE), compared with 3% of the 1,040 placebo-treated patients in those studies. The most common AE leading to discontinuation in at least 1% of the FETZIMA-treated patients was nausea (1.5%). The most commonly observed AEs in FETZIMA-treated MDD patients in placebo-controlled studies (incidence ≥ 5% and at least twice the rate of placebo) were: nausea (17% vs. 6%), constipation (9% vs. 3%), hyperhidrosis (9%

vs. 2%), heart rate increased (6% vs. 1%), erectile dysfunction (6% vs. 1% of male patients), tachycardia (6% vs. 2%), vomiting (5% vs. 1%), and palpitations (5% vs. 1%).

CONTRAINDICATIONS
FETZIMA is contraindicated with patients with hypersensitivity to levomilnacipran, milnacipran, or to any excipient. The use of MAOIs intended to treat psychiatric disorders with FETZIMA or within 7 days of stopping treatment with FETZIMA is contraindicated because of an increased risk of serotonin syndrome. The use of FETZIMA within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated, as well as starting FETZIMA in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue. FETZIMA is also contraindicated in patients with uncontrolled narrow-angle glaucoma.

WARNINGS AND PRECAUTIONS
FETZIMA has a boxed warning for the increased risk of suicidality and is not approved for use in pediatric patients. All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the first few months of treatment and when changing the dose. Consider changing the therapeutic regimen, including possibly discontinuation, in patients whose depression is persistently worse or includes symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, or suicidality that are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Serotonin syndrome has been reported with SNRIs and SSRIs alone, but particularly with concomitant use of other serotonergic drugs, and with drugs that impair metabolism of serotonin. Patients taking FETZIMA should be monitored for symptoms of serotonin syndrome. If such symptoms occur, discontinue FETZIMA and initiate supportive treatment. SNRIs, including FETZIMA, have been associated with increases in blood pressure and heart rate. SSRIs and SNRIs may increase the risk of bleeding events. Concomitant use of aspirin, NSAIDS, warfarin, and other anticoagulants may add to this risk. FETZIMA should be used cautiously in patients with controlled narrow-angle glaucoma. The noradrenergic effect of SNRIs, including FETZIMA, can cause urinary hesitation or retention. Symptoms of mania/hypomania have been reported with FETZIMA. As with all antidepressants, use FETZIMA cautiously in patients with a history or family history of bipolar disorder, mania, or hypomania. FETZIMA should be used with caution in patients with a seizure disorder. Monitor patients when discontinuing FETZIMA, and reduce the dose gradually whenever possible. Hyponatremia has occurred with SSRIs and SNRIs. Elderly patients, patients taking diuretics, or patients who are volume depleted can be at greater risk.

SPECIFIC POPULATIONS
FETZIMA is in pregnancy category C. There are no adequate and well-controlled studies in pregnant women. Nursing mothers: It is not known if FETZIMA is present in human milk. Studies have shown that FETZIMA is present in the milk of lactating rats. The safety and effectiveness of FETZIMA in the pediatric population have not been established. No dose adjustment of FETZIMA is recommended on the basis of age or gender. No dosage adjustment is recommended for patients with hepatic impairment. FETZIMA is predominantly excreted through the kidneys, and dosing adjustment is necessary for patients with moderate or severe renal impairment. The maximum recommended maintenance dose is 80 mg once daily in patients with moderate renal impairment and 40 mg once daily in patients with severe renal impairment. FETZIMA is not recommended for patients with end stage renal disease.

DOSING
The recommended dose range for FETZIMA is 40 mg to 120 mg once daily, with or without food. FETZIMA should be initiated at 20 mg once daily for 2 days, and then increased to 40 mg once daily. Based on efficacy and tolerability, FETZIMA may then be increased in increments of 40 mg at intervals of 2 or more days. The maximum recommended dose is 120 mg once daily. FETZIMA should be taken at approximately the same time each day. FETZIMA should be swallowed whole and the capsule should not be opened, chewed or crushed.

Questions and Answers
Q: Are other indications being sought?
A: No.

Viibryd® (vilazodone hydrochloride)
INDICATION
VIIBRYD® (vilazodone HCl) is indicated for the treatment of Major Depressive Disorder (MDD) in adults.

PHARMACOLOGY
VIIBRYD binds with high affinity to the serotonin transporter (SERT) and potently and selectively inhibits serotonin (5-HT) reuptake. It also binds selectively with high affinity to 5-HT_{1A} receptors and is a 5-HT_{1A} receptor partial agonist. Although not fully understood, VIIBRYD's antidepressant effect is thought to be related to enhancement of 5-HT activity in the central nervous system through selective inhibition of 5-HT reuptake. VIIBRYD is also a partial 5-HT_{1A} agonist, however, the net result of this action on 5-HT transmission and its role in the antidepressant effect are unknown.

PHARMACOKINETICS
The absolute bioavailability of VIIBRYD is approximately 72% when taken with food. It has an elimination half-life of approximately 25 hours, peak plasma concentration at 4-5 hours, and linear kinetics. *In vivo*, VIIBRYD is 96-99% protein-bound and is metabolized primarily through the liver by CYP3A4 isoenzymes. In the presence of strong CYP3A4 inhibitors, the recommended VIIBRYD dose of 40 mg/day should be reduced to 20 mg/day. Based on clinical response, consider increasing the dose of VIIBRYD up to 2-fold when used concomitantly with strong CYP3A4 inducers for greater than 14 days. The maximum daily dose should not exceed 80mg.

EFFICACY
The efficacy of VIIBRYD as a treatment for adult MDD was established in two 8-week, multicenter, randomized, double-blind, placebo-controlled studies in adult (18-70 years of age) outpatients who met the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV-TR*) criteria for MDD. In these studies, patients were titrated over 2 weeks to a dose of 40 mg of VIIBRYD with food (n = 436) or placebo (n = 433) once daily. In both trials, VIIBRYD was superior to placebo in the improvement of depressive symptoms as measured by the mean change from baseline to Week 8 in the Montgomery-Asberg Depression Rating Scale (MADRS) total score (least squares mean difference from placebo in change from baseline was -3.2 (95% CI; -5.2, -1.3) for Study 1 and -2.5 (95% CI; -4.4, -0.6) for Study 2.

CONTRAINDICATIONS
The use of MAOIs intended to treat psychiatric disorders with VIIBRYD or within 14 days of stopping treatment with VIIBRYD is contraindicated because of an increased risk of serotonin syndrome. Do not use VIIBRYD within 14 days of stopping an MAOI intended to treat psychiatric disorders. In addition, do not start VIIBRYD in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue.

WARNINGS AND PRECAUTIONS
VIIBRYD has a boxed warning for the increased risk of suicidal thoughts and behavior in children, adolescents and young adults taking antidepressants and is not approved for use in pediatric patients. **All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the first few months of treatment and when changing the dose.** Consider changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or includes symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, or suicidality that are severe, abrupt in onset, or were not part of the patient's presenting symptoms. The development of potentially life-threatening serotonin syndrome has been reported with SNRIs and SSRIs, including VIIBRYD, both when taken alone, but especially when co-administered with other serotonergic agents (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort). If such symptoms occur, discontinue VIIBRYD and initiate supportive treatment. If concomitant use of VIIBRYD with other serotonergic drugs is clinically warranted, patients should be made aware of a potential increased risk for serotonin syndrome, particularly during treatment initiation and dose increases. VIIBRYD should be prescribed with caution in patients with a seizure disorder. The use of drugs that interfere with serotonin reuptake, including VIIBRYD, may increase the risk of bleeding events. VIIBRYD should be used cautiously in patients with a history or family history of bipolar disorder, mania or hypomania. VIIBRYD is not approved for use in treating bipolar depression. Discontinuation symptoms have been reported with discontinuation of serotonergic drugs such as VIIBRYD. Gradual dose reduction is recommended, instead of abrupt discontinuation, whenever possible. Elderly patients and patients taking diuretics or who are otherwise volume depleted may be at greater risk of developing hyponatremia with SSRIs. Discontinuation of VIIBRYD in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. The pupillary dilation that occurs following use of many antidepressant drugs, including VIIBRYD, may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.

ADVERSE REACTIONS

The safety of VIIBRYD was evaluated from two double-blind placebo-controlled 8-week trials in 861 MDD patients (436 patients receiving VIIBRYD). In the 8-week trials, approximately 80% of patients completed the trials. Overall, 7.1% of the patients who received VIIBRYD discontinued treatment due to an adverse reaction compared with 3.2% of placebo-treated patients. No single adverse reaction led to discontinuation in >1% of the patients. The most commonly observed adverse reactions in VIIBRYD-treated patients (incidence ≥5% and at least twice the rate of placebo) were: diarrhea (28% vs. 9%), nausea (23% vs. 5%), vomiting (5% vs. 1%), and insomnia (6% vs. 2%). VIIBRYD had no effect on body weight as measured by the mean change from baseline in the 8-week placebo-controlled studies. The mean changes in weight were +0.16kg in the VIIBRYD group and +0.18kg in the placebo group. The safety profile of VIIBRYD is further supported by an open-label 52-week safety study in 599 MDD patients receiving 40 mg daily. The most commonly observed adverse reactions in VIIBRYD-treated patients in this open-label study were diarrhea (36%), nausea (32%), and headache (20%). VIIBRYD was not associated with any clinically significant changes in laboratory parameters, ECGs, and vital signs in the 8-week placebo controlled studies or the 52-week open-label study.

USE IN SPECIFIC POPULATIONS
Pregnancy Category C: There are no adequate and well-controlled studies of VIIBRYD in pregnant women. When treating pregnant women with VIIBRYD, carefully consider whether the potential benefits outweigh the potential risks of treatment. Nonteratogenic effects: Neonates exposed to serotonergic antidepressants late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. SSRI exposure during pregnancy may increase the risk of Persistent Pulmonary Hypertension of the Newborn (PPHN). The effect of VIIBRYD on lactation and nursing in humans is unknown. Breastfeeding in women treated with VIIBRYD should be considered only if the potential benefit outweighs the potential risk to the child. No dose adjustments are required in elderly patients, patients with mild, moderate, or severe renal impairment and in those patients with mild, moderate or severe hepatic impairment.

DOSING
VIIBRYD is available in 10, 20, and 40 mg tablets. VIIBRYD should be titrated, starting with an initial dose of 10 mg once daily for 7 days, followed by 20 mg once daily for an additional 7 days, and then increased to 40 mg once daily. VIIBRYD should be taken with food. Blood concentrations (AUC) in the fasted state can be decreased by approximately 50% compared to the fed state and may result in diminished effectiveness in some patients.

Questions and Answers
Q: Are there other indications or formulations being sought?
A: A sNDA has been submitted for a 20 mg strength and indication in anxiety has been looked at but it was decided to not pursue as a new indication.

IX. Novartis
Julia Compton, PharmD, Regional Account Scientific Director

Gilenya® (fingolimod)
Indications and Usage
Gilenya (fingolimod) is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

Mechanism of Action
Fingolimod is metabolized by sphingosine kinase to the active metabolite, fingolimod-phosphate. Fingolimod-phosphate is a sphingosine 1-phosphate receptor modulator, and binds with high affinity to sphingosine 1-phosphate receptors 1, 3, 4, and 5. Fingolimod-phosphate blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which fingolimod exerts therapeutic effects in multiple sclerosis is unknown, but may involve reduction of lymphocyte migration into the central nervous system.

First Dose Monitoring
- Observe all patients for signs and symptoms of bradycardia for at least 6 hours after first dose with hourly pulse and blood pressure measurement. Obtain ECG prior to dosing and at the end of the observation period.

- Patients who develop heart rate <45 bpm, or new onset 2nd degree or higher atrioventricular block 6 hours post-dose should be monitored until resolution. Patients at lowest post-dose heart rate at end of the observation period should be monitored until HR increases.
- In patients experiencing post-dose symptomatic bradycardia, initiate appropriate management, begin continuous ECG monitoring until the symptoms have resolved; if pharmacological intervention is required for symptomatic bradycardia, continuous ECG monitoring should continue overnight in a medical facility, and first-dose monitoring strategy should be repeated after the second dose of Gilenya.
- Patients with some preexisting conditions or receiving concomitant heart rate lowering or atrioventricular conduction slowing medications should be observed overnight with continuous ECG monitoring after first dose.
- Patients with prolonged QTc interval (>450 msec males, >470 msec females) before or during 6-hour observation, those at additional risk for QT prolongation, or taking QT-prolonging drugs with a known risk of torsades de pointes should be observed overnight with continuous ECG monitoring.

Efficacy

The efficacy of Gilenya was demonstrated in 2 studies that evaluated once-daily doses of Gilenya 0.5 mg and 1.25 mg in patients with relapsing-remitting MS (RRMS). Study 1 (FREEDOMS) was a 2-year randomized, double-blind, placebo-controlled study in 1,272 patients with RRMS who had not received any interferon-beta or glatiramer acetate for at least the previous 3 months and had not received any natalizumab for at least the previous 6 months. Study 2 (TRANSFORMS) was a 1-year randomized, double-blind, double-dummy, active-controlled study in 1,292 patients with RRMS who had not received any natalizumab in the previous 6 months. Patients were randomized to receive Gilenya or intramuscular interferon beta-1a (IFNβ-1a IM). Prior therapy with interferon-beta or glatiramer acetate up to the time of randomization was permitted. The following provides a brief summary of the randomized double-blind studies for Gilenya:

- *Gilenya significantly reduced the frequency of relapses compared with placebo and in a head-to-head clinical trial vs IFNβ-1a IM.*
  - In FREEDOMS, the annualized relapse rate (ARR) was significantly lower in patients treated with Gilenya 0.5 mg than in patients who received placebo (0.18 vs 0.40; *P*<0.001). There was a significantly higher percentage of Gilenya-treated patients without relapse over 24 months compared to placebo (70% vs 46%; *P*<0.001).
  - In TRANSFORMS, the ARR was significantly lower in patients treated with Gilenya 0.5 mg than in patients who received IFNβ-1a IM (0.16 vs 0.33; *P*<0.001). The proportion of patients who were relapse-free vs IFNβ-1a IM (83% vs 70%, respectively; *P*<0.001).
- *Gilenya delayed the accumulation of physical disability in patients with relapsing forms of MS.*
  - In FREEDOMS, Gilenya 0.5 mg significantly delayed the time to onset of 3-month confirmed disability progression compared with placebo (hazard ratio [HR] 0.70; 95% confidence interval [CI]: 0.52, 0.96; *P*=0.02).
  - In TRANSFORMS, there was no significant difference in the time to 3-month confirmed disability progression between Gilenya and IFNβ-1a IM-treated patients at 1 year (*P*=0.21).
- *Gilenya improved magnetic resonance imaging (MRI) measures in patients with relapsing forms of MS.*
  - In FREEDOMS, Gilenya 0.5 mg significantly reduced the mean number of new or newly enlarging T2 lesions compared with placebo over 24 months (2.5 vs 9.8), as well as the mean number of T1 Gd-enhancing lesions at 24 months (0.2 vs 1.1) (*P*<0.001 for each).
  - In TRANSFORMS, Gilenya 0.5 mg significantly reduced the mean number of new or newly enlarging T2 lesions compared with IFNβ-1a IM over 12 months (1.6 vs 2.6; *P*=0.002), as well as the mean number of T1 Gd-enhancing lesions at 12 months (0.2 vs 0.5; *P*<0.001).

Pooled results of study 1 and study 2 showed a consistent and statistically significant reduction of annualized relapse rate compared to comparator in subgroups defined by gender, age, prior MS therapy, and disease activity.

Adverse Event Profile

The most frequent adverse reactions (incidence ≥10% and >placebo) for Gilenya 0.5 mg were headache, influenza, diarrhea, back pain, liver enzyme elevations, and cough. The only adverse event leading to treatment interruption reported at an incidence >1% for Gilenya 0.5 mg was serum transaminase elevations (3.8%).

Contraindications

- Patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III/IV heart failure

- History or presence of Mobitz Type II 2nd degree or 3rd degree atrioventricular (AV) block or sick sinus syndrome, unless patient has a functioning pacemaker
- Baseline QTc interval ≥500 msec
- Treatment with Class Ia or Class III anti-arrhythmic drugs

Questions and Answers
Q: Do any Medicaid plans not require PA?
A: 18 states currently do not require PA for prior therapy due to TRANSFORM data, Novartis monitors and reports safety, improved efficacy and patient preference for oral medications. Gilenya is the first oral MS medication that will go generic.

X. Novo Nordisk

Leonard G Bennett, Jr, PharmD, Medical Liaison
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Norditropin® (somatropin [rDNA origin] injection)
Pronunciation: Norditropin® (somatropin [rDNA origin] injection) - (Nor-dee-tro-pin)

Norditropin® (somatropin [rDNA origin] injection) is a polypeptide hormone of recombinant DNA origin which is identical to the naturally occurring pituitary human growth hormone (GH). Norditropin® is indicated for:
Pediatric patients:
- the treatment of children with growth failure due growth hormone deficiency (GHD)
- the treatment of children with short stature associated with Noonan syndrome, Turner syndrome or short stature born small for gestational age (SGA) with no catch-up growth by age 2-4 years

Adult patients:
- the replacement of endogenous GH in adults with GHD who meet either of the following two criteria:
  - Adult Onset: Patients who have GHD, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or
  - Childhood Onset: Patients who were GH deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes

Patients who were treated with somatropin for GHD in childhood and whose epiphyses are closed should be reevaluated before continuation of somatropin therapy at the reduced dose level recommended for GHD adults. According to current standards, confirmation of the diagnosis of adult GHD in both groups involves an appropriate GH provocative test with two exceptions: (1) patients with multiple other pituitary hormone deficiencies due to organic disease; and (2) patients with congenital/genetic GHD.

Early Growth Hormone Initiation
- Changes in height standard deviation score (HSDS) per mean growth hormone (GH) dose over 4 years of GH treatment in pediatric patients with growth hormone deficiency (GHD), idiopathic short stature (ISS), and children born small for gestation age (SGA) relative to age at treatment start were assessed.
  - Patients with GHD and ISS showed significantly greater height gains (measured by change in HSDS and change in HSDS per dose of GH) over 4 years when treatment was initiated between 2 to 5 years of age compared to older age groups.

Device Features
- A closed-design, web-based questionnaire investigated device-specific features including most preferred features of GH injection devices and GH administration by evaluating the parents' willingness to pay.
  - Device features associated with ease of use, such as 'no mixing required' and 'room temperature stable', ranked higher compared to the lowest ranked feature, electronic versus manual operation.
- Norditropin® FlexPro® and NordiFlex® pens are pre-filled disposable devices which require no mixing. Stability data supports storage out of refrigeration (up to 77°F) after first use for up to three weeks.

Product Wastage

- A study investigated differences in GH wastage arising from dose increment size in four GH administration devices: NordiFlex®, NordiPen®, FlexPro® and MiniQuick® (Pfizer, Inc., New York, NY) using a simulation model to project GH dosing in pediatric patients with growth hormone deficiency, small for gestational age or Turner syndrome. This was done by calculating the nearest dose above the target dose administrable by each device and projecting the excess dose (GH wastage) over 1 year of typical use.
  - The device with the smallest dosing increment (FlexPro® 5 mg; 0.025 mg dosing increment) was projected to administer doses < 1% above the target across all indications. MiniQuick® (0.2 mg dosing increment) was projected to deliver between 5 and 6% above the target dose.
  - Sensitivity analyses were conducted and none changed the conclusion that larger dosing increments result in more GH wastage.

Questions and Answers
There were no additional questions and answers.

Victoza® (liraglutide)
Pronunciation: Victoza® (liraglutide [rDNA origin] injection) (VIC-tow-za; LIR-a-GLOO-tide)

Victoza® (liraglutide [rDNA origin] injection) is a once-daily human glucagon-like peptide-1 (GLP-1) analog indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Summary of Key Clinical Studies
- A 26-week, randomized, open-label, parallel-group study compared Victoza® 1.8 mg once-daily and exenatide ER 2 mg once-weekly in adult with type 2 diabetes treated with lifestyle modifications plus metformin, sulfonylurea (SU), and/or pioglitazone.

Table 1		Victoza® 1.8 mg	Exenatide ER 2 mg
EFFICACY			
N		450	461
A1C (%)	**Baseline**	8.4	8.5
	Week 26	6.9	7.2
Treatment difference, A1C		Treatment difference: 0·21 (95% CI 0·08–0·33) Non-inferiority was not met[a]	
A1C<7% (Week 26)		60	53
FPG Reduction (mg/dL)		-38.2	-31.7
Weight (lb)	**Baseline**	200.4	200.0
	Week 26	192.5	194.1
SAFETY			
Nausea (%)		21	9
Diarrhea (%)		13	6
Vomiting (%)		11	4
Injection site nodule (%)		1	10

[a]Non-inferiority criteria of exenatide ER were not met because the upper bound of the 95% confidence interval for the treatment difference exceeded the pre-specified non-inferiority margin of 0.25%.

- A 32-week, randomized, open-label, parallel-group study compared albiglutide 50 mg once weekly to Victoza® 1.8 mg once daily, in combination with metformin, thiazolidinediones, SU, or any combination of these.

Table 2		Victoza® 1.8 mg	Albiglutide
EFFICACY			
N		403	402
A1C (%)	**Baseline**	8.2	8.2
	Week 32	7.2	7.4
Treatment difference, A1C		Treatment difference: 0.21 (95% CI 0.08-0.34) Non-inferiority was not met[a]	
A1C<7% (Week 32)		52	42
FPG Reduction (mg/dL)		30.2	22
Weight (lb)	**Baseline**	204.2	201.7
	Week 32	199.4	200.3
SAFETY			

N	408	404
Injection site reaction (%)	5.4	12.9
Gastrointestinal events (%)	49	35.9

[a]Non-inferiority criteria of albiglutide were not met because the upper bound of the 95% confidence interval for the treatment difference exceeded the pre-specified non-inferiority margin of 0.3%.

- A 26-week, randomized, open-label, parallel-group study compared dulaglutide 1.5 mg once weekly to Victoza® 1.8 mg once daily, in combination with metformin.

Table 3		**Victoza® 1.8 mg**	**Dulaglutide**
EFFICACY			
N		300	299
A1C (%)	**Baseline**	8.1	8.1
	Week 26	6.7	6.7
Treatment difference, A1C		Treatment difference: 0.06% (95% CI –0.19 to 0.07) *P*<.0001 for non-inferiority of dulaglutide vs Victoza®	
A1C<7% (Week 26)		68	68
FSG Reduction (mg/dL)		34.2	34.7
Weight (lb)	**Baseline**	207.7	206.4
	Week 26	199.8	200.0
SAFETY			
Gastrointestinal disorders (%)		36	36
Total hypoglycemia (%)[a]		6	9

[a]Plasma glucose concentration ≤70.2 mg/dL with or without symptoms.

Questions and Answers
There were no additional questions and answers.

XI. Amgen

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Enbrel® (etanercept)
Pronunciation: Enbrel® (en-brel) (etanercept)

Primary Objectives
- Investigate efficacy of ETN + MTX in inducing and maintaining clinical remission in adults with early moderate-to-severe RA
- Investigate impact of treatment reduction or withdrawal on outcomes

Methods
- 3-period, multicenter, induction/maintenance / withdrawal study

− Phase 1: 52-week open-label induction phase in which all eligible patients received ETN 50 mg QW + MTX
− Phase 2: 39-week double-blind, randomized phase for patients who had prolonged response (DAS28 ≤ 3.2 at week 39 and DAS28 < 2.6 at week 52) during open-label phase
− Phase 3: 26-week drug withdrawal and observation phase for patients who were responders at week 39 of double-blind phase

- Inclusion criteria: Early RA (onset of symptoms within 12 months of enrollment); moderate-to-severe disease activity (DAS ESR > 3.2); paid employment or unpaid but measurable work; no prior exposure to MTX or biologics. Patients who had received other DMARDS were permitted to participate after specified washout periods.

Results – Phase I
- At week 52, 70% of patients achieved DAS28 remission, 51% achieved ACR/ EULAR Boolean remission, and 67% achieved a normal HAQ score.

Results – Phase II
- Primary endpoint: A significantly higher proportion of patients achieved sustained remission (DAS28 < 2.6 at weeks 24 and 39 and no corticosteroids between weeks 0 and 12 of phase 2) in the ETN 25 mg QW + MTX group (63%) than in the MTX-only group (40%; P < 0.001) and the PBO group (23%; P = 0.009)

- The proportion of patients in DAS28 and ACR/EULAR Boolean remission and DAS28 LDA declined more slowly between weeks 0 and 39 of phase 2 in the ETN 25 mg + MTX group than in the MTX-only and PBO groups
- Differences in the proportion of patients achieving DAS28 remission and LDA were significant between the ETN 25 mg + MTX group and the MTX-only and PBO groups from weeks 12 to 39
- Differences in the proportion of patients achieving ACR/EULAR Boolean remission and normal HAQ score, were significant between the ETN 25 mg + MTX group and PBO groups at the same time points. Similar results were seen for ACR20/50/70/90 responses in the ETN 25 mg + MTX group than those in the MTX-only and PBO groups at weeks 12, 24, and 39 of phase 2
- There was no significant radiographic progression in any treatment group during phase 2 and no difference between groups
- SAEs were reported by 5%, 3%, and 3% of patients in the ETN 25 mg + MTX, MTX only, and PBO groups, respectively

Results – Phase 3

- Significantly higher proportions of patients in the ETN 25 mg + MTX group were in DAS28 and ACR/EULAR Boolean remission and had normal HAQ scores compared to those in the PBO group (double-blind phase mITT population)
- The difference between the ETN 25 mg + MTX and MTX-only groups was no longer significant for DAS28 remission or normal HAQ at week 65 but remained significant for ACR/EULAR Boolean remission
- Patients in the ETN 25 mg + MTX group maintained remission significantly longer than did patients in the MTX-only and PBO groups ($P < 0.039$ and $P < 0.0001$, respectively)
- Mean DAS28 scores in the ETN 25 mg + MTX group remained significantly lower than those in the PBO group at weeks 52 and 65 ($P < 0.01$)
- SAEs were reported by 0%, 0%, and 6% of patients in the ETN 25 mg + MTX, MTX-only, and PBO groups, respectively

Questions and Answers

There were no additional questions and answers.

XII. Astellas

J. Darryl Harrison, Access & Reimbursement Manager
Rick Lunsford, Regional Sales Manager

Myrbetriq® (mirabegron)

Pronunciation: Myrbetriq® (mirabegron) extended-release tablets (mir-BET-rik)(mir-a-BEG-ron)

Indications & Administration

• Myrbetriq is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.
• The recommended starting dose is 25 mg once daily with or without food. Myrbetriq 25 mg is effective within 8 weeks. Based on individual patient efficacy and tolerability the dose may be increased to 50 mg once daily.

Mechanism of Action

• Mirabegron relaxes the detrusor muscle during the storage phase of the urinary bladder fill-void cycle by activation of beta-3 adrenergic receptor which increases bladder capacity.

Efficacy Profile

• Myrbetriq was evaluated in three, 12-week, double-blind, randomized, placebo-controlled, parallel group, multicenter clinical trials and one long-term safety study in patients with OAB with symptoms of urge urinary incontinence, urgency, and urinary frequency.
• The 25 mg and 50 mg doses of Myrbetriq each showed statistically significant improvements versus placebo in both coprimary efficacy endpoints of change from baseline to end of treatment (Week 12) in mean number of incontinence episodes and mean number of micturitions per 24 hours. Efficacy was maintained through the 12-week treatment period.

Safety Profile

• Myrbetriq can increase blood pressure (BP). Periodic BP determinations are recommended, especially in hypertensive patients. Myrbetriq is not recommended for use in severe uncontrolled hypertensive patients (defined as systolic BP≥180mm Hg and/or diastolic BP≥110mm Hg).
• Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients also taking Myrbetriq. Administer with caution in patients with BOO and in patients taking antimuscarinic drugs for OAB because of risk of urinary retention.
• Myrbetriq is a moderate inhibitor of CYP2D6. Appropriate monitoring is recommended and dose adjustment may be necessary for narrow therapeutic index CYP2D6 substrates.
• The most commonly reported adverse reactions (>2% and >placebo) for Myrbetriq 25 mg and 50 mg vs placebo, were hypertension, nasopharyngitis, urinary tract infection and headache.

Important Safety Information
Myrbetriq can increase blood pressure. Periodic blood pressure determinations are recommended, especially in hypertensive patients. Myrbetriq is not recommended for use in severe uncontrolled hypertensive patients (defined as systolic blood pressure ≥180mm Hg and/or diastolic blood pressure ≥110mm Hg). Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in Myrbetriq patients; however, Myrbetriq should be administered with caution to patients with clinically significant BOO. Myrbetriq should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB. Since Myrbetriq is a moderate CYP2D6 inhibitor, the systemic exposure to CYP2D6 substrates such as metoprolol and desipramine is increased when co-administered with Myrbetriq. Therefore, appropriate monitoring and dose adjustment may be necessary, especially with narrow therapeutic index drugs metabolized by CYP2D6, such as thioridazine, flecainide, and propafenone. Most commonly reported adverse reactions (>2% and >placebo) for Myrbetriq 25 mg and 50 mg vs placebo, respectively, were hypertension (11.3%, 7.5% vs 7.6%), nasopharyngitis (3.5%, 3.9% vs 2.5%), urinary tract infection (4.2%, 2.9% vs 1.8%), and headache (2.1%, 3.2% vs 3.0%).

Questions and Answers
Q: What are considered the key points?
A: Not an anticholinergic so can also use in patients who cannot tolerate anticholinergics, robust safety and efficacy data and predictable results.

Vesicare® (solifenacin succinate)
Pronunciation: (VES-ih-care), (sol-ee-FEN-a-sin)

Indication & Administration
• VESIcare tablets are indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.
• The recommended dose of VESIcare is 5 mg once daily. The dose may be increased to 10 mg once daily.

Efficacy Profile
• VESIcare was evaluated in four, 12 week, double blind randomized controlled trials for the treatment of OAB in patients having symptoms of urinary frequency, urgency and/or urge or mixed incontinence (predominance of urge).
• The primary endpoint in all four trials was mean change from baseline to 12 weeks in number of micturitions/24 hours. Secondary endpoints included mean change from baseline to 12 weeks in number of incontinence episodes/24 hours.
• Mean reduction in the number of micturitions per 24 hours was significantly greater with VESIcare 5 mg (2.3; $p<0.001$) and VESIcare 10 mg (2.7; $p<0.001$) compared to placebo, (1.4). Mean reduction in number of incontinence episodes per 24 hours was significantly greater with VESIcare 5 mg (1.5; $p<0.001$) and VESIcare 10 mg (1.8; $p<0.001$) groups compared to placebo (1.1).

Safety Profile
• VESIcare is contraindicated in patients with urinary retention, gastric retention, uncontrolled narrow-angle glaucoma, and in patients with hypersensitivity to the product.
• Reports of angioedema of the face, lips, tongue and/or larynx, in some cases occurring after the first dose or multiple doses, have been described. Anaphylactic reactions have been reported rarely. Angioedema associated with upper airway swelling may be life threatening.

• Use with caution in patients with clinically significant bladder outflow obstruction, decreased gastrointestinal motility, narrow-angle glaucoma, reduced renal or hepatic functions and a known history of QT prolongation or patients who are taking medications known to prolong the QT interval or potent CYP3A4 inhibitors.
• CNS effects have been reported with VESIcare use, including headache, confusion, hallucinations and somnolence.
• The most common adverse events reported were dry mouth, constipation, blurred vision, and urinary tract infection.

Important Safety Information
VESIcare is contraindicated in patients with urinary retention, gastric retention, uncontrolled narrow-angle glaucoma, and in patients with hypersensitivity to the product.

Angioedema of the face, lips, tongue and/or larynx have been reported with VESIcare. Cases of angioedema have been reported to occur hours after the first dose or after multiple doses. Angioedema associated with upper airway swelling may be life threatening. If involvement of the tongue, hypopharynx, or larynx occurs, VESIcare should be promptly discontinued and appropriate therapy and/or measures necessary to ensure a patent airway should be promptly provided. Anaphylactic reactions have been reported rarely in patients treated with VESIcare. VESIcare should not be used in patients with a known or suspected hypersensitivity to solifenacin succinate. In patients who develop anaphylactic reactions, VESIcare should be discontinued and appropriate therapy and/or measures should be taken.

VESIcare should be administered with caution to patients with clinically significant bladder outflow obstruction, decreased gastrointestinal motility, controlled narrow-angle glaucoma, or reduced renal or hepatic function. Doses of VESIcare higher than 5 mg are not recommended in patients with severe renal impairment, moderate hepatic impairment, or when administered with ketoconazole or other potent CYP3A4 inhibitors. Use of VESIcare in patients with severe hepatic impairment is not recommended.

Anticholinergic central nervous system (CNS) effects have been reported with VESIcare use, including headache, confusion, hallucinations and somnolence. Patients should be monitored for signs of anticholinergic CNS effects, particularly after beginning treatment or increasing dose, and be advised not to drive or operate heavy machinery until they know how VESIcare affects them. If a patient experiences these effects, dose reduction or drug discontinuation should be considered.

In placebo-controlled studies, for the 10-mg dose, three intestinal serious adverse events were reported (one fecal impaction, one colonic obstruction, and one intestinal obstruction). For the 5-mg dose, one serious adverse event (angioneurotic edema) was reported.

In placebo-controlled studies, the most common adverse reactions reported by patients were dry mouth (10.9%, 27.6%, 4.2%), constipation (5.4%, 13.4%, 2.9%), blurred vision (3.8%, 4.8%, 1.8%), and urinary tract infection (2.8%, 4.8%, 2.8%) with VESIcare 5 mg, 10 mg, and placebo, respectively.

Questions and Answers
Q: What are considered the key points?
A: Robust safety and efficacy and predictable results.

XIII. Gilead

Sunil Majethia, PharmD, Associate Director, Medical Sciences
Jennifer Harper Davidson, Manager, National Accounts

Harvoni® (ledipasvir/sofosbuvir)
HARVONI is a fixed-dose combination of ledipasvir, a hepatitis C virus (HCV) NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor. Each tablet contains 90 mg of ledipasvir and 400 mg of sofosbuvir. HARVONI is indicated for the treatment of chronic hepatitis C (CHC) genotype 1 infection in adults and the recommended dose is one tablet taken, as a complete regimen, orally once daily with or without food.

Sofosbuvir as a single agent (brand name Sovaldi®) was approved in December 2013 for the treatment of HCV genotype 1, 2, 3, or 4 infection as a component of a combination antiviral treatment regimen. Since approval, sofosbuvir-based regimens have been prescribed for more than 100,000 patients in the U.S. and Europe.2 HCV-TARGET and TRIO are ongoing studies characterizing the use of direct-acting agents across a broad spectrum of

clinical practices in North America and Europe. Real world data generated from these studies are consistent with the sofosbuvir-based clinical trial data, with similar SVR rates and discontinuations due to adverse events.

HARVONI is the only interferon-free, ribavirin-free, protease inhibitor (PI)-free, and ritonavir-free all oral complete daily regimen in a single tablet, also known as a single tablet regimen (STR). HARVONI offers a shorter duration of treatment in certain treatment-naïve, GT 1 patients without cirrhosis and is the only regimen that has evaluated patients who have failed prior treatment with either peginterferon alfa + ribavirin (PegIFN + RBV) or an HCV PI + PegIFN + RBV regimen.

Simplified Dosing Regimen: The recommended dose of HARVONI is one tablet taken once-daily with or without food with treatment duration determined by host and viral factors.

Table 1. Recommended Treatment Duration for HARVONI in Patients with CHC Genotype 1

Patient Population	Treatment Duration
Treatment-naïve with or without cirrhosis	12 weeks*
Treatment-experienced** without cirrhosis	12 weeks
Treatment-experienced** with cirrhosis	24 weeks

*HARVONI for 8 weeks can be considered in treatment-naïve patients without cirrhosis who have pre-treatment HCV RNA less than 6 million IU/mL.
**Treatment-experienced patients who have failed treatment with either PegIFN + RBV or an HCV PI + PegIFN + RBV.

Potent Efficacy with High SVR Rates

Table 2 presents the SVR results from each of the key clinical studies with HARVONI. SVR rates were consistent across age (18 – 80 years), race and BMI (18 – 56 kg/m2).

Table 2. HARVONI Key Studies in Subjects with CHC Genotype 1: SVR Results within FDA-Approved Dosing Regimens

Patient Population	Treatment Duration	SVR	Relapse Rate	Clinical Trial Source
Treatment-naïve without cirrhosis who have baseline HCV RNA <6 million IU/mL	8 weeks	97% (119/123)	2%	ION 3
Treatment-naïve without cirrhosis	12 weeks	96 (208/216) & 99% (176/177)	<1%	ION 3 & 1
Treatment-naïve with cirrhosis	12 weeks	94% (32/34)	<1%	ION 1
Treatment-experienced without cirrhosis	12 weeks	95% (83/87)	5%	ION 2
PegIFN + RBV treatment-experienced with cirrhosis	24 weeks	100% (8/8)	0%	ION 2
HCV PI + PegIFN + RBV treatment-experienced with cirrhosis	24 weeks	100% (14/14)	0%	ION 2

SVR rates based on pre-specified subgroups were evaluated: race (Black or non-Black), baseline BMI (< or ≥ 30 kg/m2), sex (male or female), baseline HCV RNA level (< or ≥ 800,000 IU/mL), *IL28B* status (CC or non-CC), response to prior therapy (relapse/breakthrough or non-responder), and prior HCV therapy (HCV PI + PegIFN + RBV or PegIFN + RBV); all achieved similar SVR rates to the overall treatment groups.

Low Discontinuation Rates

Across the HARVONI phase 3 studies, there were low rates of treatment discontinuations due to adverse events: 0%, <1% and 1% for subjects receiving 8, 12 or 24 weeks.

High Barrier to Resistance

No resistance to sofosbuvir emerged in subjects who failed treatment with HARVONI in the ION trials. The sofosbuvir-associated resistance substitution *S282T* was not detected in Phase 3 trials. In a pooled analysis of subjects who received HARVONI in phase 3 trials, 37 subjects qualified for resistance analysis due to virologic failure; 23/37 subjects had virus with emergent NS5A resistance-associated substitutions at virologic failure. The fixed-dose combination of ledipasvir and sofosbuvir provides potent antiviral activity and each agent is fully active against the other agent's resistance-associated substitutions. Both ledipasvir and sofosbuvir are active against substitutions

associated with resistance to other classes of DAAs with different mechanisms of action, such as NS5B non-nucleoside inhibitors and NS3 PIs.

Questions and Answers
Q: Do patients need to have compensated disease?
A: SOLAR-1 demonstrated efficacy in decompensated patients.

Q: Is there still a need to periodically check HCV levels?
A: By Week 4, level should be undetectable so no need to check levels to dose longer.

XIV. Zylera

Kim Hagan, Territory Manager
Matt Phillips, President

Millipred® (prednisolone sodium phosphate oral solution)

Corticosteroids are naturally occurring hormones, produced by the adrenal glands. One category of corticosteroids is glucocorticoids. Glucocorticoids impact a variety of metabolic pathways, including protein metabolism, gluconeogenesis, lipolysis, glycogenesis and may also exhibit some mineralocorticoid effects.

Since glucocorticoids produce anti-inflammatory and immunosuppressive effects, these products are commonly used to treat a wide variety of conditions. According to the PI, indications include Allergic States, Dermatologic Diseases, Edematous States, Endocrine Disorders, Gastrointestinal Diseases, Hematologic Disorders, Neoplastic Diseases, Nervous System, Ophthalmic Diseases, Respiratory Diseases, Rheumatic Disorders and Miscellaneous (Tuberculous meningitis with subarachnoid block or impending block, tuberculosis with enlarged mediastinal lymph nodes causing respiratory difficulty, and tuberculosis with pleural or pericardial effusion (appropriate antituberculous chemotherapy must be used concurrently when treating any tuberculosis complications); trichinosis with neurologic or myocardial).

Millipred® (Prednisolone Sodium Phosphate Oral Solution) (10 mg Prednisolone per 5 mL) is an intermediate-acting (12-36 hour biological half-life) glucocorticoid and is equivalent to prednisolone. Millipred is the lowest concentration prednisolone product on the market. As an active Metabolite of Prednisolone, it offers the advantage of no first pass through effect and only goes through the liver once.

Products in this category are considered to be safe and effective when used properly under strict supervision of a Physician.

Why should Millipred and all oral glucocorticoid products be available for the treatment of approved indications?

1. According to CDC Original Research article; State-Based Medicaid Costs for Pediatric Asthma Emergency Room Visits, Volume 11 – June 26, 2014. “Costs for states for pediatric ED visits vary widely. Effective January 1, 2014, the CMS rules expanded which type of providers can be reimbursed for providing preventative services to Medicaid/CHIP beneficiaries…The rule change may help states reduce Medicaid costs of asthma treatment and the severity of pediatric asthma. Specifically, the research indicates that based on 2011 actual Medicaid data, Georgia covers 132,194 children with asthma, who accounted for an estimated 24,001 ED visits at a cost of approximately $10,400,000.
2. Based on the Guidelines from the National Asthma Education and Prevention Program established in cooperation with the U.S. Department of Health and Human Services, National Institute of Health, National Heart, Lung and Blood Institute, the 6 Step Approach for Managing Asthma Long term recommends the introduction of an oral corticosteroid on Step 6 of the protocol.
3. The Statistical Brief #169 for H-CUP – Healthcare Cost and Utilization Project, Trends in Pediatric and Adult Hospital Stays for Asthma, 2000 – 2010 for January 2014 finds that “The average cost per asthma-related hospital stay for children remained relatively stable at about $3,600…”, additionally, the finding concluded that “Pediatric and adult patients in the lowest income communities had consistently higher rates of hospital stays for asthma than those in the highest income communities.”
4. Nationally, State Medicaid plans are experiencing approximately 95% generic utilization within this category without managing the class.
5. The New England Journal of Medicine published an article on May 14, 2003 entitled “Mikey Likes It: A Taste Test of Oral Steroid Preparations” in which the authors state “If the prescribed medication is unpalatable, children may not take it, and unfortunately, oral steroids are notoriously vile tasting”.

6. Pediatric Emergency Care, 2006 Jun; 22(6):397-401 – "Vomiting of liquid corticosteroids in children with asthma". Of the 96 patients who received generic prednisolone, 17.7% vomited, compared to 5.4% of the controlled group which received a branded prednisolone.

Overall, it should be concluded that oral glucocorticoid products are acute products that are used primarily in the latest stage of the recommended Asthma Guidelines. With the cost of an ED visit/hospital stay at around $3,600 it should be commonplace to provide patients and the healthcare community with a wide range of tools to effectively treat these compromised patients. A common quote in pediatric medicine is "The most expensive medicine is one which a patient will not take" and this is even more prominent within the oral steroid market where most products are "notoriously vile tasting". We offer a safe, effective and extremely palatable option for patients and healthcare professionals who deserves the option for barrier-free accessibility to these products when necessary and properly prescribed.

Veripred™ 20 (prednisolone sodium phosphate oral solution)

Corticosteroids are naturally occurring hormones, produced by the adrenal glands. One category of corticosteroids is glucocorticoids. Glucocorticoids impact a variety of metabolic pathways, including protein metabolism, gluconeogenesis, lipolysis, glycogenesis and may also exhibit some mineralocorticoid effects.

Since glucocorticoids produce anti-inflammatory and immunosuppressive effects, these products are commonly used to treat a wide variety of conditions. According to the PI, indications include Allergic States, Dermatologic Diseases, Edematous States, Endocrine Disorders, Gastrointestinal Diseases, Hematologic Disorders, Neoplastic Diseases, Nervous System, Ophthalmic Diseases, Respiratory Diseases, Rheumatic Disorders and Miscellaneous (Tuberculous meningitis with subarachnoid block or impending block, tuberculosis with enlarged mediastinal lymph nodes causing respiratory difficulty, and tuberculosis with pleural or pericardial effusion (appropriate antituberculous chemotherapy must be used concurrently when treating any tuberculosis complications); trichinosis with neurologic or myocardial)

Veripred® (Prednisolone Sodium Phosphate Oral Solution) (20 mg Prednisolone per 5 mL) is an intermediate-acting (12-36 hour biological half-life) glucocorticoid and is equivalent to prednisolone. As an active Metabolite of Prednisolone, it offers the advantage of no first pass through effect and only goes through the liver once.

Products in this category are considered to be safe and effective when used properly under strict supervision of a Physician. For full prescribing information, please refer to the Package Insert/Product Information.
Why should Veripred and all oral glucocorticoid products be available for the treatment of approved indications?

1. According to CDC Original Research article; State-Based Medicaid Costs for Pediatric Asthma Emergency Room Visits, Volume 11 – June 26, 2014. "Costs for states for pediatric ED visits vary widely. Effective January 1, 2014, the CMS rules expanded which type of providers can be reimbursed for providing preventative services to Medicaid/CHIP beneficiaries…The rule change may help states reduce Medicaid costs of asthma treatment and the severity of pediatric asthma. Specifically, the research indicates that based on 2011 actual Medicaid data, Georgia covers 132,194 children with asthma, who accounted for an estimated 24,001 ED visits at a cost of approximately $10,400,000.
2. Based on the Guidelines from the National Asthma Education and Prevention Program established in cooperation with the U.S. Department of Health and Human Services, National Institute of Health, National Heart, Lung and Blood Institute, the 6 Step Approach for Managing Asthma Long term recommends the introduction of an oral corticosteroid on Step 6 of the protocol.
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4. Nationally, State Medicaid plans are experiencing approximately 95% generic utilization within this category without managing the class.
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Overall, it should be concluded that oral glucocorticoid products are acute products that are used primarily in the latest stage of the recommended Asthma Guidelines. With the cost of an ED visit/hospital stay at around $3,600 it should be commonplace to provide patients and the healthcare community with a wide range of tools to effectively treat these compromised patients. A common quote in pediatric medicine is "The most expensive medicine is one which a patient will not take" and this is even more prominent within the oral steroid market where most products are "notoriously vile tasting". We offer a safe, effective and extremely palatable option for patients and healthcare professionals who deserves the option for barrier-free accessibility to these products when necessary and properly prescribed.

Questions and Answers
Q: What are considered the advantages of Millipred or Veripred?
A: Only products with masked taste to improve compliance and only products that are alcohol-free except for Flo-Pred. FlavRx does not mask the taste of generic prednisolone liquids.

Q: Are there studies demonstrating improved outcomes due to improved compliance as a result of better taste?
A: Not yet but working with CMS to look at data to determine if patients on Millipred and Veripred have lower hospitalization rates and improved outcomes than generic products.

XV. Biogen

Debbie Kennedy, PharmD, National Medical Outcomes Science Liaison
Glenn G. Tropf, Regional Account Manager

Plegridy™ (peginterferon beta-1a)
Multiple sclerosis (MS) is a progressive, debilitating disease that affects the CNS. It typically strikes young adults in their 30s, primarily women. PLEGRIDY was approved in August 2014, as the first pegylated beta-1a interferon with a prolonged half-life for the treatment of patients with relapsing forms of MS1. It currently has an overall exposure equivalent to 1932 person-years, and a total of 1093 patients have received at least 1 year of treatment (125 µg every 14 days and 125 µg every 28 days during the placebo controlled portion of study) and 415 patients have received at least 2 years of treatment with PLEGRIDY (only 125 µg every 14 days).

PLEGRIDY is provided as both a single-use prefilled syringe and as a single-use autoinjector, (PLEGRIDY PEN); both have pre-attached, 0.5 inch, 29 gauge needles.

- PLEGRIDY is dosed subcutaneously (SQ), every 14 days.
- Patients should be advised to rotate sites for SQ injections: abdomen, back of upper arm, and thighs.
- Each titration dose and maintenance dose is color coded to assist patients in administering the correct dose on the correct day, (63 µg Orange, 94 µg Blue; 125 µg Grey).
- The starting dose is 63 µg on day 1; Dose 2 is 94 µg on day 15; Dose 3 is 125 µg on day 29 and every 14 days thereafter as maintenance. Each dose consists of 0.5 mL of solution.
- PLEGRIDY should be stored in refrigerator between 2°C to 8°C. Do not freeze. Prior to injection, PLEGRIDY should be allowed to warm to room temperature (30 minutes) naturally. Protect from light until ready to inject.
- If refrigeration is unavailable, PLEGRIDY, may be stored between 2°C to 25°C for a period up to 30 days, protected from light.
- Once PLEGRIDY is administered, the empty prefilled syringe or PLEGRIDY PEN should be disposed of in a sharps-bin container or other hard plastic or metal container, and disposed of by following local regulations.

The mechanism by which PLEGRIDY exerts is therapeutic effect in multiple sclerosis is unknown.

The efficacy of PLEGRIDY was established in a Phase III, 2 year, multicenter, randomized, double-blind, placebo controlled (for the first year), trial with over 1500 relapsing remitting multiple sclerosis subjects2. The study was designed to evaluate the safety and efficacy of peginterferon beta-1a (125 µg given subcutaneously once every 2 or every 4 weeks) compared to placebo2. Study 1 (ADVANCE, Year 1 placebo controlled data) was published in Lancet Neurology May 2014; and Study 2 (ATTAIN), a long term safety study, is on-going. The approved dose is 125 µg administered once every 14 days.

- Treatment with PLEGRIDY significantly decreased the annualized relapse rate (ARR), (total relapses/total time on trial) with a relative reduction of 36% vs. placebo in ADVANCE (primary endpoint; p=0.0007, at one year).
- A significant reduction in proportion of patients relapsed (patients relapsed/total patient in trial) was observed with PLEGRIDY vs. placebo with a relative risk reduction of 39% (secondary endpoint; p=0.0003).

Improvement was also demonstrated on measures of disability and neuroradiologic outcomes relative to placebo.

- In ADVANCE (Study 1), the time to 12-week confirmed disability progression for PLEGRIDY had a statistically significant 38% relative risk reduction (p=0.0383) vs. placebo.
- PLEGRIDY significantly reduced MRI lesions vs. placebo including Gd+ by a relative reduction of 86% (p<0.0001), new or newly enlarging T2 lesions by a relative reduction of 67% (p<0.0001).

PLEGRIDY (every 2 weeks vs. placebo) demonstrated reductions in annualized MS-related hospitalization rate by 44% (p=-0.0148) and a reduction in the annualized rate of MS relapses requiring IV corticosteroid use by 34% (p=0.049).

PLEGRIDY's safety profile is similar to other currently available interferons for the treatment of MS.

In summary PLEGRIDY offers:

- Once every 14 day subcutaneous administration.
- Demonstrated clinical efficacy with statistically significant reductions in annualized relapse rate and proportion of patients relapsing, a statistically significant reduction in the risk of sustained disability progression, and statistically significant effects on MRI endpoints.

Questions and Answers

Q: Are there any potential differences in tolerability with peginterferon beta-1a compared to interferon beta-1a?
A: Less injection site reactions due to every 2 week dosing as well as less neutralizing antibodies with peginterferon beta-1a.

Q: Is Plegridy considered monotherapy only?
A: Yes.

Tecfidera® (dimethyl fumarate)

Multiple sclerosis is a progressive, debilitating disease that afflicts the CNS. MS typically strikes young adults in their 30s, primarily women. TECFIDERA has been available for patients with relapsing forms of MS since March 2013, and has been prescribed to over 100,000 patients worldwide.

The starting dose for TECFIDERA is 120 mg twice a day orally. After seven days, the dose should be increased to the maintenance dose of 240 mg twice a day orally.

The efficacy and safety of TECFIDERA were established in two Phase III, placebo controlled clinical trials of 2-years duration with over 2600 subjects. Study 1 (DEFINE) and Study 2 (CONFIRM) included twice-daily (BID), thrice-daily (TID), and placebo arms. CONFIRM also included an open-label comparator arm of glatiramer acetate 20mg QD. The TID dose showed no additional benefit over the BID dose. In a pre-specified integrated analysis of these 2 clinical trials, BID treatment with TECFIDERA demonstrated:

- 49% reduction in annualized relapse rates and a reduction of 43% in the proportion of patients relapsed
- at two years.
- 32% reduction in the risk of confirmed (12-week) disability progression
- 78% reduction in new/enlarging T2 lesions, 83% reduction in Gd lesions, and a 65% reduction in new T2-hypointense lesions at 2 years.

In the subgroup analysis of the phase III clinical trial data, treatment with TECFIDERA reduced the annualized relapse rate and the proportion of patients relapsed at 2 years compared with placebo in all subgroups analyzed (gender, age, number of relapses in prior year, McDonald Criteria, prior MS treatment, baseline disability score and MRI cohorts). TECFIDERA also reduced the risk of disability progression at two years compared with placebo in most subgroups.

In a post hoc analysis, patients who were newly diagnosed with RRMS (i.e., within one year of entry into DEFINE or CONFIRM and were naïve to treatment with an MS therapy) showed a clinical benefit with treatment of TECFIDERA relative to placebo.

Additional Outcomes:

- Patients treated with TECFIDERA experienced significant improvements in physical health and functioning compared with patients treated with placebo as measured by the SF-36 questionnaire. Overall, results showed that a higher proportion of patients receiving TECFIDERA experienced a clinically relevant (>5-point) improvement in both physical and mental health compared with patients receiving placebo.
- Reductions in the adjusted annualized rate of relapses requiring IV steroids was 48% vs placebo at 2 years
- ($p<0.001$).
- The adjusted annualized rate of MS-related hospitalizations vs placebo was reduced by 34% ($p=0.0146$) at 2 years.

Warnings and Precautions

- Lymphopenia: TECFIDERA may decrease lymphocyte counts. In the MS placebo controlled trials, mean lymphocyte counts decreased by approximately 30% during the first year of treatment with Tecfidera and then plateaued, with mean lymphocyte counts remaining within normal limits. Four weeks after stopping TECFIDERA, mean lymphocyte counts increased but did not return to baseline. A total of 6% of TECFIDERA patients and less than 1% of placebo patients experienced lymphocyte counts < 0.5 × 109/L (lower limit of normal, 0.91 × 109/L). The incidence of infections (60% vs. 58%) and serious infections (2% vs. 2%) was similar in patients treated with TECFIDERA or placebo, respectively. There was no increased incidence of serious infections observed in patients with lymphocyte counts <0.8 x 109/L or 0.5 x 109/L. Before initiating TECFIDERA, a recent complete blood count (CBC) (i.e., within 6 months) should be available. A CBC is recommended annually, and as clinically indicated. Withholding treatment should be considered in patients with serious infections until the infection(s) is resolved. TECFIDERA has not been studied in patients with pre-existing low lymphocyte counts.
- Flushing: TECFIDERA may cause flushing (e.g., warmth, redness, itching, and/or burning sensation). In clinical trials, 40% of TECFIDERA treated patients experienced flushing. Flushing symptoms generally began soon after initiating TECFIDERA and usually improved or resolved over time. In the majority of patients who experienced flushing, it was mild or moderate in severity. Three percent (3%) of patients discontinued TECFIDERA for flushing and <1% had serious flushing symptoms that were not life-threatening but led to hospitalization. Administration of TECFIDERA with food may reduce the incidence of flushing.

Adverse Reactions

- The most common adverse reactions (incidence ≥10% overall and ≥2% vs. placebo) were flushing, abdominal pain, diarrhea, and nausea.
- The incidence of GI events was higher early in the course of treatment (primarily in month 1) and usually decreased over time. In the clinical trials, 4% of Tecfidera patients discontinued study drug due to GI events. Less than 1% of placebo patients discontinued due to GI events. The incidence of serious GI events was 1% in patients treated with TECFIDERA.
- An increased incidence of elevations of hepatic transaminases in patients treated with TECFIDERA was seen primarily during the first six months of treatment, and most patients with elevations had levels <3 times the upper limit of normal (ULN). Elevations of alanine aminotransferase and aspartate aminotransferase to ≥3 times the ULN occurred in a small number of patients treated with both TECFIDERA and placebo and were balanced between groups. There were no elevations in transaminases ≥3 times the ULN with concomitant elevations in total bilirubin >2 times the ULN. Discontinuations due to elevated hepatic transaminases were <1% and were similar in patients treated with TECFIDERA or placebo.
- A transient increase in mean eosinophil counts was seen during the first 2 months of therapy.

Questions and Answers

Q: Is Tecfidera considered monotherapy only?
A: Yes.

Q: What are considered the advantages of Tecfidera?
A: Dosed twice daily, well tolerated over time, flushing and GI events usually subside after initial 30-day treatment period, robust efficacy profile, unique mechanism of action in how the drug confers antiinflammatory benefits and does not result in immunosuppression.

XVI. Celgene

Shelley Baugh, PharmD, Regional Medical Liaison
Bob Bexley, Senior Region Account Manager
Dan Bussert, State Account Region Manager

Otezla™ (apremilast)
Pronunciation: Oh' tez" lu (u pre' mi" last)

Apremilast is an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate (cAMP). PDE4 inhibition results in increased intracellular cAMP levels. Apremilast (Otezla®) is indicated for the treatment of: adult patients with active psoriatic arthritis and adults with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Following a 5-day titration the recommended maintenance dosage is 30 mg twice daily. Apremilast can be administered without regard to meals. The dosage should be reduced to 30 mg once daily in patients with severe renal impairment (creatinine clearance (ClCr) of less than 30 mL per minute estimated by the Cockroft-Gault equation). No dosage adjustment is required in patients with moderate to severe hepatic impairment.

PsA: The safety and efficacy of apremilast was evaluated in 3 multi-center, randomized, double-blind, placebo-controlled trials of similar design with a total of 1493 adults. Subjects were permitted to remain on stable doses of DMARDS and/or low dose oral corticosteroids during the study. The primary endpoint was the percentage of patients achieving American College of Rheumatology (ACR) 20 response at Week 16. Treatment with Apremilast compared with Placebo resulted in statistically significant improvement in ACR 20 response, (range: 32-41%).

PsO: Two multicenter, randomized, double-blind, placebo-controlled trials enrolled a total of 1257 adult subjects with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy. At week 16, treatment with Apremilast compared with Placebo resulted in statistically significant improvement in PASI-75 response (33% compared with 5% in PSOR-1; 28% compared with 5% in PSOR-2).

Select Marked Laboratory Abnormalities

- Individual, markedly abnormal values were infrequent, transient, and returned to baseline or were associated with a concurrent medical condition.
- Myelosuppression was not observed based on routine CBC.
- Laboratory monitoring before or during treatment with apremilast is not required.

Adverse Reactions

- The majority of the most common adverse reactions occurred within the first two weeks of treatment and tended to resolve over time with continued dosing. Diarrhea, headache, and nausea were the most commonly reported adverse reactions. The most common adverse reactions leading to discontinuation for patients taking OTEZLA were nausea, diarrhea, and headache.
- Gastrointestinal AEs (diarrhea, headache, and nausea) were predominantly mild or moderate in severity, presented early, were self-limited and did not recur.

Warnings and Precautions

- Depression: During the placebo controlled period of clinical trials, patients treated with apremilast reported depression or depressed mood.
- Weight Decrease: During the controlled period of the studies, weight decrease was reported in patients treated with apremilast.
- Drug Interactions: Use with strong cytochrome P450 enzyme inducers (e.g. rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended because loss of apremilast efficacy may occur.

Questions and Answers
Q: Are other indications being sought?
A: Use of apremilast is Behcet's, atopic dermatitis, rheumatoid arthritis, ankylosing spondylitis and bowel syndrome is being explored.

XVII. Merck
Jonathan R Jaffe, MD, FACC, Medical Affairs Director
Gelcys Campo, PharmD, Medical Affairs Director
Lisa Bishop, Senior Region Account Executive

Zontivity™ (vorapaxar)

Indication

ZONTIVITY is indicated for the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease (PAD). ZONTIVITY has been shown to reduce the rate of a combined endpoint of cardiovascular death, MI, stroke, and urgent coronary revascularization (UCR).

WARNING: BLEEDING RISK

Do not use ZONTIVITY in patients with a history of stroke, transient ischemic attack (TIA), or intracranial hemorrhage (ICH); or active pathological bleeding (eg, ICH or peptic ulcer). Antiplatelet agents, including ZONTIVITY, increase the risk of bleeding, including ICH and fatal bleeding.

Dosage and Administration

General Dosing Information: Take one tablet of ZONTIVITY 2.08 mg orally once daily, with or without food.
Coadministration with Other Antiplatelet Drugs: There is no experience with use of ZONTIVITY alone as the only administered antiplatelet agent. ZONTIVITY has been studied only as an addition to aspirin and/or clopidogrel. Use ZONTIVITY with aspirin and/or clopidogrel according to their indications or standard of care. There is limited clinical experience with other antiplatelet drugs.

Contraindications

History of Stroke, TIA, or ICH: ZONTIVITY is contraindicated in patients with a history of stroke, TIA, or ICH because of an increased risk of ICH in this population. Discontinue ZONTIVITY in patients who experience a stroke, TIA, or ICH**. Active Pathologic Bleeding:** ZONTIVITY is contraindicated in patients with active pathological bleeding such as ICH or peptic ulcer.

Warnings and Precautions

General Risk of Bleeding: Antiplatelet agents, including ZONTIVITY, increase the risk of bleeding, including ICH and fatal bleeding. ZONTIVITY increases the risk of bleeding in proportion to the patient's underlying bleeding risk. Consider the underlying risk of bleeding before initiating ZONTIVITY. General risk factors for bleeding include older age, low body weight, reduced renal or hepatic function, history of bleeding disorders, and the use of certain concomitant medications (eg, anticoagulants, fibrinolytic therapy, chronic nonsteroidal anti-inflammatory drugs [NSAIDS], selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors) increases the risk of bleeding. Avoid concomitant use of warfarin or other anticoagulants. Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG), or other surgical procedures. Withholding ZONTIVITY for a brief period will not be useful in managing an acute bleeding event because of its long half-life. There is no known treatment to reverse the antiplatelet effect of ZONTIVITY. Significant inhibition of platelet aggregation remains 4 weeks after discontinuation**.**
Strong CYP3A Inhibitors or Inducers: Strong CYP3A inhibitors increase and inducers decrease ZONTIVITY exposure. Avoid concomitant use of ZONTIVITY with strong CYP3A inhibitors or inducers.

Results from TRA 2°P TIMI 50 Trial

Data supporting the benefit of ZONTIVITY are from the pivotal TRA 2°P TIMI 50 (Thrombin Receptor Antagonist in Secondary Prevention of Atherothrombotic Ischemic Events) trial, one of the largest secondary prevention studies of an antiplatelet medicine. In this 26,449 patient, randomized, double-blind, placebo-controlled trial, participants had a history of spontaneous MI within the prior 2 weeks to 12 months, ischemic stroke, or documented (symptomatic) PAD. Patients were followed for up to 4 years, with a median follow-up of 2.5 years. ZONTIVITY, when used daily with standard of care that included aspirin and/or a thienopyridine (principally clopidogrel), was superior to standard of care alone in reducing the incidence of both the primary combined endpoint of CV death, MI, stroke, and UCR and a key secondary composite endpoint of CV death, MI, and stroke. In the overall study population, patients with a history of stroke or TIA showed an increased risk of ICH. Consequently, the approved use of ZONTIVITY is based on the study population with a history of MI or with PAD and without a history of stroke or TIA. Among those patients, 10,080 were randomized to treatment with ZONTIVITY and 10,090 were randomized to treatment with placebo. High-risk patients in this group included patients with diabetes (24 percent) and hypertension (65 percent). In post-MI or PAD patients

without a history of stroke or TIA, the study showed: **Efficacy:** A 17 percent relative risk reduction through 3 years for the composite primary efficacy endpoint of CV death, MI, stroke, and UCR. The composite primary efficacy endpoint occurred in 10.1 percent in the group taking ZONTIVITY compared with 11.8 percent in the placebo group (Hazard Ratio [HR]: 0.83, *P*<0.001). The treatment benefit was persistent over the course of the study and was not dependent on the elapsed time from prior MI to randomization. These results demonstrated the significant benefit of ZONTIVITY when used with aspirin and/or clopidogrel vs patients using aspirin and/or clopidogrel alone. The study also showed a 20 percent relative risk reduction through 3 years for the key secondary composite efficacy endpoint of CV death, MI, and stroke. The findings for the key secondary efficacy endpoint showed an event rate of 7.9 percent in the group taking ZONTIVITY compared with 9.5 percent in the placebo group (HR: 0.80, *P*<0.001). These results for the primary and secondary efficacy composites included an 18 percent relative risk reduction in MI (event rate: 5.4 percent vs 6.4 percent; HR: 0.82, 95 percent Confidence Interval [CI]: 0.73-0.93) and a 33 percent relative risk reduction in first stroke (event rate: 1.2 percent vs 1.6 percent; HR: 0.67, 95 percent CI: 0.52-0.87). **Safety:** Among randomized post-MI or PAD patients without a history of stroke or TIA who were treated with ZONTIVITY (n=10,059) or placebo (n=10,049), adding ZONTIVITY to standard of care (including aspirin and/or a thienopyridine) was associated with an increased rate of GUSTO moderate or severe bleeding through 3 years (3.7 percent) compared to adding placebo (2.4 percent) (HR: 1.55, 95 percent CI: 1.30-1.86). GUSTO severe bleeding occurred at a rate of 1.3 percent for ZONTIVITY vs 1.0 percent for placebo (HR: 1.24, 95 percent CI: 0.92-1.66). ICH was less common in both groups compared to GUSTO moderate and severe bleeding. The 3-year rate of ICH was numerically higher for patients adding ZONTIVITY to standard of care, 0.6 percent, compared to 0.4 percent for patients adding placebo (HR: 1.46; 95 percent CI: 0.92-2.31). Fatal bleeding occurred at a 3-year rate of 0.2 percent in both the group receiving ZONTIVITY and the placebo group, with an HR of 1.15 favoring the placebo group (95 percent CI: 0.56-2.36). Clinically significant bleeding occurred at a 3-year rate of 15.5 percent in the group taking ZONTIVITY, compared with 10.9 percent in the placebo group (HR: 1.47, 95 percent CI: 1.35-1.60).

Additional Selected Safety Information About ZONTIVITY
• ZONTIVITY is not recommended in patients with severe hepatic impairment. Withholding ZONTIVITY for a brief period will not be useful in managing an acute bleeding event because, due to its long half-life, significant inhibition of platelet aggregation remains 4 weeks after discontinuation. There is no known treatment to reverse the antiplatelet effect of ZONTIVITY. Strong CYP3A inhibitors increase and inducers decrease ZONTIVITY exposure. Avoid concomitant use of ZONTIVITY with strong CYP3A inhibitors or inducers.
• Bleeding, including life-threatening and fatal bleeding, is the most commonly reported adverse reaction with ZONTIVITY.

Questions and Answers
Q: Can Zontivity be used as monotherapy?
A: No, should be taken with aspirin or clopidogrel.

Q: Any other studies or indications being conducted?
A: No decisions yet, possibly looking at patients with peripheral artery disease without aspirin or clopidogrel.

XVIII. Supernus

Shannon Medes, PhD, Associate Director, Medical Affairs
Adriana Sanchez, Director of Corporate Accounts

Oxtellar® XR (oxcarbazepine extended-release)
Pronunciation: Oxtellar XR® (ahks-TEH-lahr eks ahr) oxcarbazepine (ox car baz' e peen)

- Oxtellar XR is a novel once-daily extended-release formulation of oxcarbazepine for adjunctive treatment of partial seizures in adults and children 6 to 17 years of age
- Oxcarbazepine immediate-release (Trileptal® OXC-IR) often has limited tolerance and adherence, preventing patients from achieving a maximum therapeutic dose and adequate trial of the antiepileptic drug (AED). Oxtellar XR utilizes Solutrol®, Supernus' novel proprietary extended-release technology, which slows absorption and provides consistent plasma levels over a 24 hour period
- **Health Outcomes Data: Treatment with Oxtellar XR or OXC-IR**
  - In a retrospective chart review of patients treated with Oxtellar XR (n=109) or OXC-IR (n=91) as adjunctive therapy, utilization of Oxtellar XR resulted in:
    - **Lower hospitalization rates (statistically significant)**

        - Lower rate of seizure-related emergency department (ED) visits
        - Two-fold higher rate of adherence
- Pharmacokinetic Data: Oxtellar XR vs OXC-IR:
    - In a steady-state crossover study in healthy volunteers (Oxtellar XR 1200mg daily vs. OXC-IR 1200mg given as 600mg twice daily), overall exposure was similar between the two drugs, however they are not bioequivalent . Oxtellar XR exhibited lower peak to trough fluctuation.
    - **Adverse events (AEs) in this study were lower for Oxtellar XR compared to OXC-IR, at comparable efficacy**
- Phase 3 Pivotal Trial (PROSPER): Oxtellar XR as adjunctive therapy
    - Oxtellar XR: AE frequency was impressively low (vs OXC-IR at comparable doses), while overall efficacy in the trial was robust and well within the range observed with other oxcarbazepine products
    - Efficacy and safety of Oxtellar XR (1200mg or 2400mg) were established in a Phase 3 pivotal trial evaluating 366 patients experiencing ≥ 3 seizures/28 days and receiving 1-3 concomitant AEDs
        - The median percent reductions in seizure frequency, (primary endpoint):
            - 29% (placebo); 38% (Oxtellar XR 1200mg); **43% (Oxtellar XR 2400mg, statistically significant)**
        - Responder rates (50% or more seizure frequency reduction):
            - 28% (placebo); 36% (Oxtellar XR 1200mg); **41% (Oxtellar XR 2400mg, statistically significant)**
        - Seizure free rates:
            - 3% (placebo); 5% (Oxtellar XR 1200mg); **11% (Oxtellar XR 2400mg, statistically significant**, one of the highest rates observed)
    - Efficacy results for the 1200mg dose approached significance; approval of the 1200mg dose by the FDA was reached through: 1) concentration-response Cmin breakpoint analysis (10 mcg/ml) showing 66% of patients receiving 1200mg daily having plasma concentrations above 10 mcg/ml, 2) FDA analysis of the exposure-response of OXC-IR vs. OXC-XR showed similar slopes, 3) North American (NA) cohort analysis
    - In the NA cohort analysis, median percent seizure reductions were:
        - 13% (placebo); **35% (Oxtellar XR 1200mg, statistically significant)**; **53% (Oxtellar XR 2400mg, statistically significant)**
- There are no head-to-head clinical trials comparing Oxtellar XR to OXC-IR. While no direct comparisons can be made:
    - Trial populations were similar and the primary efficacy endpoints in both pivotal trials appear to be similar
    - The tolerability profiles differ:
        - Discontinuations due to AEs in the OXC-IR pivotal trial:
            - 9% (placebo); 36% (1200mg per day/600mg bid); 67% (2400mg per day/1200mg bid)
        - Discontinuations due to AEs in the Oxtellar XR pivotal trial:
            - 8% (placebo); 15% (1200mg daily); 30% (2400mg daily)

SUMMARY

- Oxtellar XR is the first and only FDA-approved, once daily extended-release formulation of oxcarbazepine
- A retrospective outcomes study showed increased adherence and lower rates of hospitalizations and ED visits
- As adjunctive therapy Oxtellar XR 1)reduced seizure frequency 2)improved responder rates 3) demonstrated a high rate of seizure freedom
- Oxtellar XR therapy 1) provides consistent plasma levels over a 24 hr period 2) allows effective use of higher doses of OXC
- **In conclusion**, **we respectfully request the Georgia Medicaid P&T Committee to remove the current PA requirements and consider a PDL Preferred position, with or without an Electronic Step through the generic IR formulation.**

Questions and Answers

There were no additional questions and answers.

Trokendi® XR (topiramate extended-release)

Pronunciation: Trokendi XR® (tro-KEN-dee eks ahr) topiramate (toe pyreˈa mate)

- Trokendi XR is a *once-daily*, *extended-release* formulation of topiramate, approved for the treatment of epilepsy. Trokendi XR uses Microtrol®, Supernus' novel extended-release bead technology which has been the #1 prescribed CNS drug delivery system for the past 10 years.

    - Indicated for initial monotherapy in partial onset or primary generalized tonic-clonic seizures 10 years and older; adjunctive therapy in partial onset or primary generalized tonic-clonic seizures 6 years and older; adjunctive therapy in Lennox-Gastaut Syndrome 6 years and older[1]
    - Microtrol® has been used successfully to improve the delivery profiles of many CNS drugs (e.g., Carbatrol®, Adderall XR®). As a unique delivery system, products that use this technology cannot be substituted
- **Trokendi XR produced significantly fewer cognitive deficits than the immediate-release topiramate (TPM-IR, Topamax®) in a single blind healthy volunteer study[2], as measured by the Controlled Oral Word Association (COWA) test of verbal fluency, which is known to be sensitive to the effects of TPM-IR[3]**
    - In subjects completing both treatment arms of Trokendi XR vs TPM-IR, COWA change scores significantly favored Trokendi XR over the entire treatment period and at the 100mg/day dosage
- Trokendi XR was developed to improve adherence (e.g., taken once daily) and tolerability, thereby positively impacting health and economic outcomes.
- In fact, 93% of patients with epilepsy surveyed in a crossover study preferred Trokendi XR over TPM-IR, and 92% believed once-daily dosing facilitated adherence
- Trokendi XR was approved by the FDA without a Phase 3 trial due to its bioequivalence to the immediate-release form at every time point, along with other data:
    - Pharmacokinetic data proved **bioequivalence** at steady state between once-daily Trokendi XR and twice-daily TPM-IR over 24 hours
    - Drug safety and pharmacokinetic data obtained from patients with epilepsy
    - Safety and efficacy data from studies previously conducted with TPM-IR
    - In consideration of the above, direct safety and efficacy evaluations of Trokendi XR were not required
- While bioequivalent at steady state, Trokendi XR has a markedly slower absorption profile (Tmax of 6 hrs v. 1 hr for TPM-IR). Reduced cognitive effects for Trokendi XR may be related to this slower absorption[2]
- The relatively constant plasma concentrations with Trokendi XR result in a 35% lower peak-to-trough fluctuation compared to TPM-IR (FL: Trokendi XR 26% v. Topamax 40%)
- Bioequivalence allows patients with epilepsy on TPM-IR to be converted overnight to once-daily Trokendi XR on a mg to mg basis when switching from the immediate-release form
    - Switching TPM-IR twice daily to Trokendi XR once daily at identical dosages showed no deterioration of seizure control in a pharmacokinetic study
- Population pharmacokinetic dosing simulations showed that Trokendi XR offers the convenience of once-daily dosing without increasing patient risk from missed, delayed, or doubled doses relative to twice-daily TPM-IR

SUMMARY

- Trokendi XR is the first FDA-approved once-daily extended-release formulation of topiramate for the treatment of epilepsy
- Trokendi XR has a positive profile:
    - Reduces cognitive impairment (COWA test of verbal fluency), one the most common reasons for discontinuing TPM-IR
    - Patients prefer Trokendi XR and believe it will help improve adherence
    - Bioequivalent to twice-daily TPM-IR at every time point throughout the day
    - Has a 35% lower peak-to-trough fluctuation compared to TPM-IR
    - Once-daily dosing with 4 available dosage strengths
- Converting to Trokendi XR from TPM-IR:
    - Proceed with mg-to-mg overnight conversion
- **In conclusion, we respectfully request the Georgia Medicaid P&T Committee to remove the current PA requirements and consider a PDL Preferred position, with or without an Electronic Step through the generic IR formulation.**

Questions and Answers

Q: Were other efficacy tests performed?

A: Digit symbol substitution test was performed and found not to significantly improve over entire course of study.

XIX. Johnson & Johnson

Megan Jones, PharmD, MPA, Principal Liaison, Health Economics & Outcomes Research

J. Leigh Faircloth, Strategic Market Director

Lauren Clayton, Strategic Market Director

Invega Sustenna® (paliperidone palmitate)
Pronunciation: INVEGA SUSTENNA (In-VEY-guh Suss-TEN-uh) paliperidone palmitate **(**pal-ee-PER-i-done PAL-mi-tayt)

Summary of New Clinical Information - Use in Schizoaffective Disorder
INVEGA SUSTENNA (paliperidone palmitate) Extended-Release Injectable Suspension is an atypical antipsychotic indicated for the treatment of schizophrenia and schizoaffective disorder (monotherapy and as an adjunct to mood stabilizers or antidepressants) in adults. Paliperidone is a centrally active dopamine type 2 (D_2)/serotonin type 2 ($5HT_{2A}$) receptor antagonist.

DOSING
• For patients who have never taken oral paliperidone or oral or injectable risperidone, establish tolerability with oral paliperidone or oral risperidone prior to initiating INVEGA SUSTENNA. Each injection must be administered only by a healthcare professional.
• *Initiation Dosing (Schizophrenia and Schizoaffective Disorder)*: Therapy is initiated with a dose of 234 mg on treatment day 1 and 156 mg one week later, both administered in the deltoid muscle to help attain therapeutic concentrations rapidly. Following the second initiation dose, monthly maintenance doses can be administered in either the deltoid or gluteal muscle.
• *Maintenance Dosing (Schizoaffective Disorder)*: There is no recommended monthly maintenance dose for patients with schizoaffective disorder. The dose distribution in the long-term schizoaffective disorder study was 78 mg (4.9%), 117 mg (9.8%), 156 mg (47%), and 234 mg (38.4%). Adjust the dose based on tolerability and/or efficacy using available strengths. The 39-mg strength was not studied in the long-term schizoaffective disorder study.

CLINICAL EFFICACY – SCHIZOAFFECTIVE DISORDER
• In a long-term, double-blind, placebo-controlled, flexible-dose, randomized-withdrawal maintenance study in adults, relapse rates were significantly lower for the paliperidone palmitate versus placebo groups (15.2% [n=25] versus 33.5% [n=57], respectively; $p<0.01$).
• Risk of relapse was 2.49-fold higher for placebo versus paliperidone palmitate (95% CI: 1.55, 3.99; $p<0.001$), corresponding to a 60% decrease in relapse risk with paliperidone palmitate treatment.
• Risk ratio of relapse in favor of paliperidone palmitate did not differ across different types of mood episodes.

CLINICAL SAFETY: Paliperidone palmitate was well tolerated in clinical studies
• The most common (at least 5% in any INVEGA SUSTENNA group) and likely drug-related (adverse events for which the drug rate is at least twice the placebo rate) adverse reactions from the double-blind, placebo-controlled trials in subjects with schizophrenia were injection site reactions, somnolence/sedation, dizziness, akathisia, and extrapyramidal disorder. No occurrences of adverse events reached this threshold in the long-term double-blind, placebo-controlled study in subjects with schizoaffective disorder. In the schizoaffective disorder clinical trial, adverse reactions that occurred more frequently in the INVEGA SUSTENNA than the placebo group (a 2% difference or more between groups) were weight increased, nasopharyngitis, headache, hyperprolactinemia, and pyrexia.

ECONOMIC OUTCOMES
• **Schizoaffective**: During an international, double-blind, randomized-withdrawal study, paliperidone palmitate was associated with significantly lower relapse rates and serious treatment-emergent adverse events resulting in a greater reduction in medical cost versus placebo (-$7,140 per patient).

Questions and Answers
There were no additional questions and answers.

Stelara (ustekinumab)
Pronunciation: STELARA (stel ar' a) ustekinumab (US-te-KIN-ue-mab)

Summary of New Clinical Information – Active Psoriatic
STELARA is indicated for the treatment of adult patients (18 years or older) with active psoriatic arthritis alone or in combination with methotrexate (MTX). STELARA is indicated for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

MECHANISM OF ACTION
STELARA is a human IgG1κ monoclonal antibody that binds with specificity to the p40 protein subunit used by both the **interleukin (IL)-12 and IL-23 cytokines**

CLINICAL EFFICACY DATA IN PSORIATIC ARTHRITIS (McInnes et al, 2013; Ritchlin et al, 2014)
- PSUMMIT I (PHASE 3): A significantly greater proportion of patients who received STELARA 45 mg or 90 mg achieved the primary endpoint of ACR20 at week 24 compared to placebo (42.4% and 49.5% vs 22.8%, respectively; P<0.0001 for both comparisons)
- PSUMMIT II (PHASE 3): STELARA 45 mg or 90 mg administered at weeks 0, 4, and every 12 weeks significantly reduced signs and symptoms of active psoriatic arthritis as measured by ACR 20 response at week 24 (primary endpoint) vs placebo (43.7% and 43.8% vs 20.2%, respectively; P<0.001 for both comparisons)

CLINICAL SAFETY DATA IN PSORIATIC ARTHRITIS
- In **active psoriatic arthritis,** the safety of STELARA was assessed in 927 patients in two randomized, double-blind, placebo-controlled studies. The overall safety profile of STELARA in patients with psoriatic arthritis was consistent with the safety profile seen in psoriasis clinical studies. A higher incidence of arthralgia, nausea, and dental infections was observed in STELARA-treated patients compared with placebo-treated patients (3% vs. 1% for arthralgia and 3% vs. 1% for nausea; 1% vs. 0.6% for dental infections) in the placebo-controlled portions of psoriatic arthritis clinical trials

DOSAGE AND ADMINISTRATION IN PSORIATIC ARTHRITIS
STELARA is administered by subcutaneous injection
- The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks • For patients with co-existent moderate-to-severe plaque psoriasis weighing >100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks

Questions and Answers
Q: Where is the primary location of administration?
A: Primarily in medical setting since only administered every 12 weeks but outpatient pharmacy use is increasing.

Q: Can the subcutaneous injection be administered at home?
A: Yes, generally the first 1-2 injections are in the office for education purposes and not for safety concerns.

Xarelto® (rivaroxaban)
Pronunciation: XARELTO (zah-REL-toe); rivaroxaban (ri-va-rox'-a-ban)

Summary of New Clinical Information
The following sections were updated from August 2013 – January 2015: Boxed Warnings; Warnings & Precautions; Dosage and Administration (Hip and Knee); Adverse Reactions; Drug Interactions; Clinical Pharmacology; Patient Counseling; Medication Guide; How Supplied/Storage and Handling; and Manufactured By.
• Premature discontinuation of any oral anticoagulant, including XARELTO, increases the risk of thrombotic events. To reduce this risk, consider coverage with another anticoagulant if XARELTO is discontinued for a reason other than pathological bleeding or completion of a course of therapy. (Boxed Warning)
• Epidural or spinal hematomas have occurred in patients treated with XARELTO who are receiving neuraxial anesthesia or undergoing spinal puncture. (Boxed Warning)
• Partial reversal of prothrombin time prolongation has been seen after administration of prothrombin complex concentrates (PCCs) in healthy volunteers. (Section 5.2)
• To reduce the potential risk of bleeding associated with the concurrent use of rivaroxaban and epidural or spinal anesthesia/analgesia or spinal puncture, consider the pharmacokinetic profile of rivaroxaban. An epidural catheter should not be removed earlier than 18 hours after the last administration of XARELTO. The next XARELTO dose is not to be administered earlier than 6 hours after the removal of the catheter. If traumatic puncture occurs, the administration of XARELTO is to be delayed for 24 hours. (Section 5.3)
• The safety and efficacy of XARELTO have not been studied in patients with prosthetic heart valves. Therefore, use of XARELTO is not recommended in these patients. (Section 5.8)
• Initiation of XARELTO is not recommended acutely as an alternative to unfractionated heparin in patients with pulmonary embolism who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy. (Section 5.9)

• The following adverse reactions have been identified during post-approval use of rivaroxaban: Blood and lymphatic system disorders: thrombocytopenia; Hepatobiliary disorders: hepatitis (including hepatocellular injury). (Section 6.2)
• XARELTO should not be used in patients with CrCl 15 to 80 mL/min who are receiving concomitant combined P-gp and moderate CYP3A4 inhibitors unless the potential benefit justifies the potential risk. (Section 7.4)

02/03/2014: Management of Major Bleeding Events in Patients Treated with Rivaroxaban Versus Warfarin: Results from the ROCKET AF Trial
An analysis of the safety population within the ROCKET AF trial to determine whether management of bleeding and subsequent outcomes differed between those treated with rivaroxaban versus with those treated with warfarin.
• 5.5% (N=779) of patients experienced major bleeding, with similar event rates in each arm (rivaroxaban, N=395; warfarin, N=384). Transfusion of coagulation factors was rare in both arms and patients were largely managed with supportive measures.
• Packed red blood cells (PRBCs) (rivaroxaban: N=176, warfarin: N=143) and fresh frozen plasma (FFP) (rivaroxaban: N=45, warfarin: N=81) were administered most often for transfusions within 5 days of the major bleed. The most common agents used for pharmacologic management of post-major bleed at 0-24 hours included Vitamin K, prothrombin complex concentrates (PCCs), epsilon-aminocaproic acid, and tranexamic acid.
• Transfusion of FFP was less with rivaroxaban than warfarin. PCCs were administered less frequently in the rivaroxaban arm vs. warfarin. A greater number of major bleeds were transfused with PRBC with rivaroxaban vs. warfarin.
• All-cause death (rivaroxaban: 104 (24.8%), warfarin: 120 (29.9%)); all-cause death (rivaroxaban: 86 (20.4%), warfarin: 105 (26.1%)); and MI/UA (rivaroxaban: 11 (2.6%), warfarin: 7 (1.7%).

08/11/2014: Rivaroxaban versus Vitamin K Antagonists for Cardioversion in Atrial Fibrillation (X-VERT)
A prospective study that compared the efficacy of rivaroxaban (20 mg orally once daily; 15 mg once daily for subjects with CrCl of 30 to 49 mL/min) to dose- adjusted vitamin K antagonist (VKA) for the prevention of cardiovascular events in 1,504 patients with nonvalvular AF scheduled for early or delayed cardioversion.
• The primary efficacy endpoint was composite of stroke, TIA, peripheral embolism, myocardial infarction and cardiovascular death.
• The primary efficacy outcome occurred in 0.51% in the rivaroxaban arm and in 1.02% in the VKA arm [risk ratio 0.50; 95% CI: 0.15–1.73]. In the rivaroxaban arm, 0.71% experienced primary efficacy events following early cardioversion and 0.24% following delayed cardioversion. In the VKA arm, 1.08% had primary efficacy events following early cardioversion and 0.93% following delayed cardioversion. Compared to VKA, rivaroxaban was associated with a significantly shorter time to cardioversion (P<0.001).
• The principal safety outcome was major bleeding. Major bleeding occurred in 0.6% in the rivaroxaban group and 0.8% in the VKA group (risk ratio 0.76; 95% CI 0.21–2.67).

01/14/2015: Characterizing Major Bleeding in Patients With Nonvalvular Atrial Fibrillation: A Pharmacovigilance Study of 27,467 Patients Taking Rivaroxaban
• A post-marketing safety surveillance study to gather safety data of rivaroxaban in patients with non-valvular atrial fibrillation (NVAF).
• 496 major bleed events occurred in 478/27,467 patients with NVAF on rivaroxaban; incidence of 2.86 per 100 person-years.
• The most common site of bleeding was GI (88.8%; n=423/478) and intracranial (7.5%; n=36/478). 14 patients died; fatal bleeding rate of 0.08 per 100 person years.
• Major bleeds were more prevalent in older patients, those with hypertension, coronary heart disease, heart failure, and renal disease, along with greater CHADS2 and CHA2DS2-VASc scores.

Questions and Answers
There were no additional questions and answers.

XX. Salix
Christy Copeland, PharmD, Medical Science Liaison
Brandon Cope, Regional Account Manager

Apriso® (mesalamine) extended-release capsules
Apriso (mesalamine) extended-release capsules, are indicated for the maintenance of remission of ulcerative colitis (UC) in patients 18 years of age and older. Apriso is dosed 1.5g once daily with or without food. Unlike other pH

dependent mesalamines, Apriso provides delayed and extended release delivery which begins releasing mesalamine at a pH ≥ 6, targeting gradual distribution throughout the colon. Other pH dependent mesalamine therapies, such as Delzicol, Asacol HD, or Lialda do not release mesalamine until a pH of 6.8 or higher.

In 2010, Dr. Gary Lichtenstein and colleagues published a pivotal, phase 3 clinical trial evaluating Apriso. This randomized, double-blind, placebo-controlled trial included patients with UC in remission, defined as rectal bleeding score of 0 and mucosal appearance score of 0 or 1 on the revised Sutherland Disease Activity Index (SDAI). A total of 305 patients were randomized 2:1 to Apriso 1.5g once daily or placebo for up to 6 months. The primary efficacy endpoint was the percentage of patients who remained relapse free at month 6 (end of treatment). Relapse was defined as rectal bleeding sub-score of ≥ 1 and mucosal appearance sub-score ≥ 2 on the revised SDAI. For the intent-to-treat analysis, which designated all patients prematurely withdrawing from the study for any reason as relapse, the percent of patients who remained relapse-free was 68% with Apriso and 51% with placebo, which was statistically significant ($p<0.001$). When including only patients who withdrew due to treatment failure (modified intent-to-treat), 78.9% in the Apriso arm and 58.3% in the placebo arm remained relapse-free, a statistically significant difference ($p<0.001$). In a second, similarly designed study, comparable results were concluded.

The incidence of adverse events was similar to placebo in both studies. The most common treatment-emergent adverse events reported in the treatment group (occurring in at least 3% of patients and reported more frequently than placebo) include headache, diarrhea, upper abdominal pain, nausea, nasopharyngitis, influenza-like illness and sinustitis.

In summary, Apriso is the first and only once-daily 5-ASA featuring delayed and extended release delivery that begins releasing mesalamine at a pH ≥ 6. Apriso has proven to maintain remission in pivotal clinical trials over duration of 6 months. Apriso is generally well-tolerated in maintaining remission of patients with UC.

Questions and Answers
There were no additional questions and answers.

Uceris® (budesonide MMX)
Uceris (budesonide) extended release tablets are a glucocorticoid indicated for the induction of remission in patients with active, mild to moderate ulcerative colitis (UC). The recommended dose is one 9mg tablet, taken once daily with or without food for up to 8 weeks. Uceris is a novel formulation of budesonide that uses a Multi-Matrix (MMX) technology designed to target the release of budesonide throughout the entire colon.

The safety and efficacy of UCERIS in patients with active mild to moderate UC was established in 2, phase 3 multicenter, randomized, double-blind, double-dummy, parallel group, 8-week studies. The primary endpoint was remission at 8 weeks, defined as combined clinical and endoscopic remission with a UCDAI score ≤1 point, with subscores of 0 for both rectal bleeding and stool frequency, no mucosal friability on colonoscopy, and a ≥1-point reduction from baseline in the endoscopic index score. In the first study, the percentage of patients achieving remission was 17.9% in the Uceris 9mg group compared with 7.4% in the placebo group ($P=0.0143$). In the second study, the percentage of patients achieving remission was 17.4% in the Uceris 9mg group compared with 4.5% in the placebo group ($P=0.0047$). Treatment with Uceris was generally well-tolerated with an overall safety profile comparable to that of placebo. The most common adverse reactions (incidence ≥ 2%) included headache, nausea, decreased blood cortisol, upper abdominal pain, fatigue, flatulence, abdominal distension, acne, urinary tract infection, arthralgia, and constipation. Glucocorticoid-related side effects occurred in similar percentages of patients across all treatment groups (10.2% with Uceris 9mg compared with 10.5% with placebo).

In Summary, Uceris is a formulation of budesonide which is designed to release the drug throughout the entire colon. Uceris pivotal trials have demonstrated safety and efficacy in inducing remission in patients with active, mild to moderate UC.

Questions and Answers
Q: Is the foam formulation available yet?
A: Delayed to May 2015.

Q: Are any other indications being sought?
A: Not currently.

Q: Are there any long term studies?
A: One patient in clinical studies extended on therapy for 6 months and did not have any issues.

Q: Does therapy need to be separated from PPI therapy?
A: No, not with PPIs, but H2 antagonist therapy should be separated by 2 hours since H2 antagonist therapy is immediate release.

Q: Is a combination therapy indication being sought?
A: Uceris is for acute exacerbations so maintenance with mesalamine will be continued.

XXI. Teva
Contessa Fincher, PhD, Medical Science Liaison
Robert Pearce, National Account Manager

Copaxone® (glatiramer acetate)
Pronunciation: gla-TIR-a-mer AS-e-tate

In 2014 a new formulation was approved, COPAXONE 40 mg/ml three times per week subcutaneous injection. COPAXONE is indicated for the treatment of patients with relapsing forms of multiple sclerosis. Doses are not interchangeable.

• COPAXONE has a unique mechanism of action. COPAXONE induces the generation of anti-inflammatory Th2 cells centrally, which leads to anti-inflammatory and possible neuroprotective effects within the CNS.

• In The GALA study COPAXONE 40 mg/ml three times per week was evaluated in a double-blind, placebo-controlled study with a total of 1404 RRMS patients randomized 2:1 to receive COPAXONE® 40 mg/ml three times per week (n=943) or placebo (n=461) for 12 months. COPAXONE 40 mg/ml three times per week treatment led to 34% fewer relapses than placebo (ARR GA=0.331; placebo=0.505; P<0.0001). COPAXONE 40 mg/ml three times per week treatment reduced the annual rate of severe relapses by 35% (ARR GA=0.301; placebo=0.466; P<0.0001). At 12 months, COPAXONE 40 mg/ml three times per week treatment significantly reduced the cumulative number of new/enlarging T2 lesions (35% reduction; P<0.0001), the cumulative number of gadolinium-enhancing T1 lesions (45% reduction; P<0.0001), and reduced the odds of new active lesions evolving into black holes (24% reduction, P=0.006) compared to placebo.

• The results of the open-label 24 month extension of the GALA study have shown a durability of efficacy, resulting in 31% reduction in annualized relapse rate in patients taking COPAXONE 40 mg/ml three times per week over two years compared to patients taking COPAXONE 40 mg/ml three times per week over the last year (ARR COPAXONE 40 mg/ml three times per week early start=0.177, COPAXONE 40 mg/ml three times per week late start=0.257; P=0.0002), with no new safety issues.

• The 4 month, randomized, controlled GLACIER study of over 200 MS patients which compared the safety and tolerability of COPAXONE 40 mg/ml three times per week versus COPAXONE 20 mg/ml daily was recently completed. Treatment with COPAXONE 40 mg/ml three times per week resulted in a 50% lower mean annualized rate of injection related adverse events compared to COPAXONE 20 mg/ml daily (mean annualized injection related adverse events = 35.3 vs 70.4 for COPAXONE 40 mg/ml three times per week and COPAXONE 20mg/ml daily, respectively; P=0.0006) and also resulted in a 50% lower rate of injection site reactions compared to COPAXONE 20 mg/ml daily (mean annualized Injection site reactions = 35.2 vs 70.4 for COPAXONE 40 mg/ml three times per week and COPAXONE 20mg/ml daily, respectively; P=0.0006).

• COPAXONE has been the object of the longest, continuous prospective investigation of a drug treatment in patients with RRMS. After 10 years of ongoing COPAXONE treatment, 62% of patients were improved or unchanged from their initial neurologic status, as measured by the Expanded Disability Status Score (EDSS) level, and over 90% of patients receiving COPAXONE continuously were walking unassisted.

• Unlike other immunomodulatory agents, COPAXONE does not require routine monitoring or testing for liver function, thyroid function, blood chemistries, or neutralizing antibodies, and does not have warnings about depression, hepatic injury, or serious infections. COPAXONE is also the only agent indicated in RRMS with a pregnancy category B rating,

an important issue for a disease with a high prevalence in young women.

• COPAXONE is well tolerated with discontinuation of treatment due to an adverse reaction occurring in only approximately 5% of patients in the premarketing clinical trials. During 10 years of continuous COPAXONE treatment and formal follow-up, no unexpected safety issues emerged requiring therapy discontinuation. The most common adverse reactions in controlled studies were injection-site reactions, vasodilatation, rash, dyspnea, and chest pain.

Questions and Answers
Q: When does the patent on the 20 mg expire?
A: The patent is extended to September 2015.

Q: How will generic be approved?
A: Unsure at this point, the FDA is deciding if generic will have to conduct MRI study due to differences in manufacturing process. Teva feels that generic manufacturer will not be able to replicate manufacturing process.

Q: How are CMOs covering the 40 mg strength?
A: Peach State and WellCare cover as P; Amerigroup covers as NP.

Qnasl® (beclomethasone dipropionate)
Pronunciation: (be-kloe-METH-a-sone \(dī-ˈprō-pē-ə-ˌnāt\)

QNASL 80 mcg was the first commercially available non-aqueous intranasal steroid (INS) with an aerosolized hydrofluoroalkane (HFA) delivery. QNASL was originally indicated for the treatment of nasal symptoms associated with seasonal and perennial allergic rhinitis in patients 12 years of age and older. On December 17, 2014, the FDA approved QNASL 40 mcg for the treatment of nasal symptoms associated with allergic rhinitis (AR) in children 4 years of age and older. QNASL is now available in both 40 and 80 mcg strengths.

QNASL 40 mcg delivers effective nasal allergy symptom relief at one-fourth of the dosage approved to treat adults and is the first and only waterless HFA nasal allergy treatment to be approved for use in patients as young as four years of age.

FDA approval was based on data from three double-blind, placebo-controlled studies that evaluated the safety and efficacy of QNASL 40 mcg in children (ages 4-11) with AR. Data demonstrated that once-daily treatment with QNASL 40 mcg provided significant nasal allergy symptom relief in children with seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) in comparison to placebo. In all three studies, the safety profile of QNASL 40 mcg was similar to that of placebo and the most common adverse events were nosebleeds and ulcers, which is consistent with those seen in previous clinical studies of QNASL Nasal Aerosol.

The efficacy of QNASL has been demonstrated in multiple randomized, double blind, placebo controlled clinical trials in seasonal and perennial allergic rhinitis patients. The QNASL groups experienced statistically significant and clinically meaningful improvements in patient reported reflective and immediate total nasal symptom scores, as well quality of life measures and physician rated symptom scores.

In placebo controlled trials with seasonal allergic rhinitis or perennial allergic rhinitis patients, the most common reported adverse events after 2-6 weeks of QNASL were nasal discomfort, headache, and epistaxis. In a 52 week placebo controlled study the most common adverse events were nasopharyngitis, epistaxis, and upper respiratory tract infection. Epistaxis occurred more frequently and tended to be more severe in patients who received QNASL (11%) compared to placebo (2%).

QNASL's strengths have been shown in four areas. First, it demonstrated high nasal deposition and retention rates. Greater than 99% of QNASL was retained in the nasal cavity 45 seconds post-actuation with less than 1% deposited in the throat. Nasal deposition continued to remain high at 79%, 14 minutes post QNASL administration.

Second, patients can track how many doses are left in QNASL with its built-in dose counter.

Third, QNASL's spray characteristics include a low spray force which may increase patient comfort and provide consistent delivery of medication.

Lastly, QNASL is a nonaqueous nasal spray that may benefit patients who are dissatisfied with the sensory attributes of current aqueous INS products.

Nonaqueous intranasal sprays were widely prescribed for allergic rhinitis in the past but were taken off the market in 2003 because CFC-propellants used in their formulations were banned by the Montreal Protocol. QNASL does not contain a CFC-propellant. A retrospective claims analysis of the Florida State Medicaid system comparing medication possession ratio (MPR) and pharmacy costs of aqueous and nonaqueous therapies from 1997-2001 revealed differences between the two delivery types. Patients on the nonaqueous CFC INS sprays had a higher medication possession ratio compared to the aqueous (53.2% compared to 34.7%). The nonaqueous CFC INS sprays had significantly lower pharmacy cost for payers, with 42% lower total pharmacy costs for nonaqueous CFC INS medications over 18 months ($1,222 vs $2,115). Median MPR and economic data suggest the addition of a nonaqueous allergic rhinitis treatment may be associated with lower costs.

Thank you for the opportunity to present this information. Please consider the addition of the QNASL Nasal Aerosol to your formulary.

Questions and Answers
There were no additional questions and answers.

XXII. Purdue
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Hysingla™ ER (hydrocodone bitartrate extended-release)
Pronunciation: Hysingla™ ER [(hye-SING-luh)] (hydrocodone bitartrate [HIGH-droe-KOE-dohn by-TAR-trate]

Hysingla ER, CII, is the first and only, extended-release (ER), oral formulation of single-entity hydrocodone bitartrate with abuse deterrent properties approved for every-24-hour (once daily) dosing for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Hysingla ER does not contain acetaminophen.

Efficacy of once daily Hysingla ER, in opioid-naïve and opioid-experienced patients with moderate to severe chronic low back pain, was superior to placebo, with significantly lower “average pain over the last 24 hours” pain scores than placebo at week 12 compared with baseline.

Results of treatment effectiveness outcomes of the long-term study demonstrated consistent effectiveness of Hysingla ER over 52 weeks and continued during a 24-week extension period. The treatment effects of Hysingla ER, as measured by “average pain over the last 24 hours” scores, were obtained early, with the full extent of these effects established when a stable Hysingla ER dose was achieved, with improvements maintained during the long-term treatment and without the continued requirement for dose increases.

The overall adverse reaction profile of Hysingla ER is consistent with that of other approved oral mu-opioid analgesics and no unusual safety concerns have been identified. The most common adverse reactions (≥5%) reported by patients treated with Hysingla ER in the chronic pain clinical trials were constipation, nausea, vomiting, fatigue, upper respiratory tract infection, dizziness, headache, and somnolence.

Hysingla ER contains hydrocodone bitartrate, a Schedule II controlled substance with a high potential for abuse. The Hysingla ER Full Prescribing Information (FPI) includes a Boxed Warning describing the risks for addiction, abuse, and misuse, life-threatening respiratory depression, accidental ingestion, neonatal opioid withdrawal syndrome, and cytochrome P450 3A4 interaction.

Hysingla ER has physicochemical properties that confer resistance to crushing, dissolving and breaking – manipulations often required or preferred for abuse through intravenous and intranasal routes, and causes of some medication errors. Hysingla ER has claims in its FPI indicating that the product is formulated with physicochemical barriers to abuse and indicating the product is expected to result in a meaningful reduction in abuse. Furthermore, the Hysingla ER formulation is not susceptible to dose dumping in alcohol, based on in vitro ethanol sensitivity tests. The Committee should be aware that continued support for the development and approval of abuse deterrent formulations

for opioids was demonstrated by the submission of a document, signed by the Attorneys General for 46 states, to include Sam Olens, then Attorney General for Georgia. In a letter to FDA commissioner Margaret Hamburg, the attorneys general, writing on behalf of the National Association of Attorneys General, wrote that people who abuse opioid painkillers are increasingly using those that lack tamper-resistant features, and applauded the FDA for proposing guidelines establishing clear standards for manufacturers who develop and market tamper- and abuse-resistant opioid products.

Given all of the concerns of opioid abuse, misuse, and diversion, it would seem inherent upon this Committee to consider Hysingla ER for addition to the PDL to provide an additional choice for prescribers in the State of Georgia needing an appropriate prescription of a long-acting opioid analgesic.

Questions and Answers
Q: Is Hysingla ER on the market yet?
A: Yes, became available in January.

Q: What did the street value of OxyContin do after switch to the abuse-deterrent formulation?
A: Decreased.

XXIII. Biodelivery Sciences

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Charlotte Cavoores, Medical Science Liaison
David Acheson, Vice President, Sales and Managed Marketing

Bunavail® (buprenorphine/naloxone) buccal film, CIII
Pronunciation: BEWN-a-vale

Indication and Description
On June 6, 2014, the FDA approved BUNAVAIL® for the maintenance treatment of opioid dependence, as part of a complete treatment plan to include counseling and psychosocial support. BUNAVAIL® is the first and only buccal film approved for maintenance treatment of opioid dependence.

BUNAVAIL® is powered by BEMA (BioErodable MucoAdhesive) technology and efficiently delivers buprenorphine with twice the bioavailability of Suboxone Sublingual Tablets.[1] Pharmacokinetic studies demonstrate exposure to buprenorphine from BUNAVAIL® 4.2/0.7mg and Suboxone sublingual tablets 8/2mg was equivalent. Mean circulating levels of norbuprenorphine, the primary metabolite of buprenorphine, were approximately 40% less compared to Suboxone.

The advanced technology of the BEMA film allows BUNAVAIL® to adhere to the buccal mucosa, the mucous membrane of the cheek, upon contact, where it dissolves and delivers buprenorphine and naloxone directly to the bloodstream. BEMA technology is a unique two-layer film: the mucoadhesive layer is designed to adhere upon contact with the buccal mucosa, and the backing layer promotes unidirectional flow of the medication, and prevents drug accumulation in the mouth.

Efficacy
Data from multiple studies, including a 12-week, open-label clinical study of 249 opioid-dependent patients stabilized on Suboxone sublingual tablets or film, demonstrated the safety and efficacy of BUNAVAIL®. In this phase III safety and tolerability trial, patients were switched from their current therapy, Suboxone sublingual film (N=144) or Suboxone sublingual tablets (N=105) to a proportional dose of BUNAVAIL® and maintained for 12 weeks. The mean dose of BUNAVAIL® at the end of the open-label period was 8.0/1.4mg, which was half the Suboxone (buprenorphine) dose at baseline. This 50% reduction in buprenorphine dose after conversion from Suboxone is consistent with data seen in PK studies and reflects the increased bioavailability of BUNAVAIL®, as previously referenced.

- Additionally, BUNAVAIL® was associated with low use of non-prescribed opioids. 7.6% of patients had a positive urine test for a non-prescribed opioid.

- Among patients with a baseline Clinical Opiate Withdrawal Scale (COWS) scores ranging from 10-25 (N=34) after discontinuation of Suboxone, initiation of BUNAVAIL® resulted in a decline in mean scores from >13 to ≤ 1.1 in 3 hours.
- BUNAVAIL® was associated with a high rate of patient retention. 79.1% of patients remained on treatment over 12 weeks.

Safety/Tolerability
Constipation incidence was reduced during BUNAVAIL® treatment in the 186 subjects who completed a symptom checklist at baseline and end of study. The incidence of constipation was 40.9% at baseline on Suboxone, and was reduced to 12.9% after 12 weeks on BUNAVAIL®. This represents an overall reduction of 68% of those subjects who reported having this symptom upon entering the trial on Suboxone. Treatment-emergent constipation was reported by 2.8% (7/249) of patients. Changes in the oral mucosa were carefully followed throughout the study. Systematic assessments were performed at screening, baseline, and at 5 periodic follow up exams. Prior to treatment with BUNAVAIL®, oral mucosal abnormalities were identified in 5% (25/498) of the systematic oral exams. During treatment with BUNAVAIL®, abnormalities were seen in 0.6% (6/1073) of the oral exams. Treatment-emergent adverse events were generally mild to moderate and ameliorated over the course of 12 weeks. In patients switched from Suboxone to BUNAVAIL® in the same study, the only adverse reactions reported by at least 5% of patients were drug withdrawal syndrome, lethargy and headache. Adverse reactions reported by >1% but less than 5% of patients receiving BUNAVAIL® were: fatigue, chills, somnolence, drug dependence, insomnia, constipation, oral mucosal erythema, rhinorrhea, hyperhydrosis.

Contraindications
Hypersensitivity to buprenorphine or naloxone.

Dosage/Administration
Apply BUNAVAIL® as a single daily dose. The recommended daily dose for maintenance is 8.4mg/1.4mg. Buccal film BUNAVAIL® 2.1 mg buprenorphine/0.3 mg naloxone; BUNAVAIL ®4.2 mg buprenorphine/0.7 mg naloxone; BUNAVAIL® 6.3 mg buprenorphine/ 1.0 mg naloxone.

Questions and Answers
Q: What is the dissolution rate?
A: Approximately 15-20 minutes and saliva is not needed.

Q: What are considered the advantages of Bunavail?
A: Lower dose so can control with less adverse events, favorable administration, improved adherence and drug is going into cheek and not into oral cavity so decreased taste due to drug.

Q: How has the response been by prescribers so far?
A: Good so far.

XXIV. Sanofi/Genzyme

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Nicole Yonkers, PhD, Medical Science Liaison
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Afrezza® (insulin human inhalation powder)
Pronunciation: Afrezza (uh-FREZZ-uh

INDICATION
Afrezza is a rapid-acting inhaled insulin indicated to improve glycemic control in adult patients with diabetes mellitus.

DESCRIPTION
The Afrezza system consists of the compact, reusable, breath-powered Gen2® inhaler that delivers premeasured doses of inhalable insulin powder (Technosphere® insulin [TI]) from disposable, single-use cartridges. TI is recombinant human insulin adsorbed to biologically inert, microscopic carrier particles with a size that is ideal for deposition in the deep lung. Afrezza has an onset of action comparable to that of insulin lispro, but has an earlier peak of activity and a shorter duration of action. Time to maximum serum insulin concentrations was 8 minutes with Afrezza

vs. 48 minutes with insulin lispro, and Afrezza showed an earlier peak of action (61 minutes) vs. insulin lispro (109 minutes).

EFFICACY AND SAFETY

The safety and efficacy of Afrezza is supported by 2 phase 3 clinical trials of TI administered via the Gen2 inhaler in patients with T1DM (MKC-TI-171) or T2DM (MKC-TI-175). Study MKC-TI-171 was a 24 week phase 3, randomized, open-label, multicenter study evaluating Afrezza in patients with T1DM who were inadequately controlled on their current insulin therapy. Afrezza in combination with basal insulin was shown to be noninferior to insulin aspart + basal insulin in improving HbA1c (Afrezza: −0.2%; aspart: −0.4%). Significantly fewer patients in the Afrezza group experienced severe hypoglycemia.

Study MKC-TI-175 was a 24 week phase 3, randomized, double-blind, placebo-controlled, multicenter study of Afrezza in patients with T2DM inadequately controlled on metformin and/or 2 or more oral antidiabetic drugs (OADs). In this study, prandial inhaled Afrezza was superior to placebo (Technosphere-placebo [TP]: inhaled Technosphere powder lacking absorbed insulin) in reducing HbA1c from baseline. The treatment difference between Afrezza and TP was −0.4% (95% CI: −0.57, −0.23; *P*<0.0001). There was an increase in the incidence of severe hypoglycemia for Afrezza vs TP (5.1% vs 1.7%), but this difference did not reach statistical significance.

The safety and efficacy of TI has been evaluated in 3,017 patients, including durations of exposure of 2 years or more. The total exposure was 2,052 subject-years. No safety signals have been observed for cerebrovascular or hypersensitivity events. Malignancies, including lung malignancies, were not clustered by type of cancer or organ system, and showed a pattern consistent with expectations for the general population in the age group of the study population. TI was associated with more frequent respiratory treatment-emergent adverse events (TEAEs), but no greater incidence of respiratory serious adverse events (SAEs) compared with comparator insulin.[2] Cough, generally intermittent or single-defined and closely following inhalation, was the most common respiratory TEAE, and the incidence decreased rapidly after the first weeks of treatment. Decreases in PFTs over 24 weeks were greater for TI, however, the difference was small (~40 mL [95% CI: -80, -1]), occurred early in treatment, and did not progress over time. Differences in FEV_1 resolved within 1 month of TI discontinuation, although there are insufficient data to draw definitive conclusions regarding reversal of the effect on FEV_1 after discontinuation of Afrezza.

AFREZZA REMS

Afrezza is contraindicated in patients with chronic lung disease such as asthma or COPD due to the risk of acute bronchospasm. The Afrezza Risk Evaluation and Mitigation Strategy (REMS) is a communication strategy designed to inform healthcare providers (HCPs) of the serious risks of Afrezza in this population. The program informs HCPs of the requirements for patient evaluation and testing prior to initiating Afrezza, to ensure appropriate patient selection.

CLINICAL BENEFITS

US adults with diabetes are not meeting goals for glycemic control. As a result, patients are left vulnerable to long-term complications associated with chronic hyperglycemia. Although patients with T2DM often have significant PPG excursions and are candidates for insulin therapy, reluctance on the part of both physicians and patients leads to a significant lag in initiating insulin. There is also an unmet need among patients who are already receiving basal insulin but require the addition of prandial insulin. Patients concerns include embarrassment at having to perform injections in public and fear of injection pain, which may contribute to the reluctance to use insulin. As currently available insulin products require subcutaneous injection, Afrezza may address an unmet medical need, providing the ability to administer insulin without injections, which may in turn, improve treatment adherence and improve glucose control.

CONCLUSIONS

Inhaled Afrezza mimics endogenous mealtime insulin secretion via non-injected administration of RHI for prandial glycemic management. It provides an option that is acceptable to patients who are reluctant to take insulin injections. Afrezza may address current unmet medical needs among patients with diabetes receiving insulin, who are non-adherent to their current insulin regimen or who require the addition of prandial insulin and T2DM patients who are failing to meet treatment goals despite progressive addition of OADs.

Questions and Answers

Q: How were issues addressed from when the first inhaled insulin product was on the market?
A: Improvement in design of inhaler which is more discreet, dosing does not require conversion and not overpriced. The pulmonary speculations with the previous products were not confirmed and studies indicated no serious safety signals.

Q: What are considered the advantages of Afrezza?
A: Acceptability of inhaler over injection.

Q: How many inhalers are a 30-day supply?
A: 2 inhalers, with each inhaler needing to be changed every 15 days, packaged with 90 cartridges; cartridge must be used with 3 days once punctured.

Aubagio® (teriflunamide)
AUBAGIO is a pyrimidine synthesis inhibitor indicated for the treatment of patients with relapsing forms of multiple sclerosis. It is available as a 7 mg or 14 mg tablet and taken orally once daily, with or without food.

Four randomized, controlled, double-blind clinical trials established the efficacy of AUBAGIO in patients with relapsing forms of multiple sclerosis.

Study 1 was a double-blind, placebo-controlled clinical trial that evaluated once daily doses of AUBAGIO 7 mg and 14 mg for up to 26 months in patients with relapsing forms of multiple sclerosis. The study found a statically significant reduction in the primary end point of annualized relapse rate (ARR) for patients who received AUBAGIO 7 mg or AUBAGIO 14 mg, compared to patients who received placebo. Additionally, there was a statically significant reduction in the relative risk of disability progression at week 108 sustained for 12 weeks in the AUBAGIO 14 mg compared to placebo. Patients in both AUBAGIO groups also had significantly fewer Gd-enhancing lesions per T1-weighted MRI scan as compared to the placebo group.

Study 2 was a double-blind, placebo-controlled clinical trial that evaluated once daily doses of AUBAGIO 7 mg and AUBAGIO 14 mg for up to 40 months in patients with relapsing forms of multiple sclerosis. There was a statistically significant reduction in the primary endpoint of ARR for patients who received AUBAGIO 7 mg or AUBAGIO 14 mg compared to patients who received placebo. There was a statically significant reduction in the relative risk of disability progression at week 108 sustained for 12 weeks in the AUBAGIO 14 mg group compared to placebo.

Study 3 was a double-blind, placebo controlled clinical trial that evaluated once daily doses of AUBAGIO 7 mg and AUBAGIO 14 mg for up to 108 weeks in patients with relapsing multiple sclerosis. Patients in this study were required to have had a first clinical event consistent with acute demyelination occurring within 90 days of randomization and MRI features that were characteristic of MS. The proportion of patients free of relapse was greater in the AUBAGIO 7 mg and AUBAGIO 14 mg groups than in the placebo arm.

The effect of AUBAGIO on MRI activity was also demonstrated in Study 4, a randomized, double-blind, placebo controlled clinical trial of multiple sclerosis patients with relapse. The mean number of unique active lesions per brain MRI scan during the 36-week treatment period was lower in the AUBAGIO 7 mg and AUBAGIO 14 mg group than in the placebo group, the difference being statically significant for both AUBAGIO doses.

AUBAGIO has a boxed warning for hepatotoxicity and risk of teratogenicity. AUBAGIO is contraindicated in severe hepatic impairment, pregnancy and in patients currently on leflunomide treatment.

The most common adverse events (≥10% and ≥2% greater than placebo) are headache, diarrhea, nausea, alopecia and increased ALT. If required, elimination of AUBAGIO from the plasma can be accelerated by the administration of cholestyramine. AUBAGIO may decrease white blood cell count. A recent complete blood count (CBC) should be available before starting AUBAGIO. Patients should be monitored for signs and symptoms of infection and AUBAGIO should not be started in patients with active infection. Pregnancy must be excluded before starting AUBAGIO. If the patient develops symptoms consistent with peripheral neuropathy, they should be evaluated and discontinuation should be considered. AUBAGIO may increase blood pressure. Blood pressure should be measured at treatment initiation and monitored during treatment.

Questions and Answers
Q: What are considered the advantages of Aubagio?
A: An oral medication dosed once daily so potential for improved compliance, consistent safety (available for RA since the 90s) and efficacy profiles and only oral MS treatment that has 2 phase III trials with outcomes showing decreased disability.

Sklice® (ivermectin) – Was not presented but a one-page summary was provided for review.
Prescribing Summary
- **Sklice (ivermectin) 0.5% Lotion** is a pediculicide indicated for the Topical treatment of head lice infestations in patients 6 months of age and older.
- The active ingredient of Sklice lotion is ivermectin which causes death of parasites by hyperpolarization of their nerve and muscle cells.

Updated Information
Within the U.S., clinical failures of permethrin have been reported from many states. These findings all point to a growing problem of head lice resistance to permethrin/pyrethrins. Genetic mutations, specifically a knockdown resistance (kdr) mutation was identified in head lice collected from several areas of the country. The growing number of clinical failures of current OTC products may be due to multiple genetic changes that confer resistance, and the kdr mutation may be a marker of the resistance patterns. It should be noted that when treatment with permethrin or pyrethrins fail despite their correct use, the AAP recommends that other treatment alternatives be considered.

(Yoon KS, et al. Knockdown Resistance Allele Frequencies in North American Head Louse (Anoplura: Pediculidae) Populations. J. Med. Entomol. 2014;51(2): 450Ð457. ; DOI: http://dx.doi.org/10.1603/ME13139)

- In Vitro studies, demonstrated that Topical ivermectin formulations were 100% effective at killing lice after a single 10 minute application.
- Topical ivermectin was not ovicidal. However, of treated eggs that hatched, all lice died within 48 hours of hatching – thus never reaching maturity to mate and lay eggs.

Safety Summary
- There are NO contraindications for the use of Sklice.
- During clinical trials, adverse reactions were reported in less than 1% of subjects treated with Sklice Lotion, and included conjunctivitis, ocular hyperemia, eye irritation, dandruff, dry skin, and skin burning sensation.

Prescriber Awareness
- Topical Ivermectin has been added to 2 main online resources for physicians:
  - The AAP's Committee on Infectious Diseases REDBOOK now includes topical ivermectin
  - The CDC's Lice Infestation treatment website now includes topical ivermectin as a prescription option

XXV. Bristol-Myers Squibb

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Greg A. Martin, MBA, State Access Manager

Eliquis® (apixaban)
Pronunciation: ELL eh kwiss)

Eliquis® (apixaban) is a factor Xa inhibitor anticoagulant indicated:
• to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF).
• for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery.
• for the treatment of DVT and PE, and for the reduction in the risk of recurrent DVT and PE following initial therapy.

Clinical Studies
The efficacy and safety of apixaban was evaluated in AMPLIFY for the treatment of DVT and PE, and in AMPLIFY-EXT for the reduction in the risk of recurrent DVT and PE following 6 to 12 months of anticoagulant treatment. Both studies were randomized, parallel-group, double-blind trials in patients with symptomatic proximal DVT and/or symptomatic PE. AMPLIFY (N=5400) compared apixaban 10 mg twice daily orally for 7 days followed by apixaban 5 mg twice daily orally for 6 months, with enoxaparin 1 mg/kg twice daily subcutaneously (SC) for at least 5 days (until warfarin INR ≥2) followed by warfarin (target INR range 2.0-3.0) orally for 6 months. The primary efficacy outcome was recurrent symptomatic VTE (nonfatal DVT or nonfatal PE) or VTE-related death. The primary safety outcome was

major bleeding. Other safety outcomes included clinically relevant nonmajor (CRNM) bleeding, major or CRNM bleeding, minor bleeding and all bleeding.

- Apixaban was noninferior to enoxaparin/warfarin for the primary efficacy outcome of recurrent symptomatic VTE/VTE-related death: 2.3% vs 2.7%, respectively; relative risk (RR) with apixaban=0.84 (95% CI, 0.60 to 1.18), *P* < .0001 for noninferiority.
- Apixaban was superior to enoxaparin/warfarin for the primary safety outcome of major bleeding: 0.6% vs 1.8%, respectively; RR=0.31 (95% CI, 0.17 to 0.55), *P* < .0001 for superiority.
- Apixaban had a lower incidence of bleeding compared with enoxaparin/warfarin across several bleeding outcomes (secondary safety outcomes): CRNM bleeding (3.9% vs 8.0%), major or CRNM bleeding (4.3% vs 9.7%), minor bleeding (11.7% vs 18.8%) and all bleeding (15.0% vs 25.1%).

AMPLIFY-EXT (N=2482) compared 2 doses of apixaban (2.5 mg or 5 mg twice daily orally) with placebo for the extended treatment (12 month) of VTE in patients who had been treated for DVT and/or PE for 6 to 12 months with anticoagulant therapy without having a recurrent event. Approximately one-third of patients participated in the AMPLIFY study prior to enrollment in the AMPLIFY-EXT study. The primary efficacy outcome was recurrent symptomatic VTE (nonfatal DVT or nonfatal PE) or any-cause death. The primary safety outcome was major bleeding. Other safety outcomes included CRNM bleeding, major and CRNM bleeding, minor bleeding and all bleeding.

- Both doses of apixaban, 2.5 and 5 mg twice daily orally, were superior to placebo for the primary efficacy outcome of recurrent VTE/any-cause death respectively (3.8% and 4.2% vs 11.6%; RR=0.33; 95% CI, 0.22 to 0.48 and RR=0.36; 95% CI, 0.25 to 0.53; *P* < .0001 for superiority for both comparisons).
- Rates of bleeding for apixaban and placebo were: major bleeding (primary safety outcome): apixaban 2.5 mg, 0.2%; apixaban 5 mg, 0.1%; and placebo, 0.5%; major and CRNM bleeding, apixaban 2.5 mg, 3.2%; apixaban 5 mg, 4.3%; and placebo, 2.7%; CRNM bleeding, apixaban 2.5 mg, 3.0%; apixaban 5 mg, 4.2%; and placebo, 2.3%; minor bleeding, apixaban 2.5 mg, 8.9%; apixaban 5 mg, 12.1%; and placebo, 7.0; all bleeding: apixaban 2.5 mg, 11.2%; apixaban 5 mg, 14.9%; and placebo, 9.0%.
- Apixaban 2.5 mg twice daily is the only approved dose for the reduction in the risk of VTE recurrence following initial therapy.

Pharmacoeconomics: Medical Cost Avoidance Analyses: In a medical cost avoidance analysis, apixaban was estimated to have the greatest medical cost reduction of all NOACS in a patient-year when compared to enoxaparin/warfarin for VTE treatment. The analysis was based on the clinical endpoints from the AMPLIFY (apixaban), RE-COVER (dabigatran), RE-COVER II (dabigatran), EINSTEIN-Pooled analysis (rivaroxaban) and Hokusai-VTE (edoxaban) trials, and costs were adjusted to 2013 levels. Drug costs and other monitoring related expenses were not included. The total medical cost reductions for dabigatran, rivaroxaban, apixaban and edoxaban vs. standard therapy were estimated to be -$146, -$482, -$918 and -$344, respectively. A medical cost avoidance analysis based on published clinical trial results from AMPLIFY-EXT (apixaban), RE-SONATE (dabigatran), and EINSTEIN-EXT (rivaroxaban), evaluated the medical costs avoided when apixaban, dabigatran, and rivaroxaban were used for extended treatment of VTE compared to placebo. The total medical cost reduction for apixaban 2.5 mg, apixaban 5 mg, dabigatran, and rivaroxaban vs. placebo were estimated to be -$4,249, -$4,244, -$2,794, and -$2,948, respectively.

Selected Important Safety Information WARNINGS: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS (B) SPINAL/EPIDURAL HEMATOMA
(A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
(B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures.

Questions and Answers
Q: What is the approximate market share of the new oral anticoagulants?
A: National is 34%, GA is 6%.

Q: How are other plans covering?
A: FL, AL and LA have on PDL as P without restrictions and is on 95% of hospital formularies.

XXVI. Lilly
Jennifer Ward, RN, BSN, Outcomes Liaison
Mark Guindon, RPh, Senior Account Manager

Trulicity® (dulaglutide)
Pronunciation: Trū-li-si-tee

Medical Value Summary
- TRULICITY is a glucagon-like peptide (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM).
- Dulaglutide exhibits GLP-1-mediated effects, including glucose-dependent potentiation of insulin secretion, inhibition of glucagon secretion, slowing of gastric emptying, and increased satiety.
- The combination of these effects results in a decrease of both fasting and postprandial glucose (PPG) concentrations which can be observed after a single dose, thereby leading to improvement in overall glycemic control.
- Further enhancement in long-term glycemic control may be achieved by improvements in weight control and pancreatic β-cell function.
- Dulaglutide is the only weekly GLP-1 receptor agonist that has demonstrate noninferiority to liraglutide in HbA1c change from baseline.
- TRULICITY is available as a once weekly injection delivered via a single-dose pen device that has a hidden, attached, self-retracting needle and requires no reconstitution.

Efficacy Summary
- TRULICITY has been studied as monotherapy and in combination with metformin, metformin and thiazolidinedione metformin and sulfonylurea, and prandial insulin with or without metformin.

Trial Acronym	Concomitant therapy	Active comparator	Efficacy (% HbA1c) at primary endpoint		
			Dulaglutide 1.5mg	Dulaglutide 0.75mg	Comparator
AWARD-18	Metformin and Thiazolidinedione	Exenatide twice daily	-1.51 ±0.06	-1.30 ± 0.06	-0.99 ± 0.06
AWARD-29	Metformin and Sulfonylurea	Insulin glargine	-1.08 ± 0.06	-0.76 ± 0.06	-0.63 ± 0.06
AWARD-310	Monotherapy	Metformin	-0.78 ± 0.06	-0.71 ± 0.06	-0.56 ± 0.06
AWARD-411	Insulin lispro with/without metformin	Insulin glargine	-1.64 ± 0.07	-1.59 ± 0.07	-1.41 ± 0.07
AWARD-512	Metformin	Sitagliptin	-1.10 ± 0.06	-0.87 ± 0.06	-0.39 ± 0.06
AWARD-613	Metformin	Liraglutide	-1.42 ± 0.06	Not studied	-1.36 ± 0.06

- No overall differences in glycemic effectiveness were observed across demographic subgroups (age, gender, race/ethnicity, duration of diabetes).

Safety Summary-Please see full prescribing information for complete safety information.
- The most common adverse reactions, reported in ≥5% of patients treated with TRULICITY are: nausea, diarrhea, vomiting, abdominal pain, and decreased appetite.
- The FDA has required this safety notice as part of the TRULICITY REMS (Risk Evaluation and Mitigation Strategy) to inform healthcare providers about the following **serious risks of TRULICITY (dulaglutide):**
  - **Potential Risk of Medullary Thyroid Carcinoma (MTC).** Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide (GLP-1) receptor agonists. It is unknown whether TRULICITY causes thyroid C-cell tumors, including MTC, in humans. Counsel patients regarding the risk of MTC and the symptoms of thyroid tumors.
  - TRULICITY has **a boxed warning** on the risk of thyroid c-cell tumors. Dulaglutide causes thyroid C-cell tumors in rats. It is unknown whether TRULICITY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance could not be determined from clinical or nonclinical studies. TRULICITY is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

- **Risk of Pancreatitis**. Pancreatitis has been reported with the use of GLP-1 receptor agonists. Cases of pancreatitis have been described in association with TRULICITY during clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

TRULICITY is not recommended as first-line therapy for patients with type 2 diabetes mellitus inadequately controlled on diet and exercise.

Questions and Answers
Q: How are other Medicaid plans covering?
A: Most are moving to a 1 of 2 of the GLP-1s dosed once weekly.

Q: What are considered the advantages of Trulicity?
A: Once weekly dosing, easy single-use pen with no mixing required, hidden needle, robust efficacy, similar safety to class, minimal renal clearance, and the only GLP-1 to show non-inferiority to Victoza (liraglutide).

XXVII. Boehringer Ingelheim

Striverdi® Respimat® (olodaterol inhalation spray)
Indication and Important Limitations
• Striverdi Respimat (olodaterol) Inhalation Spray is a long-acting beta2-agonist indicated for long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.
• Important Limitations: STRIVERDI RESPIMAT is not indicated to treat acute deteriorations of COPD and is not indicated to treat asthma.

IMPORTANT SAFETY INFORMATION: WARNING: ASTHMA-RELATED DEATH
Long-acting beta2-adrenergic agonists (LABA) increase the risk of asthma-related death. Data from a large, placebo-controlled US study that compared the safety of another long-acting beta2-adrenergic agonist (salmeterol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol. This finding with salmeterol is considered a class effect of LABA, including olodaterol, the active ingredient in STRIVERDI RESPIMAT. The safety and efficacy of STRIVERDI RESPIMAT in patients with asthma have not been established. STRIVERDI RESPIMAT is not indicated for the treatment of asthma.

Executive Summary of STRIVERDI Efficacy and Safety Data
The STRIVERDI RESPIMAT clinical development program included three dose-ranging trials in COPD patients, four dose-ranging trials in asthma patients, and eight confirmatory trials in patients with COPD.

Confirmatory Trials
• The eight confirmatory trials in the STRIVERDI RESPIMAT clinical development program were four pairs of replicate, randomized, double-blind, placebo-controlled trials in 3533 COPD patients (1281 received the 5 mcg dose, 1284 received the 10 mcg dose):
  - two replicate, placebo-controlled, parallel group, 48 week trials (Trials 1 and 2)
  - two replicate, placebo- and active- [formoterol 12 mcg twice-daily] controlled, parallel group, 48-week trials (Trials 3 and 4)
  - two replicate, placebo- and active- [formoterol 12 mcg twice-daily] controlled, 6-week cross-over trials (Trials 5 and 6)
  - two replicate, placebo- and active- [tiotropium bromide 18 mcg once-daily] controlled, 6-week cross-over trials (Trials 7 and 8)
• These eight trials enrolled patients who were 40 years of age or older with a clinical diagnosis of COPD, a smoking history of at least 10 pack-years, and moderate to very severe pulmonary impairment (post-bronchodilator FEV1 less than 80% predicted normal [GOLD II – IV] and a post-bronchodilator FEV1 to FVC ratio of less than 70%).
• The majority of the 3104 patients in the 48-week trials (Trials 1 and 2, Trials 3 and 4) were male (77%), white (66%) or Asian (32%), with a mean age of 64 years. Mean post-bronchodilator FEV1 was 1.38 L (GOLD II [50%], GOLD III [40%], GOLD IV [10%]). Mean beta2-agonist responsiveness was 15% of baseline (0.16 L). With the exception of other LABAs, all pulmonary medications were allowed as concomitant therapy (e.g., tiotropium [24%], ipratropium

[25%], inhaled corticosteroids [45%], xanthines [16%]); patient enrollment was stratified by tiotropium use. In all four trials, the primary efficacy endpoints were change from pre-treatment baseline in FEV1 AUC0-3 and trough (pre-dose) FEV1 (after 12 weeks in Trials 1 and 2; after 24 weeks in Trials 3 and 4).

IMPORTANT SAFETY INFORMATION
All LABAs are contraindicated in patients with asthma without use of a long-term asthma control medication.

STRIVERDI RESPIMAT should not be initiated in patients with acutely deteriorating COPD, which may be a life threatening condition, or used as rescue therapy for acute episodes of bronchospasm. Acute symptoms should be treated with an inhaled short-acting beta2 agonist.

Questions and Answers
Q: What are considered the advantages of Striverdi Respimat?
A: Once daily dosing, improved inhaler, no refrigeration required and only has COPD indication.

Spiriva® Respimat® (tiotropium bromide inhalation spray)
A one-page summary was not able to be provided on the new Respimat inhaler formulation of Spiriva.

Questions and Answers
Q: Will the Handihaler formulation remain available?
A: Yes.

Jardiance® (empagliflozin)
Indication and Limitation of Use
• JARDIANCE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
• JARDIANCE is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Executive Summary of JARDIANCE Efficacy and Safety Data
JARDIANCE has been studied as monotherapy and in combination with metformin, sulfonylurea, pioglitazone, and insulin and also in patients with type 2 diabetes with mild or moderate renal impairment. In patients with type 2 diabetes, treatment with JARDIANCE reduced hemoglobin A1c (HbA1c), compared to placebo. The reduction in HbA1c for JARDIANCE compared with placebo was observed across subgroups including gender, race, geographic region, baseline BMI and duration of disease.
• **Monotherapy:** In a randomized, double-blind, placebo-controlled study (n=986) of treatment-naïve adults patients with inadequately controlled type 2 diabetes (A1C between 7 and 10%), JARDIANCE 10 mg or 25 mg daily demonstrated a statistically significant placebo-adjusted mean difference from baseline A1C of -0.7% and -0.9%, respectively, at 24 weeks (p<0.0001, 0.1% adjusted mean increase from baseline A1C 7.9% with placebo)
    - JARDIANCE 10 mg or 25 mg also provided a statistically significant placebo-adjusted reduction in fasting blood glucose (FPG) of -31 mg/dL and -36 mg/dL (12 mg/dL adjusted mean increase from baseline FPG of 155 mg/dL with placebo), in body weight of -2.5% and -2.8% (0.4% adjusted mean decrease from baseline a body weight of 78 kg with placebo), and in systolic blood pressure of -2.6 mmHg (p=0.0231, placebo-adjusted) and -3.4 mmHg (p=0.0028, placebo-corrected), respectively, at 24 weeks
• **Add-on combination with metformin:** In a randomized, double-blind, placebo-controlled study (n=637) of adults patients with inadequately controlled type 2 diabetes (A1C between 7 and 10%) on at least 1500 mg of metformin daily, JARDIANCE 10 mg or 25 mg in combination with metformin demonstrated a statistically significant placebo-adjusted mean difference from baseline A1C of -0.6% for both doses at 24 weeks (p<0.0001, 0.1% adjusted mean decrease from baseline A1C 7.9% with placebo)
    - JARDIANCE 10 mg or 25 mg also provided a statistically significant placebo-adjusted reduction in fasting blood glucose (FPG) of -26 mg/dL and -29 mg/dL (6 mg/dL adjusted mean increase from baseline FPG of 156 mg/dL with placebo), in body weight of -2.0% and -2.5% (0.5% adjusted mean decrease from baseline a body weight of 80 kg with placebo), and in systolic blood pressure of -4.1 mmHg (p<0.0001, placebo-corrected) and -4.8 mmHg (p<0.0001, placebo-corrected), respectively, at 24 weeks
• **Add-on combination with metformin and sulfonylurea:** In a randomized, double-blind, placebo-controlled study (n=666) of adults patients with inadequately controlled type 2 diabetes (A1C between 7 and 10%) on at least 1500 mg of metformin and a sulfonylurea daily, JARDIANCE 10 mg or 25 mg in combination with metformin and a sulfonylurea demonstrated a statistically significant placebo-adjusted mean difference from baseline A1C of -0.6% for both doses at 24 weeks (p<0.0001, 0.2% adjusted mean decrease from baseline A1C 8.2% with placebo)

- o JARDIANCE 10 mg or 25 mg also provided a statistically significant placebo-adjusted reduction in fasting blood glucose (FPG) of -29 mg/dL for both doses (6 mg/dL adjusted mean increase from baseline FPG of 152 mg/dL with placebo), and in body weight of -2.4% and -2.7% (0.5% adjusted mean decrease from baseline a body weight of 76 kg with placebo), respectively, at 24 weeks

• **Non-inferiority study versus glimepiride:** In a randomized, double-blind, glimepiride-controlled study (n=1545) of adults patients with inadequately controlled type 2 diabetes (A1C between 7 and 10%) despite metformin therapy, JARDIANCE 25 mg in combination with metformin and glimepiride with metformin resulted in an adjusted mean A1C reduction of 0.7% from a mean baseline A1C of 7.9% (mean difference in A1C between the two treatment groups was 0.07%, p=0.0001)

• **Add-on combination with pioglitazone with or without metformin:** In a randomized, double-blind, placebo-controlled study (n=498) of adults patients with inadequately controlled type 2 diabetes (A1C between 7 and 10%) on at least 1500 mg of metformin and 30 mg of pioglitazone daily, JARDIANCE 10 mg or 25 mg in combination with pioglitazone, with or without metformin, demonstrated a placebo-adjusted mean difference from baseline A1C of -0.5% and -0.6%, respectively, at 24 weeks (p<0.0001, 0.1% adjusted mean decrease from baseline A1C 8.2% with placebo)

• **Add-on combination with insulin with or without metformin and/or sulfonylurea:** In a randomized, double-blind, placebo-controlled study (n=494) of adults patients with inadequately controlled type 2 diabetes despite insulin or insulin in combination with oral drug therapy, JARDIANCE 10 mg or 25 mg in combination with insulin, with or without metformin and/or sulfonylurea, demonstrated a placebo-adjusted mean difference from baseline A1C of -0.6% and -0.7%, respectively, at 18 weeks (p<0.0001, 0% adjusted mean change from baseline A1C 8.2% with placebo), and -0.5% and -0.7%, respectively, at 78 weeks (p<0.0001, 0.1% adjusted mean increase from baseline A1C 8.2% with placebo)

• **In patients with renal impairment:** In a randomized, double-blind, placebo-controlled, parallel-group study (n=738) of adults patients with type 2 diabetes and renal impairment, JARDIANCE 25 mg demonstrated a statistically significant placebo-adjusted mean difference from baseline A1C of -0.5%, in patients with mild (eGFR 60 to less than 90 mL/min/1.73 m2) to moderate (eGFR 30 to less than 60 mL/min/1.73 m2) renal impairment, at 24 weeks (p<0.0001)
o JARDIANCE 10 mg demonstrated a statistically significant placebo-adjusted mean difference from baseline AIC of -0.5% in patients with mild (eGFR 60 to less than 90 mL/min/1.73 m2) renal impairment at 24 weeks

Safety Information

• **CONTRAINDICATIONS**

JARDIANCE should not be used in patients with a history of serious hypersensitivity to JARDIANCE or in patients with severe renal impairment, end-stage renal disease, or dialysis.

• **WARNINGS AND PRECAUTIONS**

Hypotension: JARDIANCE causes intravascular volume contraction. Symptomatic hypotension may occur after initiating JARDIANCE, particularly in patients with renal impairment, the elderly, in patients with low systolic blood pressure, and in patients on diuretics. Before initiating JARDIANCE, assess for volume contraction and correct volume status if indicated. Monitor for signs and symptoms of hypotension after initiating therapy.

• Adverse reactions (excluding hypoglycemia) reported in ≥2% of patients treated with placebo, JARDIANCE 10 mg, or JARDIANCE 25 mg in pooled placebo-controlled clinical trials of JARDIANCE monotherapy or combination therapy included: urinary tract infection (7.6%, 9.3%, 7.6%), female genital mycotic infections (1.5%, 5.4%, 6.4%), upper respiratory tract infection (3.8%, 3.1%, 4.0%), increased urination (1.0%, 3.4%, 3.2%), dyslipidemia (3.4%, 3.9%, 2.9%), arthralgia (2.2%, 2.4%, 2.3%), male genital mycotic infections (0.4%, 3.1%, 1.6%), nausea (1.4%, 2.3%, 1.1%)

• In the pool placebo-controlled trials, adverse reactions related to volume depletion (e.g., blood pressure (ambulatory) decreased, blood pressure systolic decreased, dehydration, hypotension, hypovolemia, orthostatic hypotension, and syncope) were reported by 0.3%, 0.5%, and 0.3% of patients treated with placebo, JARDIANCE 10 mg, and JARDIANCE 25mg, respectively

Questions and Answers

Q: What are considered the advantages of Jardiance?
A: Lowest EGFR use and no bladder cancer, hyperkalemia or hepatic concerns.

Tradjenta® (linagliptin)

Indication and Important Limitations of Use

• TRADJENTA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

• TRADJENTA should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

• TRADJENTA has not been studied in patients with a history of pancreatitis.

ADA/EASD Position Statement
According to the 2012 ADA/EASD position statement, DPP-4 inhibitors are appropriate as monotherapy in cases where metformin is contraindicated. In addition, DPP-4 inhibitors are appropriate add-on options for dual or triple therapy if metformin monotherapy is not effective after ~3 months.

Executive Summary of TRADJENTA Efficacy and Safety Data
The efficacy and safety of TRADJENTA was evaluated in adults with type 2 diabetes mellitus in 10 double-blind, placebo-controlled studies in 3648 patients. Statistically significant A1C reductions as monotherapy and as add-on therapy to metformin, metformin and a sulfonylurea (SU), and basal insulin at 24 weeks.
• **Monotherapy:** In a randomized, double blind, placebo-controlled study of treatment-naïve and treatment-experienced adults patients with type 2 diabetes (n=503), TRADJENTA 5 mg/day demonstrated a placebo-adjusted mean difference from baseline A1C of -0.7% ($p<0.0001$, 0.3% adjusted mean increase from baseline A1C 8.0% with placebo)
• **Add-on to metformin:** In a randomized, double blind, placebo-controlled, parallel-group study of adult patients with type 2 diabetes with insufficient glycemic control despite metformin therapy (n=701), TRADJENTA 5 mg/day in combination with metformin provided a placebo-adjusted mean difference from baseline A1C of -0.6% ($p<0.0001$, 0.15% adjusted mean increase from baseline A1C 8.0% with placebo plus metformin)
• **Add-on to metformin and sulfonylurea:** In a randomized, double-blind, placebo-controlled, parallel-group study of adult patients with type 2 diabetes with insufficient glycemic control despite metformin and sulfonylurea combination therapy (n=1058), TRADJENTA 5 mg/day as an add-on to metformin and sulfonylurea therapy resulted in a placebo-adjusted mean difference from baseline A1C of -0.6% ($p<0.0001$, 0.1% adjusted mean decrease from baseline A1C of 8.1% with placebo plus metformin and a sulfonylurea)
• **Add-on to basal insulin:** In a randomized, double-blind, placebo-controlled, parallel-group study of adult patients with type 2 diabetes with insufficient glycemic control despite treatment with basal insulin therapy (n=1263), TRADJENTA 5 mg/day as an add-on to existing basal insulin with or without metformin and/or pioglitazone demonstrated a placebo-adjusted mean difference from baseline A1C of -0.7% ($p<0.0001$, 0.1% adjusted mean increase from baseline A1C 8.3% with placebo plus basal insulin)

SELECT SAFETY INFORMATION ABOUT TRADJENTA
CONTRAINDICATIONS
TRADJENTA is contraindicated in patients with a history of hypersensitivity reaction to linagliptin, such as anaphylaxis, angioedema, exfoliative skin conditions, urticaria, or bronchial hyperreactivity.

WARNINGS AND PRECAUTIONS
Pancreatitis
There have been postmarketing reports of acute pancreatitis, including fatal pancreatitis, in patients taking TRADJENTA. Take careful notice of potential signs and symptoms of pancreatitis. If pancreatitis is suspected, promptly discontinue TRADJENTA and initiate appropriate management. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using TRADJENTA.

Questions and Answers
There were no additional questions and answers.

Jentadueto® (linagliptin and metformin)
Indication and Important Limitations of Use
• JENTADUETO tablets are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both linagliptin and metformin is appropriate.
• JENTADUETO should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
• JENTADUETO has not been studied in patients with a history of pancreatitis.

ADA/EASD Position Statement
According to the 2012 ADA/EASD position statement, DPP-4 inhibitors are appropriate add-on options for dual or triple therapy if metformin monotherapy or dual combination therapy has not achieved or maintained an A1C target over ~ 3 months.

Executive Summary of JENTADUETO Efficacy and Safety Data

The coadministration of linagliptin and metformin was studied in patients with type 2 diabetes mellitus inadequately controlled on diet and exercise and in combination with sulfonylurea. There have been no clinical efficacy studies conducted with JENTADUETO; however, bioequivalence of JENTADUETO to linagliptin and metformin coadministered as individual tablets was demonstrated in healthy subjects. Statistically significant A1C reductions at 24 weeks with the initial combination of linagliptin and metformin.

• **Initial combination therapy with linagliptin and metformin:** In a randomized, double-blind, placebo-controlled, parallel-group study of drug-naïve or previously treated adults patients with type 2 diabetes (n=791), linagliptin 2.5 mg/metformin 1000 mg twice daily demonstrated a placebo-adjusted mean difference in A1C at 24 weeks of -1.7% and linagliptin 2.5 mg/metformin 500 mg twice daily resulted in a placebo-adjusted mean difference in A1C at 24 weeks of -1.3% (0.1% adjusted mean increase from baseline A1C 8.7% with placebo). The adjusted mean treatment difference in A1C from baseline to week 24 (LOCF) was -0.5% (95% CI -0.7, -0.3; p<0.0001) for linagliptin 2.5 mg/metformin 1000 mg twice daily compared to metformin 1000 mg twice daily; -1.1% (95% CI -1.4, -0.9; p<0.0001) for linagliptin 2.5 mg/metformin 1000 mg twice daily compared to linagliptin 5 mg once daily; -0.6% (95% CI -0.8, -0.4; p<0.0001) for linagliptin 2.5 mg/metformin 500 mg twice daily compared to metformin 500 mg twice daily; and -0.8% (95% CI -1.0, -0.6; p<0.0001) for linagliptin 2.5 mg/metformin 500 mg twice daily compared to linagliptin 5 mg once daily.

• **Initial combination with linagliptin and metformin versus linagliptin:** In a randomized, double-blind, study of adult patients with type 2 diabetes with insufficient glycemic control (A1C ≥8.5% to ≤12.0%) and no prior antidiabetic therapy for 12 weeks (n=316), linagliptin 5 mg/day in combination with metformin (1500 to 2000 mg per day) resulted in a statistically significant adjusted mean A1C difference of -0.84% compared to linagliptin 5 mg/day and placebo at 24 weeks (95% CI -1.23, -0.45; P<0.0001). Mean baseline A1C: 9.8% for linagliptin and metformin group; 9.9% linagliptin and placebo group.

SELECT SAFETY INFORMATION

WARNING: RISK OF LACTIC ACIDOSIS: Lactic acidosis is a rare, but serious, complication that can occur due to metformin accumulation. The risk increases with conditions such as renal impairment, sepsis, dehydration, excess alcohol intake, hepatic impairment, and acute congestive heart failure. The onset is often subtle, accompanied only by nonspecific symptoms such as malaise, myalgias, respiratory distress, increasing somnolence, and nonspecific abdominal distress. Laboratory abnormalities include low pH, increased anion gap, and elevated blood lactate. If acidosis is suspected, JENTADUETO should be discontinued and the patient hospitalized immediately.

CONTRAINDICATIONS

JENTADUETO is contraindicated in patients with:

• Renal impairment (e.g., serum creatinine ≥1.5 mg/dL for men or ≥1.4 mg/dL for women, or abnormal creatinine clearance).

• Acute or chronic metabolic acidosis, including diabetic ketoacidosis.

• A history of hypersensitivity reaction to linagliptin, such as anaphylaxis, angioedema, exfoliative skin conditions, urticaria, or bronchial hyperreactivity.

• Hypersensitivity to metformin.

Questions and Answers

There were no additional questions and answers.

Pradaxa® (dabigatran)

Statement of PRADAXA Indications and Usage

• to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation;

• for the treatment of deep venous thrombosis and pulmonary embolism in patients who have been treated with a parenteral anticoagulant for 5-10 days;

• to reduce the risk of recurrence of deep venous thrombosis and pulmonary embolism in patients who have been previously treated

SELECT SAFETY INFORMATION

WARNING: (A) PREMATURE DISCONTINUATION OF PRADAXA INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA (A) PREMATURE DISCONTINUATION OF PRADAXA INCREASES THE RISK OF THROMBOTIC EVENTS

Dosage and Administration

Non-valvular Atrial Fibrillation:

- For patients with CrCl >30 mL/min: 150 mg orally, twice daily
- For patients with CrCl 15-30 mL/min: 75 mg orally, twice daily

Treatment of DVT and PE:

- For patients with CrCl >30 mL/min: 150 mg orally, twice daily after 5-10 days of parenteral anticoagulation

Reduction in the Risk of Recurrence of DVT and PE:

- For patients with CrCl >30 mL/min: 150 mg orally, twice daily after previous treatment

FDA Drug Safety Communication: FDA study of Medicare patients finds risks lower for stroke and death but higher for gastrointestinal bleeding with Pradaxa (dabigatran) compared to warfarin [05-13-2014]
In its ongoing review of the blood thinner Pradaxa (dabigatran), the U.S. Food and Drug Administration (FDA) recently completed a new study in Medicare patients comparing Pradaxa to the blood thinner warfarin (Coumadin, Jantoven, and generics), for risk of ischemic or clot-related stroke, bleeding in the brain, major gastrointestinal (GI) bleeding, myocardial infarction (MI), and death. Pradaxa and warfarin are used to reduce the risk of stroke and blood clots in patients with a common type of abnormal heart rhythm called non-valvular atrial fibrillation (AF).

The new study included information from more than 134,000 Medicare patients, 65 years or older, and found that among new users of blood-thinning drugs, Pradaxa was associated with a lower risk of clot-related strokes, bleeding in the brain, and death, than warfarin. The study also found an increased risk of major gastrointestinal bleeding with use of Pradaxa as compared to warfarin. The MI risk was similar for the two drugs.

Importantly, the new study is based on a much larger and older patient population than those used in FDA's earlier review of post-market data, and employed a more sophisticated analytical method to capture and analyze the events of concern. This study's findings, except with regard to MI, are consistent with the clinical trial results that provided the basis for Pradaxa's approval.

As a result of our latest findings, we still consider Pradaxa to have a favorable benefit to risk profile and have made no changes to the current label or recommendations for use. Patients should not stop taking Pradaxa (or warfarin) without first talking with their health care professionals. Stopping the use of blood-thinning medications such as Pradaxa and warfarin can increase the risk of stroke and lead to permanent disability and death. Health care professionals who prescribe Pradaxa should continue to follow the dosing recommendations in the drug label.

Questions and Answers
There were no additional questions and answers.

XXVIII. Orexo – Did not present at the Forum but provided the update on Zubsolv below.
Richard Gustin, Ph.D., Medical Science Liaison

Zubsolv (buprenorphine and naloxone) sublingual tablet (CIII)
Indication: Zubsolv is indicated for the maintenance treatment of opioid dependence and should be used as part of a complete treatment plan to include counseling and psychosocial support.

Zubsolv has the same active components (buprenorphine/naloxone) as previously approved Suboxone sublingual tablets, but includes other features which may benefit patients, including:

- Higher bioavailability which requires 30% less buprenorphine per dose to reach bioequivalence
- Results from a clinical study, in 758 opioid dependent patients comparing Zubsolv and Suboxone film, found no difference in retention in treatment, COWS, SOWS, or opioid cravings at Day 15 (primary endpoint) and after a forced switch between treatments
- Fast dissolve time
- Higher overall preference (including taste, mouthfeel, and ease of administration) compared to Suboxone film in opioid dependent patients
- Packaged in F1 child-resistant unit dose packaging (F1 represents the most stringent testing criteria for child-resistant packaging)

Zubsolv sublingual tablet are currently available in three dosage strengths:

- buprenorphine/naloxone 1.4 mg/0.36 mg, white, triangular shape
- buprenorphine/naloxone 5.7 mg/1.4 mg, white, round shape
- buprenorphine/naloxone 8.6 mg/2.1 mg, white, diamond shape

Study OX219-006
Study OX219-006 was a randomized, non-inferiority, multicenter study to assess early treatment efficacy of Zubsolv versus Suboxone film and to explore switching between treatments. The primary endpoints were retention in treatment at Day 15 and Day 3. Secondary efficacy assessments included scores on the COWS and SOWS, and opioid cravings VAS, preference, and switching between Zubsolv and Suboxone film. 758 opioid dependent adult subjects were randomized. On days 1 and 2, patients received a blinded, fixed dose of Zubsolv (5.7/1.4 mg and 5.7/1.4 or 11.4/2.8 mg, respectively) or generic buprenorphine monotherapy (8 mg and 8 or 16 mg, respectively). On Day 3, the patients on generic buprenorphine were switched to Suboxone film and patients on Zubsolv continued to receive Zubsolv. Stabilization doses were titrated to a maximum daily dose of 17.1/4.2 mg and 24/6 mg for Zubsolv and Suboxone, respectively, based upon clinical symptoms. On Day 15, patients receiving Suboxone film were switched to Zubsolv and vice versa and the effect was assessed at Day 22. (Orexo Data on File OX219-006)

There were no statistically significant differences in retention in treatment at Day 15 with Zubsolv and Suboxone film in the per protocol set [Zubsolv arm: 83% (273/329); Suboxone film arm: 82.5% (269/326) (p=0.875)] or full analysis set [Zubsolv arm: 74.9% (287/383); Suboxone film arm: 74.4% (279/375) (p=0.866)]. Similar improvements for both groups were observed in COWS, SOWS, and opioid cravings VAS total scores.

At Day 15, 11.8% of patients in the Zubsolv group and 10.8% of patients in the film group experienced treatment-related adverse events. There were no serious treatment-related adverse events in either group. The most common treatment-related adverse events (≥1%) reported at Day 15 were: constipation (Zubsolv: 2.8%, film 3.5%), headache (Zubsolv: 1.4%, film 2.0%), nausea (Zubsolv: 1.4%%, film 0.3%), somnolence (Zubsolv: 1.4%, film 0.3%), dry mouth (Zubsolv: 0.6%, film 1.2%), and vomiting (Zubsolv: 1.1%, film 0.6%). (Orexo Data on File OX219-006)

Switch Phase – Days 15 to 22
After patients switched treatment, there were no significant differences in retention in treatment or clinical response as measured by COWS, SOWS, and opioid cravings. Of the patients who switched to Zubsolv from Suboxone film at Day 15, 6.1% withdrew by Day 22 compared to 8.7% of patients who withdrew after switching to Suboxone film from Zubsolv. Improvements from baseline were maintained for Zubsolv and Suboxone film on COWS, SOWS and craving VAS scores at day 22. (Orexo Data on File OX219-006)

Patient preference ratings favored ZUBSOLV; 78%, 73%, and 72% of patients preferred the taste, mouthfeel, and ease of administration, respectively, of ZUBSOLV vs Suboxone film on day 22 ($P<0.0001$ for each). In addition, Zubsolv received significantly higher ratings for overall preference (70%) vs Suboxone film (30%; $P<0.0001$).

No clinically significant differences in doses of Zubsolv or Suboxone film were observed. Following stabilization, mean buprenorphine doses prescribed on days 15 and 22 were lower in the Zubsolv group versus Suboxone film group, respectively (day 15: 10.8 mg vs 15.9 mg; day 22: 11.3 mg vs 16.0 mg). A greater percentage of patients in the Suboxone group required the maximum 24/6-mg dose on day 22 (21%) compared with the 17.1/4.2-mg maximum dose in the Zubsolv group (15%). Throughout the study, the mean buprenorphine dose for BNX sublingual tablet was 22% to 36% lower than for BNX film. (Orexo Data on File OX219-006)

GEORGIA DEPARTMENT OF COMMUNITY HEALTH

Manufacturers' Forum

ANNOUNCEMENT

NorthStar HealthCare Consulting
Georgia Department of Community Health

On behalf of the Georgia Department of Community Health (DCH) and in service to the Georgia Medicaid Fee-for-Service (FFS) Drug Utilization Review Board (DURB), NorthStar HealthCare Consulting (NHC), in conjunction with Catamaran, announces the Manufacturers' Forum occurring Thursday, April 30, 2015.

Date: **Thursday, April 30, 2015 from 9am-5pm EST**

Location: **NorthStar HealthCare Consulting**
1121 Alderman Drive, Suite 112
Alpharetta, GA 30005

Appointments: ***The Manufacturers' Forum is by appointment only*.** Appointments may be requested and will be scheduled ***after*** the Drugs Under Review are posted to the DCH website at **http://dch.georgia.gov/durb-meeting-information** approximately 30 days prior to the Forum. Manufacturers with drugs up for review at the current DURB meeting will be granted preference when seeking appointments. All requests for appointments must be made in writing to **GAMedicaid@nhc-llc.com** and include the drug name. New drug entities are generally not reviewed by the DURB until the drug has been on the market for at least 6 months.

Guidelines for Participation:

- To ensure equitable treatment of all manufacturers, individual manufacturer participation shall be limited to one 30-minute time segment per Forum. The presentation shall be limited to 20 minutes with 10 minutes for questions and answers.
- Manufacturer presentations may be audio-recorded for review after the Forum and the associated information shall be presented by NHC in summary fashion at regularly scheduled DURB meetings.
- For new drugs, manufacturers are highly encouraged to present all clinical information pertinent and relevant to current NHC clinical presentations to the DURB, to DCH drug benefit plan design as posted on the DCH website, and to other drugs within the class.
- For existing drugs, manufacturers are highly encouraged to present new clinical information since the drug was last reviewed by the DURB, especially clinical information related to comparisons of other drugs within the class.
- An electronic **one-page** summary (front only, font 10, not including references) of the presentation should be provided one week prior to the presentation via email to **GAMedicaid@nhc-llc.com** and please include a pronunciation guide of the drug's brand and generic names. The one-page summary along with relevant questions and answers related to the presentation will be provided to the DURB as well as published in the DURB meeting handout that is provided to the public at the meetings and on the DCH website at **http://dch.georgia.gov/durb-meeting-information**.

Comments and Inquiries:

- Manufacturers with comments or inquiries related to Georgia Medicaid FFS **Preferred Drug List, Prior Authorization Criteria, Manufacturers' Forum or DURB** should submit these in writing to **GAMedicaid@nhc-llc.com**.
- Manufacturers with comments or inquiries related to Georgia Medicaid FFS **supplemental rebates** should submit these in writing to **GAOffers@ghsinc.com**.
- Manufacturers with comments or inquiries related to Georgia Medicaid FFS **claims processing** or **drug benefit plan design** should submit these to the address or phone number below:

Catamaran, Inc.
Georgia Department of Community Health
Windward Fairways I, 3025 Windward Plaza Suite 200, Alpharetta, Georgia 30005
Phone: 770-776-2000 Fax: 770-776-2050

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Georgia Department of Community Health (GDCH)

Opportunities for Pharmaceutical Manufacturer Input on Clinical Recommendations and Clinical Management Strategies by the Drug Utilization Review Board

Clinical Information and Clinical Management Strategies relevant to the GDCH Medicaid Fee-For-Service program will be presented to the Drug Utilization Review Board (DURB) at each meeting through Catamaran by its vendor NorthStar HealthCare Consulting (NHC). Manufacturer input on recommendations is welcomed and appreciated using these opportunities. **Please note that new drug entities are generally not reviewed by the DURB until the drug has been on the market for at least 6 months.**

Ongoing Opportunity:

DUR Board Meeting Process: Drugs, therapeutic classes and/or supplemental rebate classes under review will be posted to the DCH website at **http://dch.georgia.gov/durb-meeting-information** approximately 30 days prior to the Manufacturers' Forum. Input specific to the drugs under review from manufacturers are made directly to NHC via **GAMedicaid@nhc-llc.com** and reported as appropriate by NHC at subsequent DURB meetings. NHC will pass relevant manufacturer-submitted electronic materials to the DURB members via a secure FTP site.

Upon review of information, and based on its expertise and discussions, the DURB makes recommendations to GDCH.

Presentation Opportunity:

Manufacturers' Forum: A forum prior to each relevant DURB meeting whereby manufacturers may present:

1) Clinical information relevant to a new drug on the market or a drug that is part of a therapeutic or supplemental rebate class under review by the DURB at the next meeting.

2) Clinical information relevant to ongoing NHC/Catamaran clinical management strategies (e.g. review of drug benefit plan designs, new drugs coming to market, new indications, etc.) as deemed necessary by NHC/Catamaran.

Please see the Manufacturers' Forum Announcement at **http://dch.georgia.gov/durb-meeting-information**.

Opportunity to Appeal to GDCH:

GDCH Review Process: DURB recommendations are reviewed by GDCH for final decisions. Manufacturers may request an appeal meeting for review directly with GDCH within 10 business days following DURB meetings. **Contact: Shirmary Hodges at (404) 656-4044 or shodges@dch.ga.gov**

Questions not addressed in this document may be sent to NorthStar HealthCare Consulting by e-mail: GAMedicaid@nhc-llc.com

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2015

Upcoming Meetings

Drug Utilization Review Board Meeting

2 Peachtree Street, N.W.

5th Floor Board Room

Atlanta, Georgia 30303

Thursday, June 4, 2015:	9:30am – 2:30pm
Thursday, September 24, 2015:	9:30am – 1:30pm
Tuesday, December 15, 2015:	9:30am – 1:30pm

Manufacturers' Forum

NorthStar HealthCare Consulting

1121 Alderman Drive

Suite 112

Alpharetta, Georgia 30005

Thursday, April 30, 2015:	9:00am – 5:00pm
Thursday, August 6, 2015:	9:00am – 5:00pm
Thursday, November 5, 2015:	9:00am – 5:00pm

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Drug Utilization Review Board

Board Member	Credentials	Specialty/Area of Expertise	Company Name
Drew A. Miller, Chair	R.Ph.	Retail Pharmacy	Wynn's Pharmacy
Gurinder J.S. Doad, Vice-Chair	M.D.	Family Practice	Southwest Georgia Family Medicine and Mercer University School of Medicine
Mia Avery	Pharm.D.	Oncology Pharmacy	Emory University Hospital Winship Cancer Institute
Ann R. Damon	Pharm.D.	Long Term Care Pharmacy	United Pharmacy Services
Deborah W. Fincher	R.Ph., M.S.	HIV/AIDS Pharmacy	Pride Medical Pharmacy
M. Celeste Fowler	Pharm.D., HCMBA	Hospital Pharmacy	Piedmont Henry Hospital
Thomas B. Gore	M.D.	Internal Medicine, Cardiology	Southern CardioPulmonary Associates
Robyn Lorys	Pharm.D.	Managed Care	Peach State Health Plan
J. Russell May	Pharm.D.	Academia - Professor	University of Georgia College of Pharmacy
Brent L. Rollins	R.Ph., Ph.D.	Academia - Professor	Philadelphia College of Osteopathic Medicine School of Pharmacy
Robert E. Shervette, III	M.D.	Child and Adolescent Psychiatry	Ogeechee Behavioral Health Services