



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

December 10, 2013





**GEORGIA DEPARTMENT
OF COMMUNITY HEALTH**

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**DRUG UTILIZATION REVIEW BOARD MEETING
AGENDA**

*2 Peachtree Street - 5th Floor DCH Board Room
Atlanta, Georgia 30303*

**Tuesday, December 10, 2013
9:30 a.m. to 1:30 p.m.**

CALL TO ORDER	<i>Laurel Ashworth, PharmD, Chair</i>
MEDICAID UPDATE	<i>Jerry Dubberly, PharmD, MBA, Chief</i>
ADDITIONAL COMMENTS FROM THE DEPARTMENT	<i>Linda Wiant, PharmD, Director</i>
MINUTES FROM PREVIOUS MEETING	<i>Chair</i>
CONSUMER COMMENTS SESSION	<i>Chair</i>
ADJOURNMENT OF OPEN SESSION	<i>Chair</i>
EXECUTIVE SESSION	
BREAK	
RECONVENING OF OPEN SESSION	<i>Chair</i>
CLINICAL REVIEW AND DURB VOTES	<i>Emily Baker, PharmD, BCPS, MBA, MHA Tara R. Cockerham, PharmD</i>
➤ Manufacturers' Forum	
➤ New Drug Reviews	
●Cometriq	●Invokana
●Cystaran	●Nesina
●Diclegis	●Pomalyst
●Fulyzaq	●Rescula
	●Signifor
	●Sirturo
	●Tecfidera
	●Vecamyl
➤ Utilization Trends Review	
➤ Drug Information Review	
●Drug Update Newsletter	●Patent Expiration Report
●Horizon Watch Report	●Clinical Compass Newsletter
FUTURE AGENDA ITEMS	<i>Chair</i>
ADJOURNMENT	<i>Chair</i>





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**Department of Community Health
Drug Utilization Review Board (DURB)
MINUTES
Thursday, September 19, 2013**

MEMBERS PRESENT

Laurel E. Ashworth, Pharm.D., Chair
Joseph R. Bona, M.D., MBA, Vice-Chair
Karen L. Carter, M.D.
Deborah W. Fincher, M.S., R.Ph.
Thomas B. Gore, M.D.
John Greeson, M.D., MBA
Edwina L. Jones, Pharm.D.
Robyn Lorys, Pharm.D.
J. Russell May, Pharm.D.
Osgood (Drew) A. Miller, R.Ph.
Sandra L. White, M.D., MBA, FACR
Mary Virginia "Ginny" Yates, Pharm.D.

MEMBERS ABSENT

Paul D. Boyce, M.D.
Ann R. Damon, Pharm.D.
Rondell C. Jagers, Pharm.D.
Donald A. Paul, M.D.
Matthew Perri, III, R.Ph., Ph.D.

Staff

Heather Bond, Deputy Director, Policy and Provider Services
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
Peter Nguyen, Pharm. D. Candidate

NorthStar HealthCare Consulting

Emily Baker, Pharm.D., BCPS, MHA, MBA, President
Tara R. Cockerham, Pharm.D., Clinical Programs Director
Elizabeth Flores, Pharm.D., Clinical Pharmacist

Catamaran

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 (DUR Board) held its third meeting for the calendar year on September 19, 2013. The Chair, Laurel E. Ashworth, Pharm.D., called the meeting to order at 9:39am.

Comments from the Department

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

1. **Pharmacy Students** – Mercer student, Peter Nguyen and University of Georgia students, Michelle Eun, Kristey Alspaugh and Stephanie Hoge were welcomed.
2. **DUR Board** – Appreciation was expressed for the following members who were rotating off of the Board: Paul D. Boyce, M.D., Melissa D. Carter, J.D., Carl Ellis, R.Ph., Laurel E. Ashworth, Pharm.D (*term ends December 2013*), Karen L. Carter, M.D., Rondell C. Jagers, Pharm.D., Matthew Perri, III, R.Ph., Ph.D., and J. Russell May, Pharm.D. The Department is seeking nominations for a consumer advocate.

Minutes from the Previous Meeting

Dr. Ashworth asked for comments regarding the minutes from the June 6, 2013 meeting. There were no corrections. A motion was made (Joseph R. Bona, M.D., MBA, Vice-Chair), seconded (J. Russell May, Pharm.D.), and carried to approve the minutes as written.

Guest Expert Speaker

Michael Gordon, M.D. spoke on addiction treatment. He addressed questions from the Board regarding State Composite Board regulation, formulations of buprenorphine, length of therapy, tolerance, bioavailability and abuse. The Board also discussed the lack of coverage for psychotherapeutic services.

Consumer Comments Session

There were no consumer 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 USCS1396R-8B3D. The individuals recorded in attendance were from the Department of Community Health, Goold Health Services, NorthStar HealthCare Consulting, and Catamaran. Peter Nguyen (DCH pharmacy intern/Mercer University student), and Michelle Eun, Kristey Alspaugh and Stephanie Hoge (UGA students) attended the closed session with the Board members. A motion was made by Sandra L. White, M.D., MBA, FACR, and seconded by Osgood (Drew) A. Miller, R.Ph., to adjourn the open session and approve the closed session. There was a unanimous vote approving the closed session. The Chairman, Dr. Laurel Ashworth, adjourned the open session at approximately 10:13am, at which time members reconvened for the Executive (closed) Session.

Executive Session

The Executive Session was held from 10:19am to 10:52am.

Reconvening of Open Session

The DUR Board reconvened for the open session at 11:06am.

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 ten (10) manufacturers participated and provided information regarding the following drugs discussed at the September, 2013 DUR Board meeting:

Manufacturers	Drugs
GlaxoSmithKline	Relenza
Aegerion	Juxtapid
Hyperion	Ravicti
Bristol-Myers Squibb and Pfizer	Eliquis
Amarin	Vascepa
Eisai	Belviq
Sunovion	Latuda
Orexo	Zubsolv
Reckitt Benckiser	Suboxone Film

There were no questions or comments. The next forum will be held on Thursday, November 7, 2013 from 9am-5pm at the NorthStar Healthcare Consulting office: 1121 Alderman Drive, Suite 112, Alpharetta, GA 30005.

Therapeutic Class Review

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

Therapeutic Class Name
Buprenorphine-Naloxone Agents

Guest Expert Speaker

Jennifer Casarella, M.D. spoke about treatments for opioid dependence. She addressed questions from the Board and provided comments on the different formulations, place in therapy for Zubsolv, length of therapy, psychosocial treatment, maintenance dosing, drug screening and pain management treatment.

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
Anticoagulant	<i>Eliquis</i>	Tara Cockerham, Pharm.D.
Short Bowel Syndrome Agent	<i>Gattex</i>	Elizabeth Flores, Pharm.D.
Antihyperlipidemic	<i>Juxtapid</i>	Elizabeth Flores, Pharm.D.
Antihyperlipidemic	<i>Kynamro</i>	Elizabeth Flores, Pharm.D.
Urea Cycle Disorder Agent	<i>Ravicti</i>	Elizabeth Flores, Pharm.D.
Antihypertriglyceridemic	<i>Vascepa</i>	Elizabeth Flores, Pharm.D.

The Board discussed the drug information, provided comments, and raised questions about the following medications:

- Eliquis – antidotes for newer anticoagulants; no major differences between newer products; for difficult-controlled warfarin patients, newer agents may have a role; pregnancy category
- Gattex – off label usage
- Ravicti – prescriber restriction and education; hidden costs (G-tubes, surgery)

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

Therapeutic Class Review

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

Therapeutic Class Name
Influenza Agents

Subgroup Analysis for Atypical Antipsychotic Long-Acting Injectables

Dr. Bona reported that the subgroup committee has put together a comprehensive data analysis plan to look at outcomes in terms of the clinical and economic value of the atypical antipsychotic long-acting injectables.

Utilization Trends 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

Department of Community Health
Drug Utilization Review Board (DURB)
MINUTES

Thursday, September 19, 2013

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

Future Agenda Items

There were no future agenda items noted.

Upcoming Meetings

The following dates for upcoming meetings were published in the DUR Board binder:

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

Tuesday, December 10, 2013

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

Thursday, November 7, 2013

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

Anticoagulant

The DUR Board recommended *Non-Preferred* status with *Prior Authorization* for *Eliquis*[®] (*Oral*) *Tablet*. The DUR Board also recommended *Preferred* status for *Coumadin*[®] (*Oral*) *Tablet*.

Short Bowel Syndrome

The DUR Board recommended *Non-Preferred* status with *Prior Authorization* for *Gattex*[®] (*Subcutaneous*) *Kit*.

Antihyperlipidemics for Homozygous Familial Hypercholesterolemia

The DUR Board recommended *Non-Preferred* status with *Prior Authorization* for *Juxtapid™ (Oral) Capsule* and *Kynamro® (Subcutaneous) Syringe*.

Urea Cycle Disorder

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

Antihyperlipidemic for Hypertriglyceridemia

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

Therapeutic Class Reviews

The following classes were reviewed with recommendations for changes in PDL status for the following drugs.

Analgesics, Opioid Abuse, Buprenorphine-Naloxone Agents

The DUR Board recommended *Preferred* status with *Prior Authorization* for *Zubsolv® (Sublingual) Tablet*.

Antivirals, Influenza Agents

The DUR Board recommended *Non-Preferred* status for *Rimantadine (Oral) Tablet*.

Conclusion

At the conclusion of the reconvened open session and no other business for discussion, Chair Ashworth adjourned the meeting at 1:22pm.

THESE MINUTES ARE HEREBY APPROVED AND ADOPTED, THIS THE _____
DAY OF _____, 2013.

Laurel Ashworth, Pharm.D., Chair

Drug Utilization Review Board

Motions - Votes

New Drugs

September 19, 2013

ANTICOAGULANTS, ORAL (New Drug Review)				Attachment A		
Motion:		Drug	PDL Status			
		<i>Eliquis® (Oral) Tablet</i>	NP/PA			
		<i>Coumadin® (Oral) Tablet</i>	P			
Board Members - Present		Motion Maker (√)	Seconded By (√)	VOTES		
				YES (√)	NO (√)	ABSTAIN (√)
1	Ashworth, Laurel E. Pharm.D. - Chair			√		
2	Bona, Joseph R. M.D. - Co-Chair			√		
3	Carter, Karen L., M.D.	√		√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Gore, Thomas B., M.D.			√		
6	Greeson, John D., M.D., MBA			√		
7	Jones, Edwina L., Pharm.D., MBA			√		
8	Lorys, Robyn Pharm.D.			√		
9	May, J. Russell, Pharm.D.			√		
10	Miller, Osgood (Drew) A. R.Ph.		√ (Coumadin)	√		
11	White, Sandra L., M.D., MBA, FACR		√ (Eliquis)	√		
12	Yates, Mary Virginia "Ginny", Pharm.D.			√		
TOTAL				12	0	0
Board Members - Absent						
1	Boyce, Paul D., M.D.					
2	Damon, Ann R., Pharm.D.					
3	Jaggers, Rondell C., Pharm.D.					
4	Paul, Donald A., M.D.					
5	Perri, III, Matthew, R,Ph., Ph.D.					

Drug Utilization Review Board

Motions - Votes

New Drugs

September 19, 2013

SHORT BOWEL SYNDROME, AGENTS (New Drug Review)						
Motion:		Drug	PDL Status			
		Gattex [®] (Subcutaneous) Kit	NP/PA			
Board Members - Present		Motion Maker (✓)	Seconded By (✓)	VOTES		
				YES (✓)	NO (✓)	ABSTAIN (✓)
1	Ashworth, Laurel E. Pharm.D. - Chair			✓		
2	Bona, Joseph R. M.D. - Co-Chair			✓		
3	Carter, Karen L., M.D.			✓		
4	Fincher, Deborah W., M.S., R.Ph.			✓		
5	Gore, Thomas B., M.D.			✓		
6	Greeson, John D., M.D., MBA			✓		
7	Jones, Edwina L., Pharm.D., MBA			✓		
8	Lorys, Robyn Pharm.D.			✓		
9	May, J. Russell, Pharm.D.		✓	✓		
10	Miller, Osgood (Drew) A. R.Ph.	✓		✓		
11	White, Sandra L., M.D., MBA, FACR			✓		
12	Yates, Mary Virginia "Ginny", Pharm.D.			✓		
TOTAL				12	0	0
Board Members - Absent						
1	Boyce, Paul D., M.D.					
2	Damon, Ann R., Pharm.D.					
3	Jaggers, Rondell C., Pharm.D.					
4	Paul, Donald A., M.D.					
5	Perri, III, Matthew, R,Ph., Ph.D.					

Drug Utilization Review Board

Motions - Votes

New Drugs

September 19, 2013

ANTIHYPERLIPIDEMICS for HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (New Drug Review)						
Motion:		Drug	PDL Status			
		<i>Juxtapid™ (Oral) Capsule</i>	NP/PA			
		<i>Kynamro® (Subcutaneous) Syringe</i>	NP/PA			
Board Members - Present		Motion Maker (v)	Seconded By (v)	VOTES		
				YES (v)	NO (v)	ABSTAIN (v)
1	Ashworth, Laurel E. Pharm.D. - Chair			√		
2	Bona, Joseph R. M.D. - Co-Chair			√		
3	Carter, Karen L., M.D.			√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Gore, Thomas B., M.D.			√		
6	Greeson, John D., M.D., MBA		√	√		
7	Jones, Edwina L., Pharm.D., MBA	√		√		
8	Lorys, Robyn Pharm.D.			√		
9	May, J. Russell, Pharm.D.			√		
10	Miller, Osgood (Drew) A. R.Ph.			√		
11	White, Sandra L., M.D., MBA, FACR			√		
12	Yates, Mary Virginia "Ginny", Pharm.D.			√		
TOTAL				12	0	0
Board Members - Absent						
1	Boyce, Paul D., M.D.					
2	Damon, Ann R., Pharm.D.					
3	Jaggers, Rondell C., Pharm.D.					
4	Paul, Donald A., M.D.					
5	Perri, III, Matthew, R,Ph., Ph.D.					

Drug Utilization Review Board

Motions - Votes

New Drugs

September 19, 2013

UREA CYCLE DISORDER AGENTS (New Drug Review)						
Motion:		Drug	PDL Status			
Board Members - Present		Ravicti® (Oral) Liquid	NP/PA	VOTES		
		Motion Maker (v)	Seconded By (v)	YES (v)	NO (v)	ABSTAIN (v)
1	Ashworth, Laurel E. Pharm.D. - Chair			√		
2	Bona, Joseph R. M.D. - Co-Chair			√		
3	Carter, Karen L., M.D.	√		√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Gore, Thomas B., M.D.			√		
6	Greeson, John D., M.D., MBA			√		
7	Jones, Edwina L., Pharm.D., MBA			√		
8	Lorys, Robyn Pharm.D.		√	√		
9	May, J. Russell, Pharm.D.			√		
10	Miller, Osgood (Drew) A. R.Ph.			√		
11	White, Sandra L., M.D., MBA, FACR			√		
12	Yates, Mary Virginia "Ginny", Pharm.D.			√		
TOTAL				12	0	0
Board Members - Absent						
1	Boyce, Paul D., M.D.					
2	Damon, Ann R., Pharm.D.					
3	Jaggers, Rondell C., Pharm.D.					
4	Paul, Donald A., M.D.					
5	Perri, III, Matthew, R,Ph., Ph.D.					

Drug Utilization Review Board

Motions - Votes

New Drugs

September 19, 2013

ANTIHYPERLIPIDEMICS - HYPERTRIGLYCERIDEMIA (New Drug Review)						
Motion:		Drug	PDL Status			
		<i>Vascepa® (Oral) Capsule</i>	NP/PA			
Board Members - Present		Motion Maker (✓)	Seconded By (✓)	VOTES		
				YES (✓)	NO (✓)	ABSTAIN (✓)
1	Ashworth, Laurel E. Pharm.D. - Chair			✓		
2	Bona, Joseph R. M.D. - Co-Chair			✓		
3	Carter, Karen L., M.D.			✓		
4	Fincher, Deborah W., M.S., R.Ph.			✓		
5	Gore, Thomas B., M.D.	✓		✓		
6	Greeson, John D., M.D., MBA		✓	✓		
7	Jones, Edwina L., Pharm.D., MBA			✓		
8	Lorys, Robyn Pharm.D.			✓		
9	May, J. Russell, Pharm.D.			✓		
10	Miller, Osgood (Drew) A. R.Ph.			✓		
11	White, Sandra L., M.D., MBA, FACR			✓		
12	Yates, Mary Virginia "Ginny", Pharm.D.			✓		
TOTAL				12	0	0
Board Members - Absent						
1	Boyce, Paul D., M.D.					
2	Damon, Ann R., Pharm.D.					
3	Jaggers, Rondell C., Pharm.D.					
4	Paul, Donald A., M.D.					
5	Perri, III, Matthew, R,Ph., Ph.D.					

Drug Utilization Review Board

Motions-Votes

Class Review

September 19, 2013

ANALGESICS, OPIOID ABUSE						
Motion:		Drug	PDL Status			
		Zubsolv® (Sublingual) Tablet	P/PA	VOTES		
Board Members - Present	Motion Maker (v)	Seconded By (v)	YES (v)	NO (v)	ABSTAIN (v)	
1 Ashworth, Laurel E. Pharm.D. - Chair			√			
2 Bona, Joseph R. M.D. - Co-Chair			√			
3 Carter, Karen L., M.D.			√			
4 Fincher, Deborah W., M.S., R.Ph.			√			
5 Gore, Thomas B., M.D.			√			
6 Greeson, John D., M.D., MBA			√			
7 Jones, Edwina L., Pharm.D., MBA			√			
8 Lorys, Robyn Pharm.D.			√			
9 May, J. Russell, Pharm.D.	√		√			
10 Miller, Osgood (Drew) A. R.Ph.			√			
11 White, Sandra L., M.D., MBA, FACR			√			
12 Yates, Mary Virginia "Ginny", Pharm.D.			√			
TOTAL			12	0	0	
Board Members - Absent						
1 Boyce, Paul D., M.D.						
2 Damon, Ann R., Pharm.D.						
3 Jagers, Rondell C., Pharm.D.						
4 Paul, Donald A., M.D.						
5 Perri, III, Matthew, R.Ph., Ph.D.						

Drug Utilization Review Board

Motions-Votes

Class Review

September 19, 2013

ANTIVIRALS, INFLUENZA AGENTS						
Motion:		Drug	PDL Status			
		<i>Rimantadine (Oral) Tablet</i>	NP			
Board Members - Present		Motion Maker (v)	Seconded By (v)	VOTES		
				YES (v)	NO (v)	ABSTAIN (v)
1	Ashworth, Laurel E. Pharm.D. - Chair			√		
2	Bona, Joseph R. M.D. - Co-Chair			√		
3	Carter, Karen L., M.D.			√		
4	Fincher, Deborah W., M.S., R.Ph.			√		
5	Gore, Thomas B., M.D.			√		
6	Greeson, John D., M.D., MBA			√		
7	Jones, Edwina L., Pharm.D., MBA	√		√		
8	Lorys, Robyn Pharm.D.			√		
9	May, J. Russell, Pharm.D.			√		
10	Miller, Osgood (Drew) A. R.Ph.			√		
11	White, Sandra L., M.D., MBA, FACR			√		
12	Yates, Mary Virginia "Ginny", Pharm.D.		√	√		
			TOTAL	12	0	0
Board Members - Absent						
1	Boyce, Paul D., M.D.					
2	Damon, Ann R., Pharm.D.					
3	Jaggers, Rondell C., Pharm.D.					
4	Paul, Donald A., M.D.					
5	Perri, III, Matthew, R,Ph., Ph.D.					

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Manufacturers' Forum Manufacturer Presentations

Dates: November 7, 2013

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

Dan Alday, RPh, Director, Clinical Programs & Analytics

Catamaran Health Solutions

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). For the drugs presented at the Forum, the information is highlighted below. 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. Duchesnay

Eugene G. Kelly, BS, Director, Scientific Affairs and Medical Communication

John Ross, Viking, Director of National Accounts and Governments Affairs

Diclegis® (doxylamine succinate/pyridoxine hydrochloride tablets)

Pronunciation: Diclegis (dye-CLEE-gis)/doxylamine succinate/pyridoxine hydrochloride (dok-sil'ă-mĕn sŭk'si-năt/piri'dăk,sĕn HYE droe KLOR ide)

- Therapeutic Class: Nausea and Vomiting of Pregnancy (NVP)
- Dosage Form: Delayed-release white, round, film coated tablets containing 10 mg doxylamine succinate and 10 mg pyridoxine hydrochloride. The delayed-release allows for continuous pharmacotherapeutic effect, controlling nausea and vomiting symptoms that occur in the morning, throughout the day and into the night.

Approved Indications

- **Diclegis** is indicated for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management.
- **Diclegis** has not been studied in women with hyperemesis gravidarum.

Nausea and Vomiting of Pregnancy (NVP)

- **NVP** is a common condition affecting 70–85% of pregnant women. NVP typically occurs during first trimester and last 4 to 6 weeks. Nausea and vomiting of Pregnancy is a unique condition because it can affect the health of both a pregnant woman and her fetus.
- Initial management of NVP includes rest, avoidance of sensory stimuli that may provoke symptoms, frequent, small meals, avoiding spicy or fatty foods; eliminating pills with iron, eating bland or dry foods, high-protein snacks, and crackers in the morning before arising.

Efficacy & Safety

- The safety and efficacy of **Diclegis** were compared to placebo in a two week, double-blind, randomized, multi-center trial in 261 women with NVP. The mean gestational age at enrollment was 9.3 weeks. Women in this trial had failed conservative management, and typically had symptoms for 4 weeks prior to enrolling. The women experienced on average 6 hours of nausea plus 4 episodes of retching and 2 episodes of vomiting each day. **Diclegis** efficacy was significantly superior to placebo, with 19% of **Diclegis**-treated women reporting no symptoms on day two, and another 21% reporting no symptoms by day 3. At day 15, women on **Diclegis** reported no symptoms for 2 of the 3 dimensions of the PUQE score (Nausea, Vomiting, Retching) and mild symptoms for the third.
- The most common side effect of **Diclegis** is drowsiness. No other adverse reactions occurred at an incidence ≥ 5 percent and exceeded the incidence for placebo.
- **Diclegis** should be used with caution in women who have: (1) asthma, (2) increased pressure in the eye, (3) an eye problem called narrow angle glaucoma, (4) a stomach problem called stenosing peptic ulcer, (5) pyloroduodenal obstruction, or (6) a bladder problem called bladder-neck obstruction.
- **Diclegis** is the only FDA-approved treatment of NVP, and carries a Pregnancy Category A safety rating. **Diclegis** is supported by the results of multiple clinical trials in pregnant women and epidemiological studies specifically designed to detect possible teratogenicity.

Questions and Answers

Q: How are other Medicaid plans covering?

A: TennCare requires pregnancy only. Most prescribers are using as last resort.

Q: What are the usual conservative methods tried?

A: Small frequent meals, increase intake of protein, avoid smells, ginger/gingerale and sea-bands.

Q: What is the average duration of use?

A: OB/GYNs tend to write one prescription for 14 days supply with most prescriptions being written for a quantity of 60 tablets.

Q: It seems the Food and Drug Administration (FDA) has determined that previous teratogenic reports were invalid.

A: Yes, the FDA has determined the previous product, Bendectin, was not teratogenic and the FDA published in the Federal Registry that the previous product was not pulled from the market due to safety or efficacy concerns. The previous product was withdrawn from the market by the previous manufacturer due to the cost of defending litigation.

II. Biogen

Jerrica L. Dodd, PharmD, MS, Sr. Medical and Outcomes Science Liaison

Glenn G. Tropf, Regional Account Manager

Tecfidera™ (dimethyl fumarate delayed-release capsules)

Pronunciation: Tecfidera (tech-fi-der-a)/dimethyl fumarate (dye-METH-il FUE-ma-rate)

- TECFIDERA (dimethyl fumarate) is an oral medication which was approved in March 2013 by the FDA for the treatment of patients with relapsing forms of multiple sclerosis (MS).

Clinical Trials

The efficacy and safety of TECFIDERA were demonstrated 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. The TID dose showed no additional benefit over the BID dose and the approved TECFIDERA dose according to the package insert is BID. The BID results are presented below.

- Annualized Relapse Rate (ARR)
 - DEFINE: The ARR over 2 years was 0.17 in the TECFIDERA BID group and 0.36 in the placebo group, corresponding to a relative reduction of 53% ($P < 0.001$) compared with placebo.
 - CONFIRM: The ARR over 2 years was 0.22 in the TECFIDERA BID group and 0.40 in the placebo group, corresponding to a relative reduction at 2 years of 44%, compared with placebo ($P < 0.001$).
 - In a pre-specified integrated analysis that included DEFINE and CONFIRM, TECFIDERA demonstrated a reduction of 49% over placebo in ARR over two years (0.191 for TECFIDERA and 0.371 for placebo) ($P < 0.0001$).
- Proportion of Patients Relapsing

- DEFINE: The proportion of patients relapsed at 2 years was 27% in the TECFIDERA BID group compared with 46% in the placebo group. These results represented a relative reduction in the risk of relapse at 2 years in the TECFIDERA BID group of 49% ($P < 0.001$) compared with placebo.
- CONFIRM: The proportion of patients relapsed at 2 years was 29% in the TECFIDERA BID group compared with 41% in the placebo group. These results represented a relative reduction in the risk of relapse at 2 years in the TECFIDERA BID group of 34% ($P = 0.002$) compared with placebo.
- In a pre-specified integrated analysis that included DEFINE and CONFIRM, TECFIDERA demonstrated a reduction of 43% over placebo in the proportion of patients relapsed at two years (28% for TECFIDERA vs. 44% placebo) ($P < 0.0001$).
- Risk of Disability Progression
 - DEFINE: The proportion of patients who progressed by 2 years was 16% in the TECFIDERA BID group and 27% in the placebo group, representing a relative reduction in the risk of confirmed (12-week) disability progression at 2 years over placebo of 38% ($P = 0.005$).
 - CONFIRM: The proportion of patients who progressed by 2 years was 13% in the TECFIDERA BID group and 17% in the placebo group, representing a relative reduction in the risk of confirmed (12-week) disability progression at 2 years over placebo of 21% ($P = 0.25$). This reduction was not statistically significant.
 - In a pre-specified integrated analysis that included DEFINE and CONFIRM, TECFIDERA demonstrated significant reduction of 32% (15% for TECFIDERA vs. 22% for placebo) ($P = 0.0034$) for TECFIDERA BID over placebo in the risk of confirmed (12-week) disability progression at 2 years.
- Reduction in the number of lesions as measured by MRI
 - DEFINE: The adjusted mean number of new or newly enlarging T2 hyperintense lesions over 2 years was 17.0 and 2.6 in the placebo and TECFIDERA groups, respectively, corresponding to a significant reduction of 85% ($P < 0.001$) relative to placebo. The mean number of new T1 hypointense lesions over the 2-year study period was 5.6 and 1.5 for placebo and the TECFIDERA group, respectively, corresponding to a 72% significant reduction relative to placebo ($P < 0.0001$). The mean number of Gd-enhancing lesions at 2 years was 1.8 and 0.1 in the placebo and TECFIDERA groups, respectively, corresponding to a significant relative odds reduction of 90% ($P < 0.001$) with TECFIDERA as compared to placebo.
 - CONFIRM: The adjusted mean number of new or newly enlarging T2 hyperintense lesions that developed in patients receiving placebo and TECFIDERA was 17.4 and 5.1, respectively, corresponding to a significant reduction of 71% for TECFIDERA relative to placebo ($P < 0.001$). The mean number of new T1 hypointense lesions over the 2-year study period.
 - For reactive use only in response to unsolicited request. TF-US-0225 was 7.0 and 3.0 in the placebo and TECFIDERA group, respectively, corresponding to a 57% significant reduction relative to placebo ($P < 0.001$). The mean number of Gd-enhancing lesions at 2 years was 2.0 and 0.5 in the placebo and TECFIDERA groups, respectively, corresponding to a significant relative odds reduction of 74% ($P < 0.001$) with TECFIDERA as compared to placebo.

Additional Outcomes

- Patients treated with TECFIDERA experienced significant improvements in physical health and functioning and trending improvements in mental health 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 relapse requiring IV steroids at 2 years was 52% and 44% vs. placebo in DEFINE and CONFIRM, respectively ($P < 0.0001$ and $P = 0.0002$ vs placebo).
- Reductions in the adjusted annualized rate of MS-related hospitalizations at 2 years compared with placebo were 35% and 32% in DEFINE and CONFIRM, respectively ($P = 0.0708$ and $P = 0.1092$ vs placebo).

Warnings and Precautions

- Lymphopenia
- Flushing

Adverse Reactions

- The most common adverse reactions (incidence $\geq 10\%$ overall and $\geq 2\%$ vs. placebo) were flushing, abdominal pain, diarrhea, and nausea.

Questions and Answers

Q: What are considered the advantages of Tecfidera over other oral medications for MS given there are not any head-to-head studies?

A: Adverse events are not as serious and can be treated, three-fourths of MS patients are women who can use if needed while pregnant, and Tecfidera represents 25% of all new prescriptions (2nd to Copaxone) and 12% of all prescriptions for MS.

Q: What is the price of the starter kit?

A: It is priced at parity.

Q: Is there a limited distribution?

A: Availability is through 16 specialty pharmacies.

Q: What were the most common reasons for discontinuations in the clinical trials?

A: Flushing, diarrhea and the other gastrointestinal (GI) adverse events.

Q: Are you finding most prescribers are using the 120mg for 1 month instead of 7 days before titrating up to the 240mg strength?

A: Yes, though this is not FDA approved.

III. Takeda

Charlie Kelly, PharmD, Regional Scientific Manager

Jennifer Hooks, Regional Account Manager

Nesina[®] (alogliptin tablets)

Pronunciation: Nesina (nes-see'-na)/alogliptin (al-oh-GLIP-tin)

Indication

NESINA is a dipeptidyl peptidase-4 inhibitor (DPP-4) indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

How Supplied

6.25, 12.5, and 25 mg tablets

Dosage and Administration

Recommended dose: 25 mg once daily, as monotherapy or combination therapy. Adjust dose for patients with moderate renal impairment (CrCl \geq 30 to $<$ 60 mL/min; 12.5 mg/day), and severe renal impairment or end-stage renal disease (CrCl $>$ 15 to $<$ 30 mL/min or CrCl $<$ 15 mL/min or requiring hemodialysis, respectively; 6.25 mg/day).

Contraindications

NESINA is contraindicated in patients with a history of serious hypersensitivity reaction to alogliptin-containing products, such as anaphylaxis, angioedema or severe cutaneous adverse reactions.

Warnings and Precautions

- There have been postmarketing reports of acute pancreatitis in patients taking NESINA. If pancreatitis is suspected, promptly discontinue NESINA.
- There have been postmarketing reports of serious hypersensitivity reactions in patients treated with NESINA such as anaphylaxis, angioedema and severe cutaneous adverse reactions. In such cases, promptly discontinue NESINA, assess for other potential causes, institute appropriate monitoring and treatment, and initiate alternative treatment for diabetes.
- Postmarketing reports of hepatic failure, sometimes fatal. Causality cannot be excluded. If liver injury is detected, promptly interrupt NESINA and assess patient for probable cause, then treat cause if possible, to resolution or stabilization. Do not restart NESINA if liver injury is confirmed and no alternative etiology can be found.
- A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with NESINA.
- There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with NESINA or any other antidiabetic drug.

Efficacy

A total of 8673 patients with type 2 diabetes were randomized in 10 double-blind, placebo- or active-controlled clinical safety and efficacy studies conducted to evaluate the effects of NESINA on glycemic control. In patients with type 2 diabetes, treatment with NESINA produced clinically meaningful and statistically significant improvements in

glycosylated hemoglobin A1C (A1C) compared to placebo in pivotal studies (Table). As is typical for trials of agents to treat type 2 diabetes, the mean reduction in A1C with NESINA appears to be related to the degree of A1C elevation at baseline. Improvements in A1C were not affected by gender, age, or baseline body mass index.

Table: Baseline and Mean Change From Baseline in A1C (%) at Week 26

Study	Parameter	Mean Baseline A1C (%)	Adjusted Mean Change from Baseline A1C (%)
Monotherapy Study	NESINA 25 mg (n = 128)	7.9	- 0.6
	Placebo (n = 63)	8.0	0
Combination Study 1	NESINA 25 mg + metformin (n = 203)	7.9	- 0.6
	Placebo + metformin (n = 103)	8.0	- 0.1
Combination Study 2	NESINA 25 mg + pioglitazone ± metformin ± sulfonylurea (n = 195)	8	- 0.8
	Placebo + pioglitazone ± metformin ± sulfonylurea (n = 95)	8	- 0.2
Combination Study 3	NESINA 25 mg + glyburide (n = 197)	8.1	- 0.5
	Placebo + glyburide (n = 97)	8.2	0
Combination Study 4	NESINA 25 mg + insulin ± metformin (n = 126)	9.3	- 0.7
	Placebo + insulin ± metformin (n = 126)	9.3	- 0.1

Abbreviation: A1C, glycosylated hemoglobin A1C. ^aLeast squares mean values.

Most Common Adverse Reactions

Approximately 8500 patients with type 2 diabetes have been treated with NESINA in randomized, double-blind controlled clinical trials. The most common adverse reactions reported in ≥ 4% of patients treated with NESINA 25 mg and more frequently than in patients who received placebo were: nasopharyngitis (4.4%), headache (4.2%) and upper respiratory tract infection (4.2%).

Questions and Answers

Q: What are considered the advantages of Nesina over other DPP-4 inhibitors given there are not any head-to-head trials?

A: Higher selectivity for DPP-4 receptor so can have less adverse events, no clinically significant drug-drug interactions and safe in cardiovascular patients.

Q: What was the incidence of pancreatitis in the clinical trials?

A: 0.2%.

Q: Are any additional studies being conducted?

A: Kaiser is conducting a study looking at pancreatitis.

Q: What was the incidence of skin lesions in the clinical trials?

A: 0.4%.

IV. Johnson & Johnson

Megan L. Jones, PharmD, MPA, Senior Liaison, Health Economics & Outcomes Research

J. Leigh Faircloth, Strategic Market Director

Invokana™ (canagliflozin tablets)

Pronunciation: Invokana (in-vo-KAHN-uh)/canagliflozin (kan" a gli floe' zin)

Product Description

- INVOKANA is a sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM). By inhibiting SGLT2, INVOKANA reduces reabsorption of filtered glucose and lowers the renal threshold for glucose, thereby increasing urinary glucose excretion.
- INVOKANA is available as 100- and 300-mg film-coated tablets, dosed before the first meal of the day alone or in combination with other antihyperglycemic agents (AHAs). Starting dose of INVOKANA is 100 mg daily and can be increased to 300 mg daily if tolerating 100 mg, have an eGFR ≥60 mL/min/1.73 m², and require additional glycemic control. Limit INVOKANA to 100 mg daily if eGFR ≥45 to <60 mL/min/1.73 m². Do not initiate or discontinue INVOKANA if eGFR is <45 mL/min/1.73 m². If a UGT inducer must be given with INVOKANA, consider

increasing INVOKANA to 300 mg if tolerating 100 mg, has an eGFR ≥ 60 mL/min/1.73 m², and needs further glycemic control.

Efficacy of INVOKANA studied in 9 pivotal phase 3, double-blind, randomized studies enrolling ~10,300 patients

- *Placebo-Controlled Studies*: Significant A1C reduction vs placebo reported at 18 and 26 weeks ($p < 0.001$); A1C reductions also seen at 52 weeks. For prespecified secondary endpoints at 26 weeks, INVOKANA showed a greater proportion of patients achieving A1C $< 7\%$, and greater reductions in fasting plasma glucose (FPG) and body weight (BW) ($p < 0.001$ for all parameters vs placebo). Significant reductions in systolic blood pressure (SBP) from baseline with INVOKANA were reported in 3 studies. Dose-related drops in A1C, FPG, BW, and SBP were seen at 52 weeks.
- *Active-Controlled Studies (vs sitagliptin and vs glimepiride)*: As add-on to metformin, both INVOKANA doses were noninferior to glimepiride 6-8 mg in A1C reduction at 52 weeks. INVOKANA 300 mg showed statistically superior reduction in A1C versus glimepiride 6-8 mg (added to metformin) and vs sitagliptin 100 mg (added to metformin and sulfonylurea) at 52 weeks. For prespecified secondary endpoints at 52 weeks, both INVOKANA doses provided reductions in percent BW change vs glimepiride 6-8 mg ($p < 0.0001$). INVOKANA 300 mg provided improvement in percent BW versus sitagliptin ($p < 0.001$) at 52 weeks. Greater mean drop from baseline seen in SBP with INVOKANA vs sitagliptin 100 mg. At 104 weeks, A1C reductions were maintained; reductions in FPG, BW, and SBP were similar to 52-week data.
- *Specific Populations (55 to 80 years of age and moderate renal impairment)*: In patients 55 to 80 years and in patients with eGFR ≥ 30 to < 50 mL/min/1.73 m², both INVOKANA doses significantly improved A1C vs placebo at 26 weeks; at 52 weeks, drops in A1C seen in moderate renal impairment. Analyses of CV outcomes in patients with or at high risk for CV disease on INVOKANA (as add-on to insulin +/- AHAs and as add-on to a sulfonylurea) are ongoing.

Overall Safety

- In 4 pooled placebo-controlled studies, AEs $\geq 5\%$ with either INVOKANA dose were female genital mycotic infections (GMI), urinary tract infections, and increased urination. Other AEs ($\geq 2\%$ with INVOKANA) were male GMI, vulvovaginal pruritus, thirst, constipation, and nausea. In a pool of 8, placebo- and active-controlled studies, the types and frequency of common AEs were consistent with the 4 pooled placebo-controlled studies.
- INVOKANA results in an osmotic diuresis, which may lead to reductions in intravascular volume. In the 8 pooled studies, patients on loop diuretics, patients with moderate renal impairment (eGFR, 30 to < 60 mL/min/1.73 m²), and patients ≥ 75 years of age had the largest increase in volume depletion-related AEs. INVOKANA was associated with a dose-dependent increase in the incidence of volume depletion-related AEs, a dose-dependent increase in serum creatinine, and a concomitant decrease in eGFR; patients with moderate renal impairment at baseline had larger mean changes.
- In monotherapy or in combination with metformin, the incidence of hypoglycemia observed with INVOKANA was similar to the incidence with placebo. Hypoglycemia occurred at a higher rate when INVOKANA was coadministered with insulin or a sulfonylurea.
- In 4 pooled placebo-controlled studies, dose-related increases in LDL-C and non-HDL-C with INVOKANA were observed. Mean changes from baseline in LDL-C relative to placebo were 4.4 mg/dL (100 mg) and 8.2 mg/dL (300 mg); mean changes from baseline in non-HDL-C relative to placebo were 2.1 mg/dL (100 mg) and 5.1 mg/dL (300 mg). (*Note: the sitagliptin-controlled study was not included in pooled analyses of adverse reactions.*)

Clinical Value, Place in Therapy, and Cost Effectiveness

- INVOKANA (as monotherapy or add-on to metformin) had significant reduction in A1C levels vs placebo. INVOKANA 300 mg provided statistically superior A1C reduction from baseline to 52 weeks vs sitagliptin 100 mg (added to metformin and a sulfonylurea). In combination with metformin, both INVOKANA doses were noninferior to glimepiride 6-8 mg and 300 mg provided statistically superior A1C reduction at 52 weeks from baseline. INVOKANA had been shown to lower glucose levels in triple therapy with metformin and either a sulfonylurea or pioglitazone. Glycemic control was also significantly better with both doses of INVOKANA vs placebo when added to stable insulin therapy alone or in combination with other AHAs. Significant reduction in A1C was observed with INVOKANA in subjects with moderate renal impairment and in older patients. Greater reductions in A1C vs placebo observed in patients with higher baseline A1C or eGFR values.
- INVOKANA was associated with some BP reduction, BW reduction, and improvement in β -cell function indices. In studies up to 52 weeks or 104 weeks, both doses maintained reductions in A1C, FPG, BW, and SBP, with small increases in HDL-C and LDL-C vs comparator.
- INVOKANA can be placed as an oral treatment option for adults with T2DM as monotherapy or add-on to metformin in those requiring further glycemic control, for those intolerant to metformin, or in dual/triple therapy (+/- insulin) for further glycemic control. INVOKANA 300 mg (a) demonstrated cost savings and superior cost efficiency

as compared with sitagliptin 100 mg in a 1-year cost and cost-efficiency analysis and was found to dominate (i.e., is more effective and less costly than) sitagliptin, showing an increase in QALYs and lower costs than sitagliptin over 10-, 20-, and 30-year time horizons in the longer-term cost-effectiveness model.

Questions and Answers

Q: Have any head-to-head studies been conducted?

A: Yes, vs. sitagliptin that showed canagliflozin was non-inferior and superior to sitagliptin.

Q: Have any outcomes studies been conducted?

A: An outcomes study is in progress.

Q: Are any combinations products being developed?

A: A combination with metformin is being explored.

Q: Is there any use of a 200mg dose?

A: A 200mg dose has not been studied or approved; the dose should be either 100mg or 300mg once daily.

Sirturo™ (bedaquiline tablets)

Pronunciation: Sirturo (ser toor' oh)/bedaquiline (bed ak' wi leen)

Product Description

- SIRTURO is a diarylquinoline antimycobacterial drug that inhibits mycobacterial ATP (adenosine 5'-triphosphate) synthase, an enzyme that is essential for the generation of energy in *Mycobacterium tuberculosis*. SIRTURO is indicated as part of combination therapy in adults (≥ 18 years) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Reserve SIRTURO for use when an effective treatment regimen cannot otherwise be provided.
- The safety and efficacy of SIRTURO has not been established for the treatment of latent infection due to *M. tuberculosis*, the treatment of drug-sensitive TB, the treatment of extra-pulmonary TB (e.g., central nervous system), or infections caused by non-tuberculous mycobacteria. Therefore, use of SIRTURO in these settings is not recommended.
- The dosing for SIRTURO for pulmonary MDR-TB is 400 mg once daily with food for 2 weeks followed by 200 mg three times per week with food for 22 weeks. Swallow SIRTURO tablets whole with water. SIRTURO should be administered by directly observed therapy.

Efficacy from Phase 2 Clinical Studies: The C208 (stage 1 and stage 2) and the C209 trial

- The **C208 trial (stage 1)** was an 8 week, multicenter, double-blind, placebo-controlled study. The study population included patients from South Africa with newly diagnosed pulmonary MDR-TB. Patients received SIRTURO 400 mg daily (n=23) or placebo (n=24) for weeks 1 and 2, followed by SIRTURO 200 mg three times weekly or placebo during weeks 3-8. Patients also received a background regimen (BR) of 5 drugs during the 8 week treatment phase, and was continued after the 8 week treatment phase. At weeks 8 and 24, the difference in culture conversion proportions between the SIRTURO and placebo groups was 38.9% (95% CI:12.3%-63.1%; *P*-value=0.004), and 15.7% (95% CI:-11.9%, 41.9%; *P*-value=0.32), respectively.
- The **C208 trial (stage 2)** was a multicenter, double-blind, placebo-controlled study. The study population included international patients with newly diagnosed pulmonary MDR-TB. Patients received SIRTURO (n=79) or placebo (n=81) with 5 other anti-TB drugs for MDR-TB. The dosing of SIRTURO was the same as stage 1, except the treatment period was 24 weeks instead of 8 weeks. At week 24 of this ongoing trial, the median time to culture conversion was 83 days for the SIRTURO group compared to 125 days for placebo. At weeks 24 and 72, the difference in treatment success rates between the SIRTURO and placebo groups was 20% (95% CI:4.5%-35.6%; *P*-value=0.014) and 14.1% (95% CI:-2.1%, 30.3%; *P*-value=0.092).
- The **C209 trial** is an open-label, noncomparative study. The study population included patients with sputum smear positive pulmonary MDR-TB infection. During the initial 24 weeks of the study, patients received SIRTURO with a BR. SIRTURO was administered as 400 mg daily for 14 days, followed by 200 mg three times a week for 22 weeks. After 24 weeks, the patients continued to receive the BR until a total of 18-24 months of MDR-TB treatment was achieved. The median time to culture conversion was 8 weeks for patients with MDR-TB (n=93). The response rate at 24 weeks for MRD-TB patients was 87.1%.

Safety

• WARNINGS

- **An increased risk of death was seen in the SIRTURO™ treatment group (9/79, 11.4%) compared to the placebo treatment group (2/81, 2.5%) in one placebo-controlled trial. Only use SIRTURO when an effective treatment regimen cannot otherwise be provided.**

- **QT prolongation can occur with SIRTURO. Use with drugs that prolong the QT interval may cause additive QT prolongation.**
- The most common adverse drug reactions reported in greater >10.0% of patients treated with SIRTURO compared to the placebo treatment group are nausea (38.0% vs. 32.1%), arthralgia (32.9% vs. 22.2%), headache (27.8% vs. 12.3%) and additional adverse events reported in ≥10.0% of patients are hemoptysis (17.7% vs. 11.1%) and chest pain (11.4% vs. 7.4%).

Questions and Answers

No questions and answers followed.

V. Celgene

Michelle Watson, PhD, Hematology Regional Medical Liaison
Phillip Lafferty, Regional Account Manager
Brian Hall, Associate Director, Regional Account Group

Pomalyst® (pomalidomide capsules)

Pronunciation: Pomalyst (POM-uh-list)/pomalidomide (poe" ma lid' oh mide)

- Multiple myeloma (MM) is an incurable hematologic cancer of plasma cells. MM is characterized by increased monoclonal (M) protein levels in the serum and/or urine due to proliferation of malignant clonal plasma cells. MM accounts for 1% of all cancers and 15% of estimated new hematologic malignancies. The age-adjusted incidence rate for MM is 5.8 per 100,000 (2005-2009 data) and the prevalence is approximately 23 per 100,000. The median age at diagnosis is 69 years (2005-2009 data). The Goals of MM therapy can include: eliminating all measurable disease, controlling disease burden, maintaining/improving quality of life, and managing disease symptoms.
- FDA granted Fast Track designation to POMALYST (pomalidomide) based upon the potential to treat relapsed and refractory patients who no longer respond to existing therapies. Fast Track allows for expedited FDA review of drugs that fill an unmet medical need in the treatment of a serious disease. Phase 2 data can be submitted with Phase 3 data to follow.

Indications

- POMALYST is a thalidomide analogue indicated for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy.
- Approval is based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

Dosing and Administration

4 mg per day taken orally on days 1-21 of repeated 28-day cycles until disease progression.

Contraindications: Pregnancy

POMALYST can cause fetal harm when administered to a pregnant female.

Warnings/Precautions

- **WARNING: EMBRYO-FETAL TOXICITY and VENOUS THROMBOEMBOLISM POMALYST is only available through a restricted distribution program called POMALYST REMS.**
- Venous Thromboembolism, Hematologic Toxicity, Hypersensitivity Reactions, Dizziness and Confusional State, Neuropathy and Risk of Second Primary Malignancies

Clinical Studies

MM-002 was a Phase 2, multicenter, randomized open-label study in patients with relapsed multiple myeloma who were refractory to their last myeloma therapy and had received lenalidomide and bortezomib. Patients were considered relapsed if they had achieved at least stable disease for at least one cycle of treatment with at least one prior regimen and then developed progressive disease. Patients were considered refractory if they experienced disease progression on or within 60 days of their last therapy. A total of 221 patients were randomized to receive pomalidomide alone (POM alone) or pomalidomide with Low dose dexamethasone (POM+LoDex). In MM-002, the safety and efficacy of pomalidomide 4 mg, once daily for 21 of 28 days, until disease progression, were evaluated alone and in combination with Low dose Dex (40 mg per day given only on Days 1, 8, 15 and 22 of each 28-day cycle

for patients 75 years or younger, or 20 mg per day given only on Days 1, 8, 15 and 22 of each 28-day cycle for patients greater than 75 years of age). Patients in the POM alone arm were allowed to add Low dose Dex upon disease progression. The overall response rate (ORR), defined as \geq partial response (PR), in the ITT population was 29.2% for POM+LoDex vs. 7.4% for POM alone. Duration of response (DOR): was 7.4 months for POM+LoDex vs. not reached for POM alone in patients who achieved at least a PR.

Adverse Reactions

Of the 219 patients who received POM alone (n=107) or POM + LoDex (n=112), all patients had at least one treatment-emergent adverse reaction. In the POM alone versus POM + LoDex arms, respectively, most common adverse reactions (\geq 30%) included fatigue and asthenia, neutropenia, anemia, constipation, nausea, diarrhea, dyspnea), upper respiratory tract infection, back pain, and pyrexia. The most common hematologic Grade 3/4 treatment-emergent AEs (TEAEs) included neutropenia, thrombocytopenia, leukopenia and anemia. Common non-hematologic Grade 3/4 TEAEs included pneumonia, fatigue, dyspnea and back pain.

Drug Interactions

No formal drug interaction studies have been conducted with POMALYST. Pomalidomide is primarily metabolized by CYP1A2 and CYP3A and is also a substrate for P-glycoprotein (P-gp). Coadministration of POMALYST with drugs that are strong inhibitors or inducers of CYP1A2, CYP3A, or P-gp should be avoided. Smoking may reduce pomalidomide exposure due to CYP1A2 induction.

Use in Specific Populations

Pregnancy, Nursing Mothers, Pediatric use, Geriatric use, Renal and Hepatic Impairment are listed in Section 8 of the POMALYST Prescribing Information. For additional information on the use of POMALYST in these populations, please see the POMALYST Prescribing Information.

Questions and Answers

Q: How many providers are enrolled for distribution?

A: Approximately 30 specialty pharmacies and 180 physician sites.

Q: Has the phase 2 study been published yet?

A: Some study results have been published in *Blood*.

Q: When will the phase 3 results be available?

A: The data are still being evaluated and plan to be published.

Q: Is Celgene the manufacturer of the 3 omide products for multiple myeloma?

A: Yes.

Q: What are the differences between lenalidomide, pomalidomide and thalidomide?

A: They are slightly different in adverse events.

VI. Salix

Christy Copeland, PharmD, Medical Science Liaison

Fulyzaq™ (crofelemer delayed-release tablets)

Pronunciation: Fulyzaq (Full-eh-zac)/crofelemer (kroe-FEL-e-mer)

Overview

- Fulyzaq (crofelemer) is indicated for symptomatic relief of non-infectious diarrhea in adult patients with HIV/AIDS on anti-retroviral therapy.
- The recommended dose is one 125 mg delayed-release tablet taken orally twice a day (BID), with or without food. Fulyzaq tablets should not be crushed or chewed. The tablets should be swallowed whole. Fulyzaq (crofelemer) delayed-release tablets are an anti-diarrheal, enteric-coated drug product for oral administration. Each delayed-release tablet contains 125 mg of crofelemer, a botanical drug substance derived from the red latex of *Croton lechleri* tree that is harvested from South America.
- Crofelemer is an inhibitor of both the cyclic adenosine monophosphate (cAMP)-stimulated cystic fibrosis transmembrane conductance regulator (CFTR) chloride ion (Cl-) channel, and the calcium-activated Cl- channel (CaCC) at the luminal membrane of enterocytes. The CFTR Cl- channel and CaCC regulate Cl- and fluid secretion

by intestinal epithelial cells. Crofelemer acts by blocking Cl⁻ secretion and accompanying high volume water loss in diarrhea, normalizing the flow of Cl⁻ and water in the GI tract.

- The absorption of crofelemer is minimal following oral dosing in healthy adults and HIV-positive patients and concentrations of crofelemer in plasma are below the level of quantitation (50 ng/mL). Therefore, standard pharmacokinetic parameters such as area under the curve, maximum concentration, and half-life cannot be estimated.

Efficacy and Safety

- A randomized, double-blind, placebo-controlled trial was conducted to evaluate the safety and efficacy of crofelemer for the treatment of non-infectious diarrhea in HIV-positive individuals. HIV-positive patients on anti-retroviral therapy with CD4⁺ cell counts > 100 cells/μL with diarrhea (watery bowel movements on ≥ 5 of 7 days prior to enrollment) and no evidence of intra-luminal pathogens were enrolled in the study. In the first stage of the study, patients were randomly assigned to received 125 mg, 250 mg, or 500 mg of crofelemer BID or placebo for 4 weeks to determine the optimal dose. In the second stage of the study, safety and efficacy of the optimal crofelemer dose was compared to placebo during 4 weeks of therapy (placebo-controlled phase) (see Figure). The primary endpoint was the proportion of subjects with ≤ 2 watery bowel movements/week for ≥ 2 of 4 weeks of the placebo-controlled phase (Stages I and II combined). Patients who reached the primary endpoint were considered clinical responders. Following the placebo-controlled phase, all patients continued in a placebo-free phase and received crofelemer for 5 months. A total of 374 patients received crofelemer (n = 236) or placebo (n = 138).¹ Most patients were male (84%), and the mean age was approximately 45 years. The mean weekly number of watery stools at baseline was 18.9 in the crofelemer group and 21.0 in the placebo group. The most common anti-retroviral medications were tenofovir/emtricitabine, ritonavir, lopinavir/ritonavir, and efavirenz/tenofovir/emtricitabine. The percentage of clinical responders (Stage I and II combined) was 18% of patients treated with crofelemer 125 mg BID and 8% of patients treated with placebo (P = 0.01). Response rates in Stage I were reported as 20.5% with crofelemer 125 mg, 9.3% with crofelemer 250 mg, 19.6% with crofelemer 500 mg, and 2% with placebo. Therefore, crofelemer 125 mg BID was selected as the optimal dose. Response rates in Stage II were reported as 16.3% with crofelemer 125 mg BID (n = 136) and 11.4% with placebo (n = 138). Upon switching to crofelemer in the placebo-free extension phase, clinical response was higher in patients previously treated with placebo at 1 month (36% vs. 9%; P < 0.0001) and these patients had greater odds of achieving clinical response in each of the remaining 4 months (P < 0.0001) compared with their 1-month placebo experience.
- In the placebo-controlled phase, the incidence of adverse events was lower in patients receiving crofelemer compared with those receiving placebo for all adverse events (27% vs. 33%), adverse events leading to discontinuations (0% vs. 3%), and serious adverse events (SAEs) (1% vs. 3%). Treatment-emergent AEs occurred most frequently in the infections and infestations (10% vs. 11%) and GI disorders (9% vs. 6%) system organ classes. None of the SAEs in either treatment group was related to study drug. Changes from baseline in HIV status (as measured by CD4 counts and HIV viral load) were low in both treatment groups.

Questions and Answers

Q: Had patients failed previous therapy in the clinical trial?

A: Some patients had failed previous therapy, some had not.

Q: Has the pivotal trial been published yet?

A: No, should be published early next year.

Q: How are most providers prescribing?

A: Most physicians are prescribing after trial of previous therapy.

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 on Thursday, February 6, 2014, with an overflow day on Wednesday, February 12, 2014 if needed.

Date: **Thursday, February 6, 2014 from 9am-5pm EST**
Wednesday, February 12, 2014 from 9am-5pm EST (overflow day if needed)

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.

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 first time the names are introduced in the summary. The one-page summary along with relevant questions and answers from 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 DURB 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 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.

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**

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 drug indications, etc.) as deemed necessary by NHC/Catamaran.

Please see the Manufacturers' Forum Announcement at

<http://dch.georgia.gov/durb-meeting-information>.

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

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2014

Upcoming Meetings

Drug Utilization Review Board Meeting

2 Peachtree Street, N.W.

5th Floor Board Room

Atlanta, Georgia 30303

Tuesday, March 18, 2014: 9:00am – 4:00pm

Thursday, June 5, 2014: 9:30am – 2:30pm

Thursday, September 18, 2014: 9:30am – 1:30pm

Tuesday, December 9, 2014: 9:30am – 1:30pm

Manufacturers' Forum

NorthStar HealthCare Consulting

1121 Alderman Drive

Suite 112

Alpharetta, Georgia 30005

Thursday, February 6, 2014: 9:00am – 5:00pm

Wednesday, February 12, 2014 (if needed) 9:00am – 5:00pm

Thursday, May 1, 2014: 9:00am – 5:00pm

Thursday, August 7, 2014: 9:00am – 5:00pm

Thursday, November 6, 2014: 9:00am – 5:00pm