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

September 15, 2011

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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
September 15, 2011 – 10:00 a.m. to 2:00 p.m.

CALL TO ORDER — *Gary Williams, MD, Chairman*

COMMENTS FROM THE DEPARTMENT — *Jerry Dubberly, PharmD, MBA, Chief, Medical Assistance Plans*

MINUTES FROM PREVIOUS MEETING — *Chairman*

PDL MANAGEMENT — *Emily Baker, PharmD, BCPS, MBA, MHA; Tara R. Cockerham, PharmD; Tami Sweat, PharmD*

- **Prior Authorization Overview**
- **Manufacturers' Forum**
- **New Drug Reviews**
  - ♦ Butrans™
  - ♦ Cuvposa™
  - ♦ Egrifta™
  - ♦ Kapvay™
  - ♦ Lastacaft™
  - ♦ Latuda™
  - ♦ Makena™
  - ♦ Nuedexta™
  - ♦ Teflaro™
- **Follow-Up Reviews**
  - ♦ Ella™
  - ♦ Gilenya™
  - ♦ Pradaxa™
  - ♦ Alpha-1 Proteinase Inhibitors
- **Clinical Utilization Reviews**
  - ♦ Long-Acting Beta-Agonist Containing Products in Asthma
  - ♦ Simvastatin 80mg Containing Products in Dyslipidemia
- **Utilization Trend Review**
- **Drug Information**
  - ♦ Drug Update Newsletter
  - ♦ Horizon Watch Report
  - ♦ Patent Expiration Report
  - ♦ Clinical Compass Newsletter

FUTURE AGENDA ITEMS — *Chairman*

CONSUMER COMMENTS SESSION

ADJOURNMENT OF OPEN SESSION — *Chairman*

EXECUTIVE SESSION

BOARD'S RECOMMENDATIONS TO DCH — *Chairman*

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Department of Community Health
Drug Utilization Review Board (DURB)
MINUTES
Thursday, June 16, 2011

MEMBERS PRESENT	MEMBERS ABSENT
Gary M. Williams, M.D., Chairman	Ryan Beddingfield, R.Ph.
Laurel E. Ashworth, Pharm.D., Vice-Chairperson	Joseph R. Bona, M.D., MBA
Karen L. Carter, M.D.	Marilane Brookes Bond, Ed.D.
Paul D. Boyce, M.D.	Truddie Darden, M.D.
Arvind Gupta, M.D.	Carl Ellis, R.Ph.
Kimberly S. Carroll, M.D.	Mary Rhee, M.D., M.S.
Rondell C. Jaggers, Pharm.D.	Richard S. Singer, DDS
Robyn Lorys, Pharm.D.	
J. Russell May, Pharm.D.	
Osgood A. Miller, R.Ph.	
Michael S. O'Connor, Pharm.D.	
Matthew Perri, III, R.Ph., PhD.	

Staff
Turkesia Robertson-Jones, Pharm.D., Pharmacy Operations Manager, Pharmacy Services
Gilletta Gray, R.Ph., Clinical Manager, Pharmacy Services
Lori Garner, MHS, MBA, R.Ph., Pharmacy Services
Rose Marie Duncan, Program Associate, Pharmacy Services
Erin Powel, Pharm.D. Candidate

NorthStar HealthCare Consulting
Emily Baker, Pharm.D., BCPS, MHA, MBA, President
Tara R. Cockerham, Pharm.D., Clinical Programs Director
Annie Oyanontaruk, Pharm.D. Candidate

SXC Health Solutions, Inc.
Susan McCreight, Account Manager
Talmahjia “Tami” Sweat, Pharm.D., Clinical Systems Product Manager

Goold Health Services
Doug Martin, Pharm.D., Pharmacy Project Manager

Department of Community Health
Drug Utilization Review Board (DURB)
MINUTES
Thursday, June 16, 2011

Call to Order

The Drug Utilization Review Board (DURB/DUR Board) held its second meeting for the calendar year on June 16, 2011. The Chairman, Gary M. Williams, M.D., called the meeting to order at 10:23am after achieving quorum with (10) members in attendance.

Comments from the Department

Gilletta Gray, R.Ph., Clinical Manager, Pharmacy Services, commented on the following items:

1. Medicaid Management Information System (MMIS) – The MMIS implementation with HP Enterprise Solutions is being cited around the country as the most successful in recent history. The Department is now working to complete CMS requirements for certification of the system to be able to receive enhanced federal matching funds.
2. Medicaid Design Consultant - The Department released a Request for Proposal (RFP) for a Medicaid Design Consultant to assist the Department with identifying what has been done well and what opportunities exist. The Consultant would also hold 30 stakeholder forums around the State.
3. RFP for PBM Services – The Department will be releasing a RFP for PBM Services in the near future. Board members and other stakeholders interested in providing suggestions for consideration during the RFP development phase should do so in writing to DCH Pharmacy Department.
4. Revised Agenda – The agenda was revised to remove the Executive Session due to new procedural requirements by the Attorney General that will be implemented for future meetings. The Board will not break for Executive Session. Future meetings will include an Executive Session.
5. Future Agenda Items – Future agenda items mentioned by the Board have been noted and will be considered for future meetings.
6. Turkesia Robertson-Jones – Turkesia Robertson-Jones was introduced as the Department's new Pharmacy Operations Manager which was previously occupied by Etta Hawkins.

Comments from the Board

Comments were made from DUR Board members regarding the decision that the Executive Session would not be held at today's meeting. The Chairman, Gary M. Williams, M.D. read a prepared statement noted in Attachment A.

Minutes from the Previous Meeting

Dr. Williams asked for comments regarding the minutes from the March 17, 2011 meeting. There were no corrections or discussions. A motion was made, seconded, and carried to approve the minutes as written.

Manufacturers' Forum

Emily Baker, Pharm.D., BCPS, reviewed information regarding the Manufacturers' Forum that was provided in the Manufacturer Information section in the DUR Board binder. A total of four (4) manufacturers participated and provided information regarding the following drugs discussed at the June 2011 DURB meeting:

Manufacturers	Drugs
Boehringer Ingelheim Pharmaceuticals	Pradaxa
Jazz Pharmaceuticals	Xyrem
CSL Behring	Zamaira
Baxter	Glassia, Aralast-NP

Comments and questions were received from the Board. The next forum is Thursday, August 11, 2011 from 9am-5pm at the NorthStar Healthcare Consulting office: 1121 Alderman Drive, Suite 112, Alpharetta, GA 30005.

New Drugs

Clinical information for the following new drugs, in the market six months or more, was presented for discussion and recommendation. The complete detailed drug summary is in the New Drugs for Review section of the June 2011 DUR Board binder.

THERAPEUTIC CLASS	DRUGS	PRESENTER
Contraceptive, Oral	*Beyaz*	Emily Baker, Pharm.D., BCPS
Urea Cycle	*Carbaglu*	Emily Baker, Pharm.D., BCPS
Contraceptive, Oral Emergency	*Ella*	Emily Baker, Pharm.D., BCPS
Multiple Sclerosis	*Gilenya*	Emily Baker, Pharm.D., BCPS
Anticoagulant	*Pradaxa*	Emily Baker, Pharm.D., BCPS

The Board discussed the drug information, provided comments, raised questions, and made recommendations for each of the drugs presented during the open session.

Therapeutic Class Review

Clinical information for the Alpha-1 proteinase inhibitors therapeutic class was presented for discussion. The complete detailed therapeutic class review was provided in the Therapeutic Class Review section of the June 2011 DUR Board binder.

THERAPEUTIC CLASS	DRUGS	PRESENTER
Alpha-1 Proteinase Inhibitors	*Aralast-NP, Glassia, Prolastin-C, Zemaira*	Tara Cockerham Pharm.D.

The Board discussed the drug information, provided comments, raised questions, and made recommendations for the therapeutic class presented during the open session.

Clinical Utilization Reviews

Clinical information for the following Clinical Utilization Review topics was presented for discussion. The complete detailed clinical reviews were provided in the Clinical Utilization Review section of the June 2011 DUR Board binder.

Clinical Topic	Description	PRESENTER
Acetaminophen-Containing Combination Products	*Clinical review of the Food and Drug Administration's action to limit acetaminophen-containing combination prescription products*	Tara Cockerham, Pharm.D.
Cough and Cold Products	*Clinical review of the Food and Drug Administration's action to remove unapproved cough and cold products from the market*	Tara Cockerham, Pharm.D.

Comments and questions were received from the Board. After discussions, the Board had the following recommendations:

Acetaminophen-Containing Combination Products

- It was moved and seconded to impose restrictive quantity limit guidelines to disallow any request exceeding 3 grams. The motion did not carry (5 against and 4 in favor)
- It was moved and seconded to let the FDA phase-out continue for the products on the market and to continue performing drug utilization review and sending letters to physicians. The motion carried.

Cough and Cold Products

- It was moved and seconded to place this class of drugs in a Non-Covered status. The motion carried.

Utilization Trend Review

Utilization trends for Georgia Medicaid Fee-for-Service were presented for discussion and provided in detail in the Utilization Trend Review section of the June 2011 DUR Board binder. Comments and questions were received from the Board.

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

Dr. Williams noted the following future agenda items:

1. All information presented in the closed session should list all combinations that are available to use to make a scenario and the drugs be identified as to what their status is on the PDL
2. Beta-2 agonists
3. Opioids and Duplicate therapy
4. Drug categories that don't need further monitoring by the DURB

Consumer Comments Session

There were no consumer comments.

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, September 15, 2011
  Tuesday, December 13, 2011

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

  Thursday, August 11, 2011
  Thursday, November 3, 2011

Disclosure Forms

All disclosure forms were received and reviewed by the Department for completeness.

Adjournment of Open Session

The Chairman, Dr. Gary Williams, adjourned the open session at approximately 11.54am**,** at which time members took a 30 second break and then reconvened for the open session again.

Department of Community Health
Drug Utilization Review Board (DURB)
MINUTES
Thursday, June 16, 2011

Executive Session

There was no executive session held.

Board's Recommendations to the Department

After all clinical evaluations and discussions, the DUR Board presented the Department with the following recommendations for changes to the Preferred Drug List (PDL):

New Drug Reviews

Oral Contraceptive

The DUR Board recommended ***Non-Preferred*** status with ***Prior Authorization*** for ***Beyaz***.

Hyperammonemic

The DUR Board recommended ***Preferred*** status with ***Prior Authorization*** for ***Carbaglu***.

Emergency Contraceptive

The DUR Board voted to table a recommendation until the next Executive Session for ***Ella***.

Multiple Sclerosis

The DUR Board voted to table a recommendation until costs and toxicities are discussed for ***Gilenya***.

Anticoagulant

The DUR Board voted to table a recommendation for further discussion and costs for ***Pradaxa***.

Therapeutic Class Review

Alpha-1 Proteinase Inhibitors

The DUR Board recommended ***Prior Authorization*** for all agents, ***Aralast-NP, Glassia, Prolastin-C*** and ***Zemaira*** until further discussion at the next Executive Session.

Clinical Utilization Reviews

Acetaminophen-Containing Combination Products

The DUR Board recommended ***to leave the category as is, continue educational letters,and let higher product doses be phased out.***

Cough and Cold Products

The DUR Board recommended ***Non-Covered*** status for all ***Cough & Cold Products***.

Conclusion

The open session reconvened after a 30 second break at 11:54am and audience participants remained in the Board room to hear the Board's recommendations submitted to the Department. Dr. Williams presented the recommendations from the Board to the Department.

With no other business for discussion, Chairman Williams adjourned the meeting at 11:56am.

Attachment A

As read by Dr. Gary Williams at the June 16, 2011 DURB Meeting:

At 4:45 pm, on the afternoon of June 14, 2011, I received a telephone call from representatives of the Department that was concerning. I was informed that the DURB can only conduct our closed or executive sessions with permission of the Attorney General's office.

More so, I was informed that no permission had been given to conduct today's meeting (at least at the time that the telephone call occurred).

The Chair would like for the Department to explain to the board the process through which that decision was made and upon which statutes this decision was based. Secondly, the Chair would request that a member of the Department and or proper representatives of the Attorney General's office address the board in a public forum and in writing as to the process that lead to this edict.

I would ask specifically that this statement be included in the minutes of this session and that the board be allowed to discuss this new process during this session.

Please note that as chair of this board, and as authorized of Section 1903(3) A of the Omnibus Budget Reconciliation Act of 1990 (OBRA), the Board has the following functions:
1) To promote patient safety through an increased review and awareness of outpatient prescribed drugs
2) To recommend medical criteria, standards and educational intervention used in the DUR program
3) It also advises DCH about products considered to be most clinically effective for members of the Departments plans
4) The Board reviews drug therapy, drug studies and utilization information, thus enabling the Department to identify the most cost- effective policies for its members.

It is the intention of this Chair, to conduct the business of the Board as stated.

If there are issues with the conduct of this Board's business, then let that be addressed to the Board openly and directly. Let those who wish to affect the conduct of the Board do so in a way that exhibits the same transparency that is asked of this Board.

Please note that the Chair intends to conduct the business of this board without political influence or pressure.

There can be no political issues of influence on the process or decisions of the DURB.

Please note too that the Board is amenable to any legal and ethical suggestions or statutes. All attempts to affect the conduct of this Board must be done in a manner dictated by the laws of this state.

Please note also, that without written and proper notification, the business of the Board will be conducted as usual in the September Quarterly Meeting.

I again request that this statement be included as a formal part of the minutes of this, the June 16, 2011 session.

THESE MINUTES ARE HEREBY APPROVED AND ADOPTED, THIS THE _____ DAY OF _____, 2011.

_____

Gary Williams, M.D., Chairman

Department of Community Health
Drug Utilization Review Board (DURB)
MINUTES
Thursday, June 16, 2011

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Manufacturers' Forum
Manufacturer Presentations

Date: August 11, 2011

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

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

Drug Summary Documents
Please note that relevant, electronic materials that were provided by manufacturers on the drugs that were posted to the Department of Community Health (DCH) website as under review for the September 15, 2011 meeting were provided to the Drug Utilization Review Board (DURB). For the drugs that were also presented at the Forum, the drug summary documents that highlighted the presentations are also included 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. EMD Serono

Alberto Avendano, MD, Field Associate Medical Director, HIV, Medical Affairs
Rob Bindner, Regional Account Manager, Managed Markets
Sherrie DeLoach Howe, Key Account Manager

Egrifta™ (tesamorelin)

- The first and only treatment indicated to reduce excess abdominal fat in HIV-infected patients with lipodystrophy.
- Limitations of use:
    - Since the long-term cardiovascular safety and potential long-term cardiovascular benefit have not been studied and are not known, careful consideration should be given whether to continue treatment in patients who do not show a clear efficacy response as judged by the degree of reduction in visceral adipose tissue (VAT) measured by waist circumference (WC) or CT scan.
    - Not indicated for weight loss management (weight neutral effect).
    - There are no data to support improved compliance with antiretroviral therapies.

Clinical Efficacy
- The efficacy and safety was evaluated in two phase 3, multi-center, randomized, double-blind, placebo-controlled, 52-week clinical trials consisting of a 26-week main phase and a 26-week extension phase of 816 HIV-infected patients with excess abdominal fat associated with lipodystrophy.
- In both Phase 3 studies, patients received either tesamorelin or placebo for 26 weeks. Patients initially randomized to tesamorelin were then re-randomized to receive either tesamorelin or placebo for an additional 26-week treatment period, whereas patients receiving placebo were switched to tesamorelin. In the first study, at baseline, mean VAT was 178 cm2 for the patients who received and was 171 cm2 for the patients who received placebo. In the second study, at baseline, mean VAT was 186 cm2 for the patients who received tesamorelin and was 195 cm2 for the patients who received placebo. Patients treated with tesamorelin experienced a statistically significant least-squares mean (LSM) decrease from baseline in VAT of 27 cm2 compared to an increase of 4 cm2 for patients on placebo [(95% CI for the mean treatment difference of -31 cm2 (-39 cm2, -24 cm2)] in the first study, and a statistically significant decrease from baseline in VAT of 21 cm2 compared to no change in VAT for patients on placebo [(95% CI for the mean treatment difference of -21 cm2 (-29 cm2, -12 cm2)] in the second study during the 26-week main phase.

- This represents a statistically significant LSM decrease from baseline in VAT of 18% for patients treated with tesamorelin compared to an increase of 2% for patients on placebo [(95% CI for the mean treatment difference of -20% (-24%, -15%)] in the first study, and a statistically significant decrease from baseline of 14% for patients treated with tesamorelin compared to a decrease of 2% for patients on placebo [(95% CI for the mean treatment difference of -12% (-16%, -7%)] in the second study during the 26-week main phase.
- In the first study, at baseline, mean waist circumference was 104 cm for the patients who received tesamorelin and was 105 cm for the patients who received placebo. In the second study, at baseline, mean waist circumference was 105 cm for the patients who received tesamorelin and for the patients who received placebo. Treatment with tesamorelin resulted in a statistically significant least-squares mean decrease from baseline in waist circumference of -3 cm compared to a decrease of -1 cm for patients on placebo [(95% CI for the mean treatment difference of -2 cm (-2.8 cm, -0.9 cm)] in the first study, and a statistically significant decrease from baseline of -2 cm compared to a decrease of -1 cm for patients on placebo [(95% CI for the mean treatment difference of -1 cm (-2.5 cm, -0.3 cm)] in the second study during the 26-week main phase. The decreases in VAT and waist circumference observed after 26 weeks of treatment were sustained in patients who received tesamorelin over 52 weeks.

Clinical Safety

- Contraindicated in patients with disruption of the hypothalamic-pituitary axis; in patients with active malignancy and any preexisting malignancy should be inactive and its treatment complete prior to instituting therapy; in patients with known hypersensitivity to mannitol; and in women who are pregnant.
- Neoplasms: For patients with a history of non-malignant neoplasms, therapy should be initiated after careful evaluation of the potential benefit of treatment. For patients with a history of treated and stable malignancies, therapy should be initiated only after careful evaluation of the potential benefit of treatment relative to the risk of re-activation of the underlying malignancy.
- Elevated IGF-1: Stimulates growth (GH) production and increases serum IGF-1. Given that IGF-1 is a growth factor and the effect of prolonged elevations in IGF-1 levels on the development or progression of malignancies is unknown, IGF-1 levels should be monitored closely during therapy.
- Fluid Retention: Fluid retention may occur during therapy and is thought to be related to the induction of GH secretion, resulting in a variety of adverse reactions (eg, edema, arthralgia, carpal tunnel syndrome) which are either transient or resolve with discontinuation of treatment
- Glucose Intolerance: Treatment may result in glucose intolerance. Patients treated with tesamorelin are at an increased risk of developing diabetes (HbA1c ≥ 6.5%). In clinical trials at week 26, a greater percentage of patients had elevated HbA1c (≥6.5%) in the tesamorelin group than in the placebo group (4.5% vs 1.3%).
- Hypersensitivity Reactions**:** Hypersensitivity reactions occurred in 3.6% of patients. These reactions included pruritis, erythema, flushing, urticaria, and other rash.
- Injection Site Reactions: Treatment may cause injection site reactions, including injection site erythema, pruritus, pain, irritation, and bruising.
- Acute Critical Illness: Increased mortality in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure**.**
- Adverse Reactions: The most common adverse reactions (incidence >5% and more frequent than placebo) included arthralgia (13.3% vs 11.0%), injection-site erythema (8.5% vs 2.7%), injection-site pruritis (7.6% vs 0.8%), pain in extremities (6.1% vs 4.6%), peripheral edema (6.1% vs 2.3%), and myalgia (5.5% vs 1.9%).

Questions and Answers

Q: Is tesamorelin only effective in reducing abdominal adipose tissue?
A: Studies only evaluated abdominal, but there is anecdotal information of reducing adipose tissue associated with HIV hump as well as breast tissue.

Q: Are there studies being conducted in patient populations other than HIV?
A: Not at this time.

Q: Were all the trials presented today?
A: Yes, and they are published.

Q: Approximately, what percentage of HIV patients is tesamorelin appropriate for?

A: Estimated that approximately 3% of HIV patients are appropriate for use, especially patients that have been on HIV treatment for a long time.

Q: Are any outcomes studies being conducted to evaluate whether tesamorelin decreases cardiovascular (CV) events due to decreased lipodystrophy?
A: As part of FDA approval, the manufacturer is required to evaluate CV outcomes, so a study is in process. Also, the manufacturer will be conducting studies to ensure tesamorelin does not cause neuropathy in diabetic patients and to decrease the dose to 1mL.

Q: Is tesamorelin being studied in other indications?
A: Additional indications are not currently being sought, but there have been propositions to study the drug in non-HIV patients with lipodystrophy.

Q: How are other Medicaid plans covering?
A: Some are covering now; others have decided to wait to on coverage status until their DURB/P&T reviews.

Q: Are any additional long-term studies being conducted?
A: A 10-year study is in process, but no results are available yet.

Q: How long can it take for response to therapy?
A: Evaluation in clinical trial was at Week 26, but working on analyzing data to determine if earlier response.

Q: Is weight distributed?
A: No, tesamorelin is weight neutral and only effects hypertrophy.

Q: Is there a study being conducted to evaluate impact of effects from tesamorelin on compliance with HIV regimen?
A: Not in the works now, but may be included in 10-year study.

Q: Is there a REMS program?
A: Yes there is a REMS program, patient support program and the product is distributed through approximately 10 specialty pharmacies.

II. Novartis

Julia Compton, PharmD, Regional Account Scientific Associate Director

Gilenya™ (fingolimod)

- First once-daily oral disease-modifying therapy (DMT) indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical relapses and to delay the accumulation of physical disability.

Clinical Efficacy

- Evaluated in the largest Phase 3 clinical trial program ever conducted in MS, which included two studies (one of which was an active comparator study) in addition to long-term extension studies.
- Fingolimod is the only MS treatment with Phase 3 clinical trial evidence demonstrating significant efficacy in a randomized, double-blind, double-dummy study vs. IM IFNβ-1a, a current standard of care (TRANSFORMS; N=1,292). Fingolimod demonstrated efficacy across all clinical measures of inflammatory disease activity compared with IM IFNβ-1a in this 1-year study and with placebo in a 2-year study (FREEDOMS; N=1,272).
- Fingolimod was effective in patients with relapsing forms of MS as it significantly reduced relapse frequency compared with placebo and in a head-to-head clinical trial vs. IM IFNβ-1a.
    - In FREEDOMS, the annualized relapse rate (ARR) was significantly lower in patients treated with Fingolimod 0.5 mg than in patients who received placebo (0.18 vs 0.40; $P<0.001$), representing a relative reduction of 54%. There was a significantly higher percentage of Fingolimod-treated patients without relapse after 24 months of therapy compared to placebo (70% vs 46%; $P<0.001$).
    - In TRANSFORMS, the ARR was significantly lower in patients treated with Fingolimod 0.5 mg than in patients who received IM IFNβ-1a (0.16 vs 0.33; $P<0.001$), representing a relative reduction of 52%. Fingolimod reduced the frequency time to first confirmed relapse. The proportion of patients who were relapse-free vs IM IFNβ-1a (83% vs 70%, respectively; $P<0.001$).

- Fingolimod delayed the accumulation of physical disability in patients with relapsing forms of MS.
    - In FREEDOMS, Fingolimod 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*=0.024).
    - In TRANSFORMS, confirmed disability progression over 12 months was infrequent in the Fingolimod 0.5 mg and IM IFNβ-1a groups. There were no significant differences in the time to 3-month confirmed disability progression between treatments.
- Fingolimod improved magnetic resonance imaging (MRI) measures in patients with relapsing forms of MS.
    - In FREEDOMS, Fingolimod 0.5 mg significantly reduced the mean number of new or newly enlarging lesions on T_2-weighted images (a sign of active inflammation) compared with placebo over 24 months (2.5 vs 9.8 lesions; *P*<0.001) (Kappos 2010). The mean of T1-Gd enhancing lesions at 24 months (0.2 vs. 1.1; *P*<0.001).
    - In TRANSFORMS, Fingolimod 0.5 mg significantly reduced the mean number of new or newly enlarging lesions on T_2-weighted images compared with IM IFNβ-1a (1.6 vs 2.6 lesions; *P*=0.002) (Cohen 2010). The mean number of T1 Gd enhancing lesions at 12 months (0.2 vs 0.5; *P*<0.001).

Clinical Safety

- The most frequent adverse reactions (incidence ≥10% and greater than placebo) for Fingolimod 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 Fingolimod 0.5 mg was serum transaminase elevations (3.8%).
- Bradyarrhythmia and Atrioventricular Blocks: Initiation of Fingolimod treatment results in a decrease in heart rate. Observe all patients for signs and symptoms of bradycardia for 6 hours after first dose. Obtain baseline ECG before first dose if not recently available in those at higher risk of bradyarrhythmia. After the first dose of Fingolimod, the heart rate decrease starts within an hour and the Day 1 decline is maximal at approximately 6 hours. Following the second dose a further decrease in heart rate may occur when compared to the heart rate prior to the second dose, but this change is of a smaller magnitude than that observed following the first dose. With continued dosing, the heart rate returns to baseline within 1 month of chronic treatment. Initiation of Fingolimod treatment has resulted in transient AV conduction delays.
- Infections: Fingolimod causes a dose-dependent reduction in peripheral lymphocyte count to 20% to 30% of baseline values because of reversible sequestration of lymphocytes in lymphoid tissues. Fingolimod may therefore increase the risk of infections, some serious in nature. Monitor for signs and symptoms of infection during treatment and for 2 months after discontinuation. Do not start Fingolimod treatment in patients with active acute or chronic infections.
- Macular Edema: In patients receiving Fingolimod 0.5 mg, macular edema occurred in 0.4% of patients. An ophthalmologic evaluation should be performed before starting Fingolimod and at 3-4 months after treatment initiation. Monitor visual acuity at baseline and during routine evaluations of patients. Patients with diabetes mellitus or a history of uveitis are at increased risk and should have regular ophthalmologic evaluations.
- Respiratory Effects: Dose-dependent reductions in forced expiratory volume over 1 second (FEV_1) and diffusion lung capacity for carbon monoxide (DLCO) were observed in patients treated with Fingolimod as early as 1 month after treatment initiation. The changes in FEV_1 appear to be reversible after treatment discontinuation; there is insufficient information to determine the reversibility of the decrease of DLCO after drug discontinuation.
- Hepatic Effects: Elevations of liver enzymes may occur in patients receiving Fingolimod. Recent liver enzyme results should be available before initiating treatment with Fingolimod. Assess liver enzymes if symptoms suggestive of hepatic injury develop. Discontinue Fingolimod if significant liver injury is confirmed.
- Fetal Risk: Based on animal studies, Fingolimod may cause fetal harm. Women of childbearing potential should use effective contraception during and for two months after stopping Fingolimod treatment.
- Blood Pressure Effects: In MS clinical trials, patients treated with Fingolimod 0.5 mg had an average increase of approximately 2 mmHg in systolic pressure, and approximately 1 mmHg in diastolic pressure, first detected after approximately 2 months of treatment initiation, and persisting with continued treatment. Blood pressure should be monitored during treatment with Fingolimod.
- Immune System Effects Following Fingolimod Discontinuation: Fingolimod remains in the blood and has pharmacodynamic effects, including decreased lymphocyte counts, for up to 2 months following the last dose of Fingolimod. Lymphocyte counts generally return to the normal range within 1-2 months of stopping therapy.

Because of the continuing pharmacodynamic effects of fingolimod, initiating other drugs during this period warrants the same considerations needed for concomitant administration.

Questions and Answers
Q: Have all studies been published?
A: Yes, all studies are available.

Q: Are there any studies currently being conducted?
A: There are studies in progress evaluating use in primary progressive MS, Pregnancy Registry, long-term observations and lower dose.

Q: Any other head-to-head studies in process?
A: None at this time.

Q: How are other Medicaid plans covering?
A: Some are requiring step with interferon; others are not requiring step with interferon since switch data showed improved results.

Q: Are there any cost comparison studies?
A: The American Academy of Neurology showed decreased costs.

Q: Has patient satisfaction with oral vs. injection been evaluated?
A: There is an ongoing study assessing patient satisfaction and results will most likely be available in 1-1½ years.

Q: Is there a REMS program?
A: Yes, the REMS program requires education on Warnings/Precautions.

Q: What was the bottom heart rate in clinical trial(s)?
A: 55 beats per minutes

Q: What is the thought on the cause of macular edema?
A: Thought is due to affect on S1P1 receptors, is dose-related and age-related, occurred in 0.4% of patients treated with fingolimod, patients were not treated for the macular edema and were discontinued resulting in improvement.

Q: What are presenter's thoughts on NICE not recommending Gilenya for NHS formulary?
A: This was a draft guide; Avonex is not used as much in Europe, Tysabri is used more; and recommendation was more economic.

III. Sunovion

Andrei a. Pikalov, III, MD, PhD, Senior Medical Director
Kitty Rajagopalan, PhD, Vice President, Health Economics & Outcomes Research
Daniel Van Deventer, Account Director

Latuda™ (lurasidone)

Efficacy and Safety
- The efficacy of lurasidone in adult patients with schizophrenia was established in four 6-week, double-blind, randomized, placebo-controlled trials (D1050006, D1050196, D1050229, and D1050231) as described in the *Clinical Studies* section (14.1) of the enclosed prescribing information. In addition to these four trials, a fifth trial (D1050049) was included as part of the safety evaluation. The safety and efficacy data from these trials were provided previously to the Drug Utilization Review Board. Data from trials completed after FDA approval (studies D1050233, D1050237, and D1050231E) have not been reviewed by the FDA. These trials are summarized below.

Study D1050233
- Study D1050233 was a 6-week, multicenter, randomized, double-blind, placebo- and active-controlled study to evaluate the efficacy and safety of lurasidone (80 mg/day and 160 mg/day) in patients with an acute exacerbation of schizophrenia. Quetiapine XR 600 mg/day was included as an active control to confirm assay sensitivity.

- At study endpoint, lurasidone at both 80 mg/day and 160 mg/day, as well as the active control (quetiapine XR 600mg/day) showed significant improvement in efficacy parameters from baseline compared to placebo. Mean changes in PANSS from baseline were -22.2 ($p<0.001$) for lurasidone 80 mg/day and -26.5 ($p<0.001$) for lurasidone 160 mg/day, vs. -10.3 for placebo. Quetiapine XR also showed significantly greater changes (-27.8; $p<0.001$) vs. placebo, verifying assay sensitivity of the study. On CGI-S, statistically significant endpoint improvement was also observed for both doses of lurasidone and quetiapine XR compared to placebo. There was a significant decrease from baseline in the Epworth Sleepiness Scale (ESS) in the lurasidone 80 mg group (-1.1; $p = 0.001$), the lurasidone 160 mg group (-0.7, $p = 0.038$), and the placebo group (-0.9; 0.006). There was no significant change from baseline in the quetiapine XR group (0.6; $p = 0.081$).
- The most common adverse events (incidence $\geq$5% and at least twice placebo) in the lurasidone dose groups were akathisia, nausea, parkinsonism, dizziness, and somnolence. The most common adverse events in the quetiapine XR group were dizziness, somnolence, dry mouth, constipation, weight increased, arthralgia, and upper respiratory tract infection. At study endpoint, mean change in weight was +0.1 kg for placebo, +0.6 kg for lurasidone 80 mg and 160 mg, and +2.1 kg for quetiapine XR. Changes in glucose, total cholesterol, and triglycerides in patients treated with lurasidone 80 mg/day and 160 mg/day were similar to placebo. Treatment with the active control (quetiapine XR 600mg/day) resulted in increases in each of these parameters, compared to decreases observed with placebo.

Study D1050231E

- Patients who successfully completed Study D1050231, a 6-week, multicenter, randomized, double-blind, placebo- and active-controlled study with lurasidone 40 mg/day, lurasidone 120 mg/day and olanzapine 15 mg/day (to confirm assay sensitivity), had the option to enter a 6-month, open-label (OL) extension study (D1050231E) with lurasidone. Dosing was fixed at 80 mg/day for the first week and flexible dosing (40-120 mg/day) was permitted thereafter.
- Subjects who received open-label treatment with lurasidone maintained improvement on PANSS total score regardless of initial treatment assignment during the acute 6-week study. The mean (SD) PANSS total score, for patients from all treatment arms (N=246) continuing into the open-label phase, was 66.6 (16.9) at the baseline of the open-label phase. Patients completing open-label treatment (n=117) had a mean (SD) PANSS total score of 54.9 (16.0) at the end of the extension phase. The mean (SD) CGI-S score also decreased from 3.3 (0.9) at OL baseline to 2.7 (1.0) at the end of OL.
- The two adverse events that occurred with an incidence >10% in lurasidone-treated patients were akathisia (13.0%) and insomnia (11.0%). Except for patients who received olanzapine 15 mg in the initial double-blind phase, 6 months open-label treatment with lurasidone did not result in meaningful changes in body weight and body mass index (BMI). Patients who were switched from olanzapine 15 mg/day to lurasidone and completed open-label treatment (n=31) experienced a mean (SD) reduction of -1.9 (5.7) kg in weight. Laboratory findings for patients who continued on lurasidone and completed open-label treatment (n=55) included mean changes from open-label baseline to endpoint in cholesterol (-4.9 mg/dL), triglycerides (-11.6 mg/dL), insulin (-3.2 mU/L), and glucose (6.7 mg/dL). Patients switched from olanzapine to lurasidone showed sustained decreases in lipids. Prolactin, which had increased during the double-blind phase of the study (+3.2 ng/mL in the lurasidone arms (combined) and +3.4 ng/mL on olanzapine arms), showed a median decrease -1.3 ng/mL (LOCF) during the open-label extension.

Study D1050237

- Study D1050237 was a 1-year, double-blind trial that evaluated the long-term safety and tolerability of lurasidone in the treatment of schizophrenia or schizoaffective disorder and included risperidone as an active comparator. Patients were randomized in a 2:1 ratio, to 12-months of double-blind, once-daily treatment with either lurasidone (dosed at 80 mg/day on Days 1-7; flexibly dosed between 40-120 mg/day on Day 8), or risperidone (dosed at 2 mg/day on Days 1-2; 4 mg/day on Day 3; flexibly dosed between 2-6 mg/day on Day 8).
- The most common adverse events (incidence $\geq$10%) in lurasidone treatment group were nausea, insomnia, sedation, akathisia, somnolence, headache, and vomiting. The most common adverse events in the risperidone treatment group were weight increased, somnolence, headache, sedation, insomnia, and nausea. Mean weight change in subjects who completed 12 months of treatment was -1.0 kg for lurasidone and +2.2 kg for risperidone. Median changes in total cholesterol, triglycerides, glucose, and prolactin were -3.0 mg/dL, -3.5 mg/dL, -0.5 mg/dL, and +0.1 ng/mL respectively for lurasidone and -7.0 mg/dL, -1.0 mg/dL, +3.0 mg/dL, +9.1 ng/mL for risperidone.
- Least Squares (LS) mean reduction in PANSS total score was -4.7 for the lurasidone treatment group and -6.5 for the risperidone treatment group at month 12. Relapse rates were low, occurring in 20% of lurasidone-treated subjects and 16% of risperidone-treated subjects. On an mixed model for repeated measures (MMRM) analysis, the CGI-S score decreased from baseline to month 12 in both the lurasidone group (-0.4, 95% CI: -0.5, -0.3; n=410) and the risperidone group (-0.4, 95% CI: -0.5, -0.2; n=198).

Questions and Answers
Q: Are any other indications being sought?
A: Bipolar depression, maintenance of bipolar and maintenance of schizophrenia in pediatrics.

Q: Are any other head-to-head trials being conducted?
A: Not at this time.

Q: Are other dosage forms in development?
A: Yes, looking at a long-acting injection.

IV. Avanir

Gary L. Engelmann, PhD, Senior Medical Science Liaison
Terry Turner, Regional Account Manager

Nuedexta™ (dextromethorphan/quinidine)

- First and only FDA-approved treatment for PBA (10/29/2010)
  - Pseudobulbar Affect, or PBA, is a neurological condition characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. PBA episodes typically occur out of proportion or incongruent to the underlying emotional state.
  - PBA occurs secondary to a variety of otherwise unrelated neurological conditions, including ALS, MS, Stroke, Parkinson's, Alzheimer's and Traumatic Brain Injury (TBI).
  - Dextromethorphan/quinidine has not been shown to be safe and effective in other types of emotional lability that can commonly occur, for example, in Alzheimer's disease and other dementias.
- PBA is believed to occur following disruption of input to, or modulation of, the brainstem, resulting in an inappropriate response to the patient's underlying mood.
- Nuedexta is a combination of dextromethorphan (DM) 20 mg and quinidine (Q) 10 mg.
- DM is believed to modulate excitatory neurotransmission through action at both sigma-1 and NMDA receptors.
  - DM is thought to inhibit the release of glutamate and attenuate post-synaptic responses
- Q is required to prevent the rapid metabolism of DM by selective inhibition of CYP2D6, resulting in a near 25-fold increase in DM plasma levels.

Clinical Efficacy
- In the pivotal Nuedexta study, the primary outcome measure, laughing and crying episodes, was statistically significantly lower in the Nuedexta arm compared to placebo, based on an analysis of the sums of the episode counts over the 12 week double-blind study.
- Additional analyses show 51% of Nuedexta patients achieved remission, compared to 29% of placebo patients.
- Prior clinical trials at higher doses (dextromethorphan 30 mg/quinidine 30 mg) provided supportive evidence.

Clinical Safety
- Nuedexta can interact with other medications causing significant changes in blood levels of those medications and/or Nuedexta. Nuedexta is contraindicated in patients receiving drugs that both prolong QT interval and are metabolized by CYP2D6 (e.g., thioridazine and pimozide) and should not be used concomitantly with other drugs containing quinidine, quinine, or mefloquine. Nuedexta is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs within the preceding 14 days. Nuedexta is contraindicated in patients with a known hypersensitivity to its components.
- Nuedexta may cause serious side effects, including possible changes in heart rhythm. Nuedexta is contraindicated in patients with a prolonged QT interval, congenital long QT syndrome or a history suggestive of torsades de pointes, in patients with heart failure as well as patients with, or at risk of, complete atrioventricular (AV) block, unless the patient has an implanted pacemaker.
- Nuedexta causes dose-dependent QTc prolongation. When initiating Nuedexta in patients at risk of QT prolongation and torsades de pointes, electrocardiographic (ECG) evaluation of QT interval should be conducted at baseline and 3-4 hours after the first dose.
- The most common adverse reactions in patients taking Nuedexta are diarrhea, dizziness, cough, vomiting, weakness, swelling of feet and ankles, urinary tract infection, flu, elevated liver enzymes, and flatulence.
- Precautions to reduce the risk of falls should be taken, particularly for patients with motor impairment affecting gait or a history of falls.

Questions and Answers
Q: Were all studies presented?
A: Yes.

Q: Are there studies looking at lower dosing?
A: No, 20/10 will be lowest does for PBA.

Q: Was Nuedexta approved as an orphan drug?
A: No, but was granted priority review by the FDA.

Q: Is there a REMS program and/or distribution program?
A: No, a REMS or distribution program was not required by the FDA.

V. Ther-Rx and KV

Jennifer Gudeman, PharmD, Director, Medical Communications
Jeff Cameron, National Account Director

Makena™ (hydroxyprogesterone)

- Preterm birth has been declared a national healthcare crisis. In spite of advances in perinatal care, the incidence of preterm birth increased 36% between 1981 and 2006. In 2008, the preterm birth rate in the US was 12.3%, which translates to approximately 500,000 premature babies per year or about 1 out of every 8 births in the US. In 2008, the rate of preterm births in the state of Georgia was 13.4%.
- Infants born preterm are at increased risk of developing potentially serious complications including intraventricular hemorrhage (IVH), respiratory distress syndrome (RDS), periventricular leukomalacia, necrotizing enterocolitis (NEC), apnea, jaundice, anemia, and infections due to immature immune systems. Significant long-term morbidities such as retinopathy of prematurity (ROP), intellectual disability, and cerebral palsy are also associated with preterm birth. Because some of these complications and consequences require lifelong medical care, preterm births impart a substantial financial burden on the US healthcare system. In 2005, direct and indirect costs associated with preterm birth cost the nation at least $26 bi llion, which translates to approximately $51,600 per infant.
- Makena is the first and only product indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth.
- Makena is an orphan drug," defined by the FDA as a drug for a condition affecting fewer than 200,000 people a year. Approximately 3% of pregnant women are estimated to be clinically indicated for treatment.

Clinical Efficacy

- The effectiveness of Makena is based on improvement in the proportion of women who delivered <37 weeks of gestation.
- There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity. While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.
- The Maternal Fetal Medicine Units (MFMU) Network, in conjunction with the National Institute of Child Health and Human Development (NICHD), conducted a multicenter, randomized, double-blind, placebo-controlled study of 463 women pregnant with a singleton, with a history of singleton spontaneous preterm birth, to evaluate the safety and efficacy of Makena in reducing the risk of recurrent preterm birth. Makena demonstrated a 32% reduction in delivery prior to 37 weeks gestation (37.1% v. 54.9%, 95% CI, [-28.0%, -7.4%]) compared to placebo, with reductions at 35 and 32 weeks gestation as well.

Clinical Safety

- Most common adverse reactions reported in >2% of subjects and at a higher rate in the Makena group than in the control group are injection site reactions (pain [35%], swelling [17%], pruritus [6%], nodule [5%]), urticaria (12%), pruritus (8%), nausea (6%), and diarrhea (2%).
- Rates of miscarriage (2.4% v. 0%) and stillbirth (2.0% v. 1.3%) were numerically higher in the Makena group, but were not statistically significant. The fetal deaths were considered by the investigator "unlikely" or "definitely not" related to the study drug.

- A follow-up study was conducted that examined children born to women enrolled in Meis et al at an average of 4 years of age and provides reassurance that Makena appears to be safe for the fetus when administered in the second and third trimesters.
- A large (n=1700), multinational, Phase 3b trial is currently underway with sufficient power to address the impact of neonatal morbidity and mortality; this randomized, placebo-controlled Makena trial also includes a follow-up observational study.

Summary
- Before the introduction of Makena, patients who were prescribed 17P were only able to obtain preparations from compounding pharmacies, which may be associated with logistical and financial barriers.
- The introduction of FDA-approved Makena is a significant milestone in obstetrical medicine.
- Makena is produced under stringent cGMP conditions, which helps to ensure that pharmaceutical companies manufacture medicines that meet specific FDA requirements for identity, strength, quality, and purity.
- Makena is the first and only product with an FDA-approved indication for reducing the risk of preterm birth in women with a singleton pregnancy with a history of singleton spontaneous preterm birth.
- Ther-Rx recommends listing Makena as a preferred product. Please refer to the Makena PI for complete prescribing and safety information.

Questions and Answers
Q: Were all studies presented today?
A: Yes.

Q: How are other Medicaid plans covering?
A: Amerigroup – NP/PA; WellCare – NP/PA; PSHP – NP/PA; Maryland and Virginia – P

Q: Where should product be administered?
A: Should be administered by health care provider and can be administered in MD office or home health.

Q: How will adding to FFS help?
A: CMOs tend to follow FFS PDL.

Q: Is manufacturer looking to expand indication?
A: Not at this time; 17P has been evaluated in multiple pregnancies and was shown to be ineffective.

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Manufacturers' Forum
Manufacturer Presentations

The following presentations were presented at the May 5th Manufacturers' Forum on drugs that are being re-reviewed at the September 15th Drug Utilization Review Board meeting.

Date: May 5, 2011

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

Attendees
NorthStar HealthCare Consulting
Emily Baker, PharmD, BCPS, MBA, MHA, President
Tara R. Cockerham, PharmD, Clinical Programs Director
Dan Alday, RPh, Director, Clinical Programs & Analytics

SXC Health Solutions
Tami Sweat, PharmD, Director, Public Sector

Drug Summary Documents
Please note that relevant, electronic materials that were provided by manufacturers on the drugs that were posted to the Department of Community Health (DCH) website as under review for the June 16, 2011 meeting were provided to the Drug Utilization Review Board (DURB). For the drugs that were also presented at the Forum, the drug summary documents that highlighted the presentations are also included 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. Boehringer Ingelheim Pharmaceuticals
Patricia Grossman, PharmD, MBA, Associate Director, Healthcare Quality and Outcomes
Kimberly Cullen, Regional Account Manager, Managed Care
Tammy Martin, Regional Director, Managed Markets SE Region

Pradaxa™ (dabigatran etexilate)

Indications and Usage
Pradaxa is a direct thrombin inhibitor indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (AF).

Clinical Efficacy
- The Randomized Evaluation of Long-term anticoagulant therapy (RE-LY) trial was a prospective, multicenter, randomized, parallel-group trials of N=18,113 patients, comparing efficacy and safety in the reduction in risk of stroke and systemic embolism in patients with nonvalvular AF of 2 blinded doses of Pradaxa vs. open-label warfarin, adjusted locally to an international normalized ration (INR) of 2.0 to 3.0 with the INR measured at least monthly. For subjects randomized to warfarin, the median percentage of the study period (excluding the first week of therapy and after discontinuation of the study drug) during which the INR was within therapeutic range (TTR), calculated using the Rosendaal method, was 67%.
- Relative to warfarin and to Pradaxa 110mg twice daily, Pradaxa 150mg twice daily significantly reduced the primary composite endpoint of stroke and systemic embolism (p=0.0001).
- The risk of major bleeds was similar with Pradaxa 150mg and warfarin across major subgroups defined by baseline characteristics, with the exception of age, where there was a trend towards a higher incidence of major bleeding on Pradaxa (HR 1.2, 95% CI: 1.0 to 1.4) for patients $\geq$75 years of age.
- There was a higher rate of major gastrointestinal (GI) bleeds in patients receiving Pradaxa 150mg than in patients receiving warfarin of 1.5, 95% CI: 1.2 to 1.9), and a higher rate of any GI bleeds (6.1% vs. 4.0%, respectively).

Clinical Safety

- Pradaxa is contraindicated in patients with active pathological bleeding and patients with a known serious hypersensitivity reaction (e.g., anaphylactic reaction or anaphylactic shock) to Pradaxa.
- Pradaxa increases the risk of bleeding and can cause significant and, sometimes, fatal bleeding.
- Risk factors for bleeding include medications that increase the risk of bleeding in general (e.g., antiplatelet agents, heparin, fibrinolytic therapy, and chronic use of nonsteroidal antiinflammatory drugs) and labor and delivery.
- Discontinuing Pradaxa for active bleeding, elective surgery, or invasive procedures places patients at an increased risk of stroke. Lapses in therapy should be avoided, and if Pradaxa must be temporarily discontinued for any reason, therapy should be restarted as soon as possible.
- The concomitant use of Pradaxa with P-gp inducers (e.g., rifampin) reduces dabigatran exposure and should generally be avoided. P-gp inhibitors (ketoconazole, verapamil, amiodarone, quinidine and clarithromycin) do not require dose adjustments. These results should not be extrapolated to other P-gp inhibitors.
- In the pivotal trial comparing Pradaxa to warfarin, the most frequent adverse reactions leading to discontinuation of Pradaxa were bleeding and GI events. Pradaxa 150mg resulted in a higher rate of major GI bleeds and any GI bleeds compared to warfarin. In patients $\geq$75 years of age, the risk of major bleeding may be greater with Pradaxa than with warfarin. Patients on Pradaxa 150mg had an increased incidence of GI adverse reactions. These were commonly dyspepsia (including abdominal pain, abdominal discomfort and epigastric discomfort) and gastritis-like symptoms (including GERD, esophagitis, gastritis and GI ulcer). Drug hypersensitivity reactions were reported in <0.1% of patients receiving Pradaxa.
- The risk of myocardial infarction was numerically greater in patients who received Pradaxa 150mg than in those who received warfarin.

Questions and Answers

Q: Were all phase III studies that have been conducted presented?
A: Yes, all pivotal trials were presented.

Q: Have guidelines been updated to include Pradaxa?
A: Yes, the guidelines have been updated to include Pradaxa as an alternate to warfarin for prevention of stroke and system embolism.

Q: Has a cost analysis been conducted vs. warfarin?
A: A U.K. cost-effectiveness study conducted by Freeman et al concluded that in patients 65 years or older with nonvalvular AF at increased risk for stroke, dabigatran may be a cost-effective alternative to warfarin depending on pricing in the U.S. In addition, Boehringer developed a Markoff budget impact model that estimated by adding Pradaxa to the PDL was cost neutral to Georgia Medicaid.

Q: Does the budget impact model take into account GI bleeds?
A: GI bleeds are captured, but are not separated out.

Q: How are other Medicaid plans covering?
A: Some of preferred with or without prior authorization and some have non-preferred with or without prior authorization.

Q: Is a supplemental rebate being offered?
A: Yes.

Manufacturers' Forum
Manufacturer Presentations

The following presentations were presented at the May 26th Manufacturers' Forum on drugs that are being re-reviewed at the September 15th Drug Utilization Review Board meeting.

Since the Alpha-1 Proteinase Inhibitors therapeutic class was added as under review at the June 16, 2011 Drug Utilization Review Board (DURB) meeting after the May 5, 2011 Forum, a second Forum was held for manufacturers to present clinical information on these products.

Date: May 26, 2011

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

Attendees
NorthStar HealthCare Consulting
Tara R. Cockerham, PharmD, Clinical Programs Director
Dan Alday, RPh, Director, Clinical Programs & Analytics
Annie Oyanuntaruk, PharmD Candidate

SXC Health Solutions
Tami Sweat, PharmD, Director, Public Sector

Drug Summary Documents
Please note that relevant, electronic materials that were provided by manufacturers on the alpha-1 proteinase inhibitors drugs were provided to the DURB. For the drugs that were also presented at the Forum, the drug summary documents are also included 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. CSL Behring
Christine Donahue, MSN, CRNP, Medical Science Liaison, Pulmonary
Lynn Szott, RN, CCM, Manager, Reimbursement

Zemaira™ (alpha-1 proteinase inhibitor [human])

Alpha 1 Antitrypsin (AAT): Protease inhibitor primarily synthesized by hepatocytes.
- Protects normal body tissue from proteolytic enzyme damage
- Especially neutrophil elastase (NE) released by white blood cells
- Theoretical protective threshold = 11 µM/L/80mg/dL

Role of AAT
- Neutrophils release NE to destroy antigens (i.e. pathogens, irritants)
- NE can digest lung elastin
- AAT released by liver binds and inactivates NE

Pathophysiology: Polymerization of alpha 1 protein.
- Deficiency in alpha 1 protein (A1ATD) quantity and quality

A1ATD Prevalance: 2-3 % of all COPD patients are reported to have A1ATD (80-100,000 people).
- Only 7000 individuals identified thus far

Genetics: Autosomal co-dominant disorder. Description of Disease Risk description by AAT Serum Levels and Phenotype
- Clinical Manifestations: Lung disease, liver disease, systemic manifestations and imaging.

- Delay in diagnosis of AATD: 7.2 years
- ATS Guideline recommendations for alpha 1 testing

Diagnostic Considerations and Available Treatment:
- Lifestyle changes, Pharmacologic therapy, Surgery, A1 Augmentation Therapy

Zemaira Overview
- Phase III Multi-Center Study: The Biochemical Efficacy, Safety, Tolerability of a new Alpha-1 Proteinase Inhibitor, Zemaira
- Phase IV RAPID Study Protocol
  - Primary objective
    - To investigate the effect of Zemaira® on the progression of emphysema, assessed by the decline of lung density, measured by computed tomography (CT)
  - Secondary objectives
    - To assess the effect of treatment with A1-PI on the number, severity, and duration of exacerbations

Questions and Answers
Q: Where is the product usually administered?
A: Infusion centers, home health care or self-administration after training.

Q: Should the first dose at least be administered in a medical setting to assess for allergic/hypersensitive/anaphylaxis reactions?
A: Yes, it is recommended that the first dose be administered in a medical setting.

Q: Can allergic-type reactions occur with subsequent doses?
A: It is possible. The presenter will research the incidence and follow-up.

Q: Do you know if general practitioners prescribe the drug?
A: General practitioners usually do not and general pulmonologist usually do not either and will refer these patients to a pulmonologist that specialized in emphysema.

Q: How do other Medicaid and Commercial plans cover?
A: Most do have a PA on the drug and some cover under pharmacy only, some cover under medical only and some cover under both.

Q: What are the advantages of Zemaira over the other alpha-1 proteinase inhibitors?
A: It is the only product classified as highly-purified by the FDA, has the fastest infusion time, low fluid required, does not require refrigeration, multiple support programs provided and patients in CSL Behring support programs are blinded to the manufacturer.

Q: If patient does not respond to one alpha-1 proteinase inhibitor, is it appropriate to try another?
A: Alpha-1 proteinase inhibitors are augmentation therapy that do not treat symptoms, but are used to preserve lung function. Due to differences in manufacturing processes of the drugs, if a patient has a reaction to one product, another product may be cautiously tried and patients may do well on another product.

Q: Are any additional clinical trials being conducted?
A: An outcomes trial has been conducted evaluating the primary endpoint of disease progression assessed by the decline of lung density. The data should be available in 2012.

II. Baxter

George O. Kitchens, RPh

Glassia® and Aralast-NP® (alpha-1 proteinase inhibitor [human])

Indication

- Glassia and Aralast-NP are indicated for chronic augmentation and maintenance therapy in individuals with emphysema due to congenital deficiency of alpha$_1$-proteinase inhibitor (Alpha$_1$-PI), also known as alpha1-antitrypsin (AAT) deficiency

Dosing
- Glassia is ready to use liquid solution of Alpha$_1$-Proteinase Inhibitor
- Aralast-NP is sterile, non-pyrogenic, lyophilized powder of Alpha$_1$-Proteinase Inhibitor that requires reconstitution
- 60mg/kg body weight, given weekly by intravenous infusion

AATD
- Alpha1 Antitrypsin Deficiency (AATD)
- Under diagnosed hereditary condition that has similar symptoms to other respiratory diseases like asthma and emphysema
- Two primary symptoms are cough and shortness of breath
- Less than 10% diagnosed
- Accounts for approximately 0.7% - 3% of COPD patients

Screening
- American Thoracic Society/European Respiratory Society Statement-2003
    - "Furthermore, it is recommended that all subjects with COPD or asthma characterized by incompletely reversible airflow should be tested once fir quantitative AAT determination"
- WHO Statement-1997
    - "All patients with COPD and adults as wells as adolescents with asthma, should be screened once in their lifetime for AAT deficiency"

Safety
- Most common adverse reactions (>3%) in clinical studies were headache and dizziness
- Clinical data demonstrating the long-term effects of chronic augmentation and maintenance therapy of individual with Glassia and Aralast-NP are not available

Clinical Trials
- Clinical and biochemical studies have demonstrated that with such therapy, Aralast is effective in maintaining target serum Alpha$_1$-Proteinase Inhibitor trough levels and increasing levels in epithelial lining fluid

Distribution
- Selected Specialty Pharmacy Providers

Questions and Answers
Q: What are the advantages of these products over others?
A: Glassia is ready to use.

Q: Why does Glassia require a longer infusion time than the others?
A: This is the infusion time that was conducted in the clinical trial and thus approved by the FDA.

Q: So, the longer infusion time is not related to any safety issues?
A: No.

Q: Are any additional clinical trials being conducted?
A: No, not at this time.

Q: Is Aralast-NP going to be discontinued in favor of Glassia?
A: Baxter is working on a nebulized formulation of alpha-1 proteinase inhibitor, so Aralast-NP will most likely be discontinued at some point.

Q: How are other Medicaid and Commercial plans covering?
A: The presenter noted that prior authorization is expected, but the presenter stated he was unaware of any plans preferring one alpha-1 proteinase inhibitor product over another.

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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 SXC Health Solutions, announces the next Forum occurring on Wednesday, November 2, 2011.

Date: **Wednesday, November 2, 2011 from 9am to 5pm EST**

Location: **Manufacturers' Forum - Georgia Department of Community Health**
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, therapeutic classes and/or supplemental rebate classes up for review are posted to the DCH website at **http://dch.georgia.gov** (under Providers – Pharmacy – Drug Utilization Review Board) approximately 30 days prior to the Forum. Those 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**.

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 ***only*** new clinical information since the drug was last reviewed by the DURB, especially clinical information related to comparisons of other drugs within the class.
- **A one-page summary of the presentation should be provided electronically 1 week prior to the presentation via email to GAMedicaid@nhc-llc.com.**

Comments and Inquiries:
- Manufacturers with comments or inquiries related to Georgia Medicaid FFS **Preferred Drug List, 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 **drug benefit plan design** should submit these to the address or phone number below:

SXC Health Solutions
Georgia Department of Community Health
Windward Fairways I, 3025 Windward Plaza Suite 200
Alpharetta, Georgia 30005
Phone: 1-800-282-3232 Fax: 630-268-0008

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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 SXC Health Solutions by its vendor NorthStar HealthCare Consulting (NHC). Manufacturer input on recommendations is welcomed and appreciated using these opportunities.

Ongoing Opportunity:

DUR Board Meeting Process: Drugs, therapeutic classes and/or supplemental rebate classes up for review will be posted to the DCH website at **http://dch.georgia.gov** (under Providers – Pharmacy – Drug Utilization Review Board – 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 the NHC clinical information and based upon 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 either a new drug on the market or a drug that is part of a supplemental rebate class under review by the DURB at the next meeting.

2) Clinical information relevant to ongoing NHC/SXC Clinical Management Strategy development (e.g. review of drug benefit-plan designs, new drugs coming to market, new drug indications, etc.) as deemed necessary by NHC/SXC.

Please see the Manufacturers' Forum Announcement at **http://dch.georgia.gov** under Providers – Pharmacy – Drug Utilization Review Board – 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: Rose Marie Duncan 404-657-7247**

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

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2011

Upcoming Meetings

Drug Utilization Review Board Meeting

2 Peachtree Street, N.W.

5th Floor Board Room

Atlanta, Georgia 30303

Tuesday, December 13, 2011: 10:00am – 2:00pm

Manufacturers' Forum

NorthStar HealthCare Consulting

1121 Alderman Drive

Suite 112

Alpharetta, Georgia 30005

Wednesday, November 2, 2011: 9:00am – 5:00pm