



GEORGIA DEPARTMENT  
OF COMMUNITY HEALTH

## Georgia Department of Community Health

### DRUG UTILIZATION REVIEW BOARD MEETING

Department of Community Health  
2 Peachtree Street - 5<sup>th</sup> Floor Board Room  
Atlanta, Georgia 30303

**March 19, 2013**





**GEORGIA DEPARTMENT  
OF COMMUNITY HEALTH**

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**DRUG UTILIZATION REVIEW BOARD MEETING  
AGENDA**

*2 Peachtree Street - 5<sup>th</sup> Floor DCH Board Room*

*Atlanta, Georgia 30303*

**March 19, 2013 – 9:00 a.m. to 4:00 p.m.**

**CALL TO ORDER**

*Laurel Ashworth, PharmD, Chair*

**COMMENTS FROM THE DEPARTMENT**

*Linda Wiant, PharmD, Director*

**MINUTES FROM PREVIOUS MEETING**

*Chair*

**PDL MANAGEMENT**

*Tara R. Cockerham, PharmD*

➤ **Manufacturers’ Forum**

➤ **New Drug Reviews**

- Neupro™
- Prepopik™
- Sklice™
- Xtandi™

➤ **Therapeutic Class Review**

- Oral nonsteroidal antiinflammatory drugs

➤ **Supplemental Rebate Classes Review**

- Clinical updates

➤ **Utilization Trends Review**

➤ **Drug Information Review**

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

**FUTURE AGENDA ITEMS**

*Chair*

**CONSUMER COMMENTS SESSION**

*Chair*

**ADJOURNMENT OF OPEN SESSION**

*Chair*

**EXECUTIVE SESSION**

**RECONVENING OF OPEN SESSION**

➤ Board’s Voting on Recommendations to DCH

*Chair*

**ADJOURNMENT OF MEETING**

*Chair*





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**Department of Community Health  
Drug Utilization Review Board (DURB)  
MINUTES  
Tuesday, December 11, 2012**

**MEMBERS PRESENT**

Laurel E. Ashworth, Pharm.D., Chair  
Joseph R. Bona, M.D., MBA, Vice-Chair  
Paul D. Boyce, M.D.  
Karen L. Carter, M.D.  
Ann R. Damon, Pharm.D.  
Carl Ellis, R.Ph.  
Deborah W. Fincher, M.S., R.Ph.  
Thomas B. Gore, M.D.  
John Greeson, M.D., MBA  
Rondell C. Jagers, Pharm.D.  
Edwina L. Jones, Pharm.D., MBA  
Robyn Lorys, Pharm.D.  
J. Russell May, Pharm.D.  
Osgood (Drew) A. Miller, R.Ph.  
Donald A. Paul, M.D.  
Matthew Perri, III, R.Ph., Ph.D.  
Sandra L. White, M.D., MBA, FACR  
Mary Virginia "Ginny" Yates, Pharm.D.

**MEMBERS ABSENT**

Melissa D. Carter, J.D.  
Arvind Gupta, M.D.

**Staff**

Linda Wiant, Pharm.D., Pharmacy Director, Pharmacy Services  
Turkesia Robertson-Jones, Pharm.D., Pharmacy Operations Manager, Pharmacy Services  
Gilletta Gray, R.Ph., Clinical Manager, Pharmacy Services  
Lori Garner, MHS, MBA, R.Ph., Pharmacist, Pharmacy Services  
Shimary Hodges, Administrative Assistant, Pharmacy Services

**NorthStar HealthCare Consulting**

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

**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 (DURB/DUR Board/Board) held its fourth meeting for the calendar year on December 11, 2012. The Chair, Laurel E. Ashworth, Pharm.D., called the meeting to order at 10:01am. Board members introduced themselves.

### **Comments from the Department**

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

1. **New Members** – A welcome was extended to new members: Ann Damon, Pharm.D., Deborah Fincher, M.S., R.Ph, Thomas Gore, M.D, and Donald Paul, M.D.
2. **Resignation** – Dr. Gary Williams resigned from the Board. He was thanked for his service.
3. **Georgia Society of Health-Systems Pharmacists** – Rondell Jagers, Pharm.D. was awarded Pharmacist of the Year Award.
4. **Department of Community Health (DCH)** – Staff members were introduced.
5. **Medicaid Reform Update** – Linda Wiant, Pharm.D., Pharmacy Director, Pharmacy Services, presented an overview of the Medicaid Redesign Refresh, DCH's direction and key improvements the Department will be engaged in (see Attachment A). Questions were addressed on benchmarking and the centralized provider portal.

### **Minutes from the Previous Meeting**

Board members reviewed the minutes from the September 20, 2012 meeting. There was one correction in the 'Minutes from Previous Meeting' section to change the date 'September 2012 meeting' to 'June 21, 2012 meeting'. A motion was made and seconded to approve the minutes with the noted correction. The motion carried unanimously to approve the minutes with corrections.

### **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 six (6) manufacturers participated and provided information regarding the following drugs discussed at the December 2012 DURB meeting:

<b>Manufacturers</b>	<b>Drugs</b>
Bristol-Myers Squibb	Reyataz, Sustiva
Merck	Isentress
GlaxoSmithKline	Potiga
Gilead	Atripla, Stribild
Corcept	Korlym
Abbott	Kaletra

There were no questions or comments. The next forum is Thursday, February 7, 2013 and Tuesday, February 12, 2013 (if needed) from 9am-5pm at the NorthStar Healthcare Consulting office: 1121 Alderman Drive, Suite 112, Alpharetta, GA 30005.

**New Drug Reviews**

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

Therapeutic Class	Drugs	Presenter
Enzyme Replacement	<i>Elelyso</i>	Emily Baker, Pharm.D., BCPS
Hormone Modifier	<i>Korlym</i>	Emily Baker, Pharm.D., BCPS
Anticonvulsant	<i>Potiga</i>	Emily Baker, Pharm.D., BCPS

There was one question raised regarding the discontinuation rate due to neuropsychiatric side effects. Dr. Baker noted the following discontinuation rates: Confusion – Potiga (4%) vs. Placebo (< 1%) and Psychosis/Hallucinations – Potiga (<1%) vs. Placebo (0%).

**Therapeutic Class Review**

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

Therapeutic Class
Antiretrovirals for Human Immunodeficiency Virus (HIV)

There were no questions or comments.

**Clinical Utilization Reviews**

Clinical information for the following Clinical Utilization Review topic was presented for discussion by Dr. Cockerham. The complete detailed clinical review was provided in the Clinical Utilization Review section of the DUR Board binder.

Clinical Topic	Description	Presenter
Angeliq	<i>Clinical utilization review of drospirenone containing agents for hormone replacement therapy</i>	Tara Cockerham, Pharm.D.

There was a question regarding the difference in incidences with non-drospirenone agents. It was noted there were no differences with regards to hormone replacement therapy but there were with birth control therapy.

**DCH Decisions**

DCH decisions from the September 2012 DURB meeting were provided in the DCH Decisions section of the DUR Board binder.

### **Utilization Trend Review**

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

### **Drug Information**

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

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

### **Future Agenda Items**

There were no future agenda items noted.

### **Acknowledgement of new DURB Chair and Vice-Chair**

Linda Wiant, Pharm.D., Pharmacy Director, Pharmacy Services, thanked and congratulated Dr. Laurel Ashworth and Dr. Joseph Bona for taking over the positions of DURB Chair and Vice-Chair, respectively. Dr. Bona will move into the Chair position in January 2014.

### **Consumer Comments Session**

Dr. Bona conducted the Consumer Comments Session. Consumer comments were presented to the Board from the following:

- Jeff Graham, Executive Director, Georgia Equality – preferred drug list for antiretrovirals
- David Resnik, M.D., Grady Health Systems, Infectious Disease Program – HIV antiretrovirals
- Harold Catner, M.D., Department of Public Health, Mercer University – prior approval of antiretrovirals
- Leisha McKinley-Beach - Dr. Cockerham presented consumer comments to the Board from a letter from Leisha McKinley-Beach, The Black AIDS Institute, regarding restrictions on HIV antiretrovirals

### **Upcoming Meetings**

The following upcoming meetings were published in the DURB binder:

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

Tuesday, March 19, 2013

Thursday, June 6, 2013

Thursday, September 19, 2013

Tuesday, December 10, 2013

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

Thursday, February 7, 2013  
Tuesday, February 12, 2013 (if needed)  
Thursday, May 2, 2013  
Thursday, August 1, 2013  
Thursday, November 7, 2013

### **Disclosure Forms**

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

Dr. Donald Paul disclosed program support from a manufacturer and abstained from voting for products or classes of medications from this manufacturer.

### **Adjournment of Open Session**

The DUR Board voted to close the open meeting pursuant to the Open Meeting Act of Georgia Section 50-14-1 – 50-14-6 and pursuant to Federal Law Section 1396R-8B3D. The individuals recorded in attendance from the Department of Community Health, Goold Health Services, NorthStar HealthCare Consulting, Catamaran and pharmacy student Kamilah Rashid attended the closed session with the Board members. There was a unanimous vote to adjourn the open session and approve the closed session. The Chairman, Dr. Laurel Ashworth, adjourned the open session at approximately 11:38 am, at which time members took a break and reconvened for the executive (closed) session at 11:58 am.

### **Executive Session**

The executive session was held from 11:58am to 1:33pm.

### **Board's Recommendations to the Department**

After all clinical and financial evaluations and discussions, the DUR Board reconvened in the open session, 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 B.

## **New Drug Reviews**

### **Enzyme Replacement**

The DUR Board recommended *Preferred* status with *Prior Authorization* for *Elelyso*<sup>™</sup>.

### Hormone Modifier

The DUR Board recommended *Preferred* status with *Prior Authorization* for *Korlym*<sup>™</sup>.

### Anticonvulsant

The DUR Board recommended *Non-Preferred* status with *Prior Authorization* for *Potiga*<sup>™</sup>.

## Class Reviews

### Antiretrovirals for Human Immunodeficiency Virus (HIV)

The DUR Board recommended *No Changes* from the current PDL status. The DUR Board also recommended the Department report on prior authorization and utilization data at the June 6, 2013 meeting.

### Conclusion

At the conclusion of the executive session, the open session reconvened at 1:41pm, and the audience was invited back in to hear the Board's recommendations submitted to the Department. Dr. Laurel Ashworth presided over the voting and presented the recommendations from the Board to the Department.

With no other business for discussion, Laurel Ashworth, Pharm.D., Chair, adjourned the meeting at 1:45pm.

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

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Laurel Ashworth, Pharm.D., Chairperson



GA MMIS DDI Project – Requirements Analysis Activities

August 28, 2008



GEORGIA DEPARTMENT OF  
COMMUNITY HEALTH



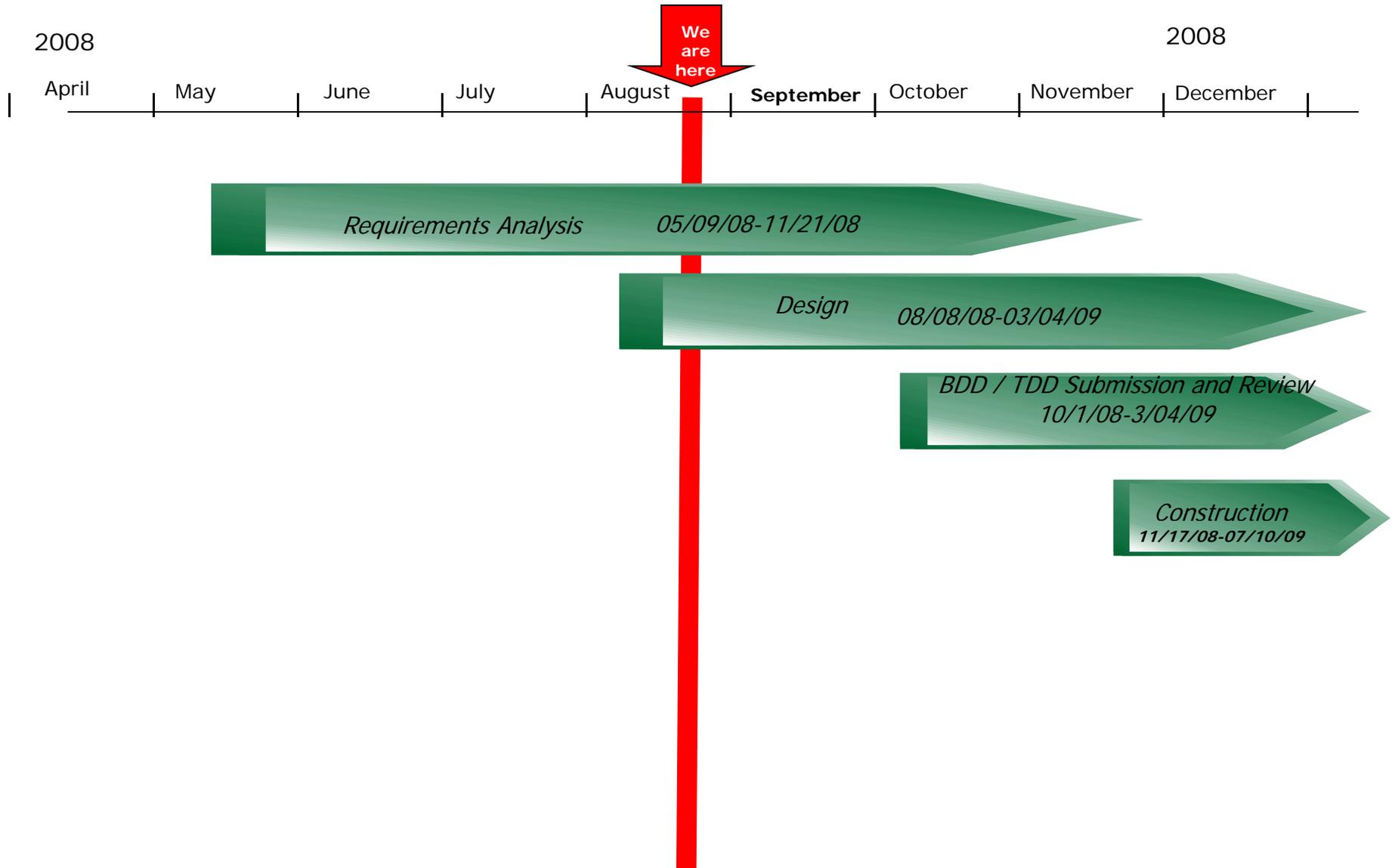
# Goals

Attachment A

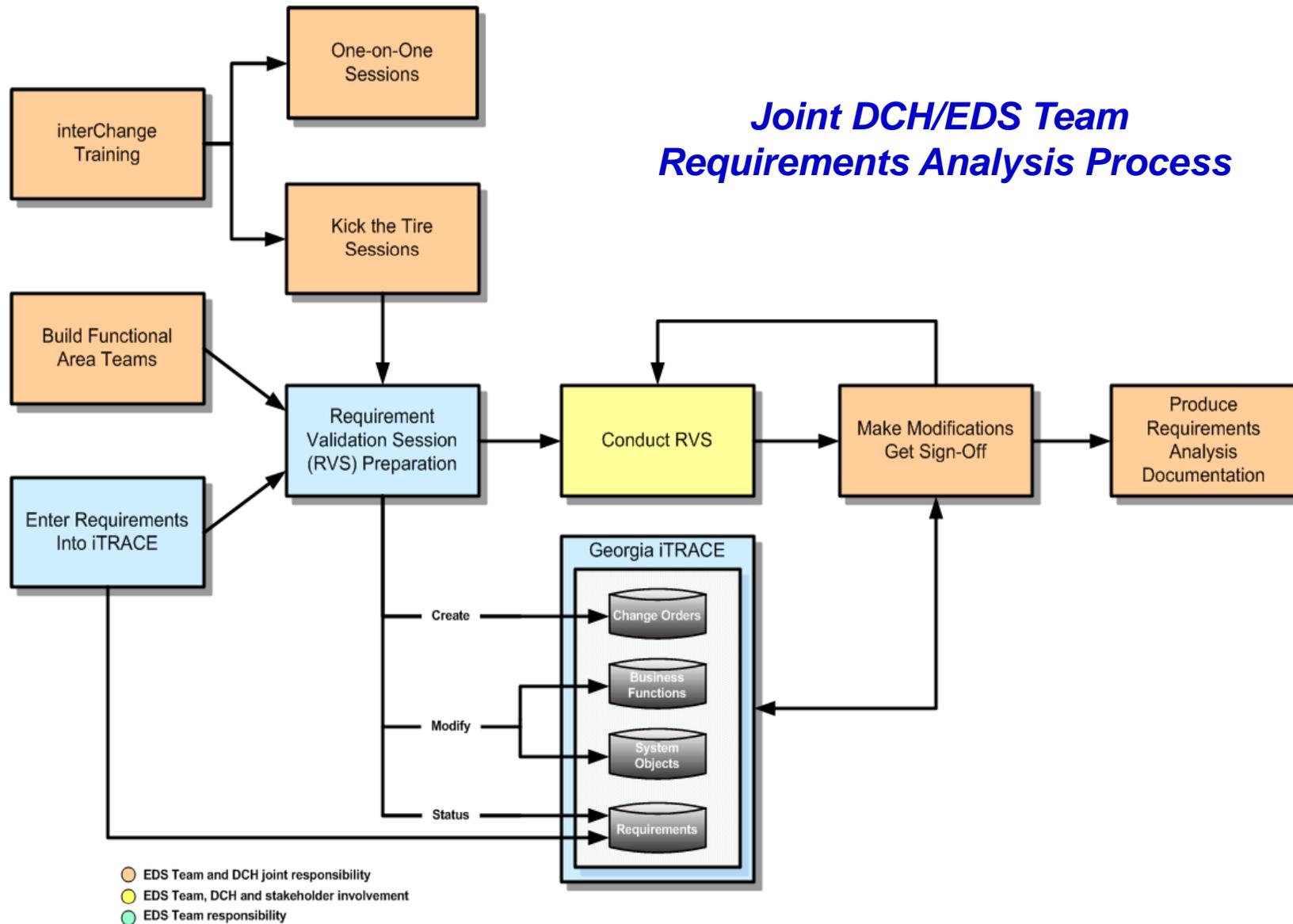
- ✓ Understand the Schedule
- ✓ Review the Requirements Analysis Process Flow
- ✓ Understand the outputs of Requirements Analysis
- ✓ How does the RAD feed into Design
- ✓ Understand the next steps

# Schedule

Attachment A



## Joint DCH/EDS Team Requirements Analysis Process



# *What To Expect When a Business Requirement Is Transferred*

## Attachment A

- The EDS PM who is transferring the requirement informs the EDS PM who is receiving the requirement of the transfer
- The receiving EDS PM contacts the receiving DCH Business Lead and coordinates a review time to discuss and clarify the requirement.
- The receiving EDS TFAL maps any system objects and/or creates any Change orders necessary to demonstrate an understanding of the requirement.
- The receiving DCH Business Lead determines if there are any other DCH team members that will need to be in the review session
- The functional project team, including the DCH Business Lead, DCH SME, DCH PMO, EDS PM, EDS TFAL and EDS Lead BA, review the requirement.
- The necessary clarifications are documented and the requirement with the associated documentation is printed and signed by the EDS PM, TFAL or Designee and the DCH Business Lead
- If the RAD has been delivered regardless of approval status, supplemental pages are printed and delivered to DCH for review and approval

# *What To Expect In The Requirements Analysis Document*

Attachment A

## **Purpose**

- The purpose of the Requirements Analysis Document (RAD) is to present the understanding of each requirement for a given business area.

## **Organization**

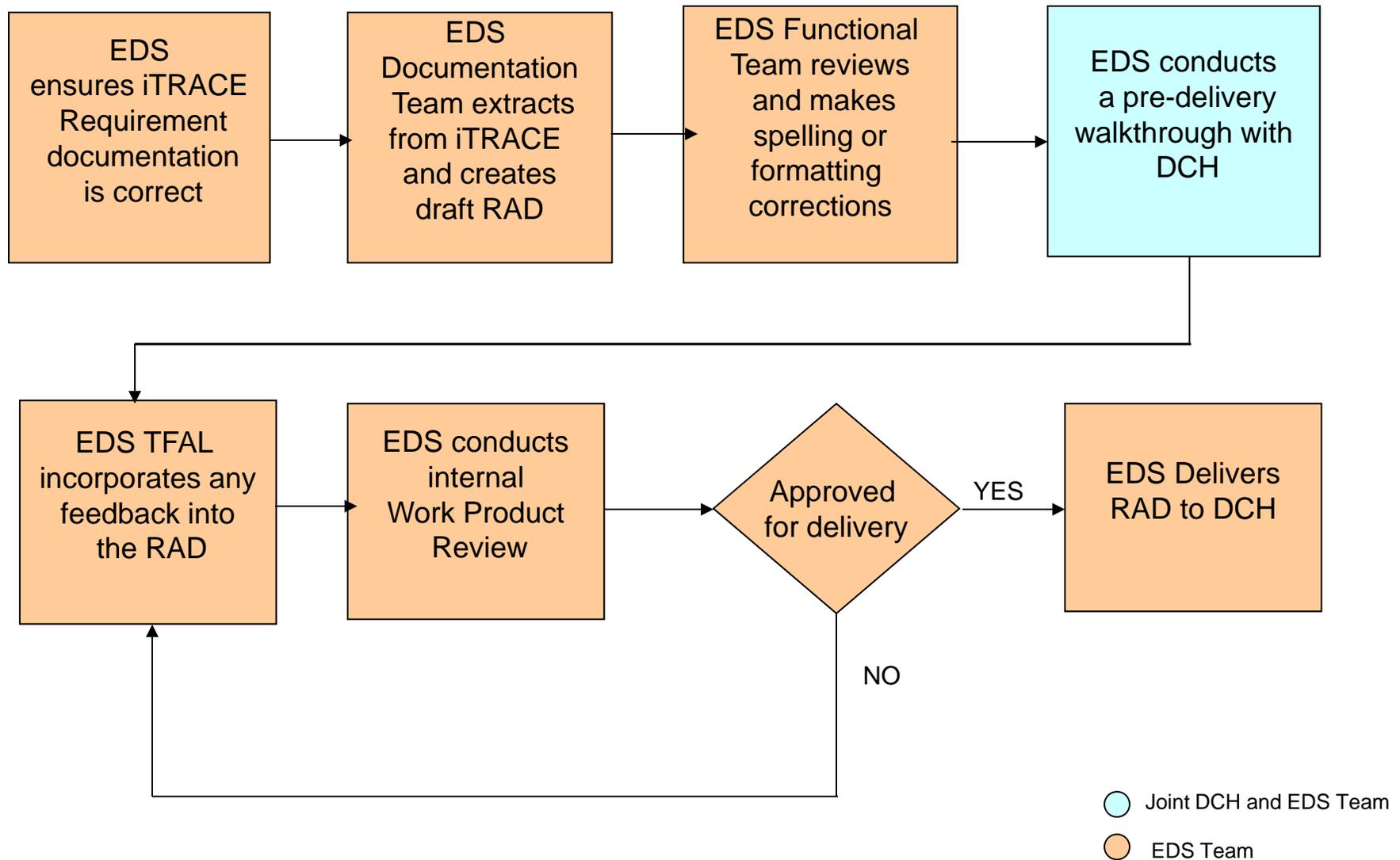
- There will be a separate RAD for each business process. In addition, there is a Cross Functional RAD which includes the general requirements.

## **Content**

- Acclimation to the document
- Requirements along with the clarifications. From this point forward requirements with status codes of RAD Ready, Informational, State, Interim RV Sign off or CCB/Deferred will be included in the RAD.
- Business function interfaces
- Any base system objects mapped to a requirement including reports and panels. (the revised objects will be presented in the Technical Design Document after the changes have been approved by DCH)
- The short description of the Change Orders that have been identified for a requirement (the details of Change Order's business and technical description will be determined during design and will be included in the Technical Design Document)

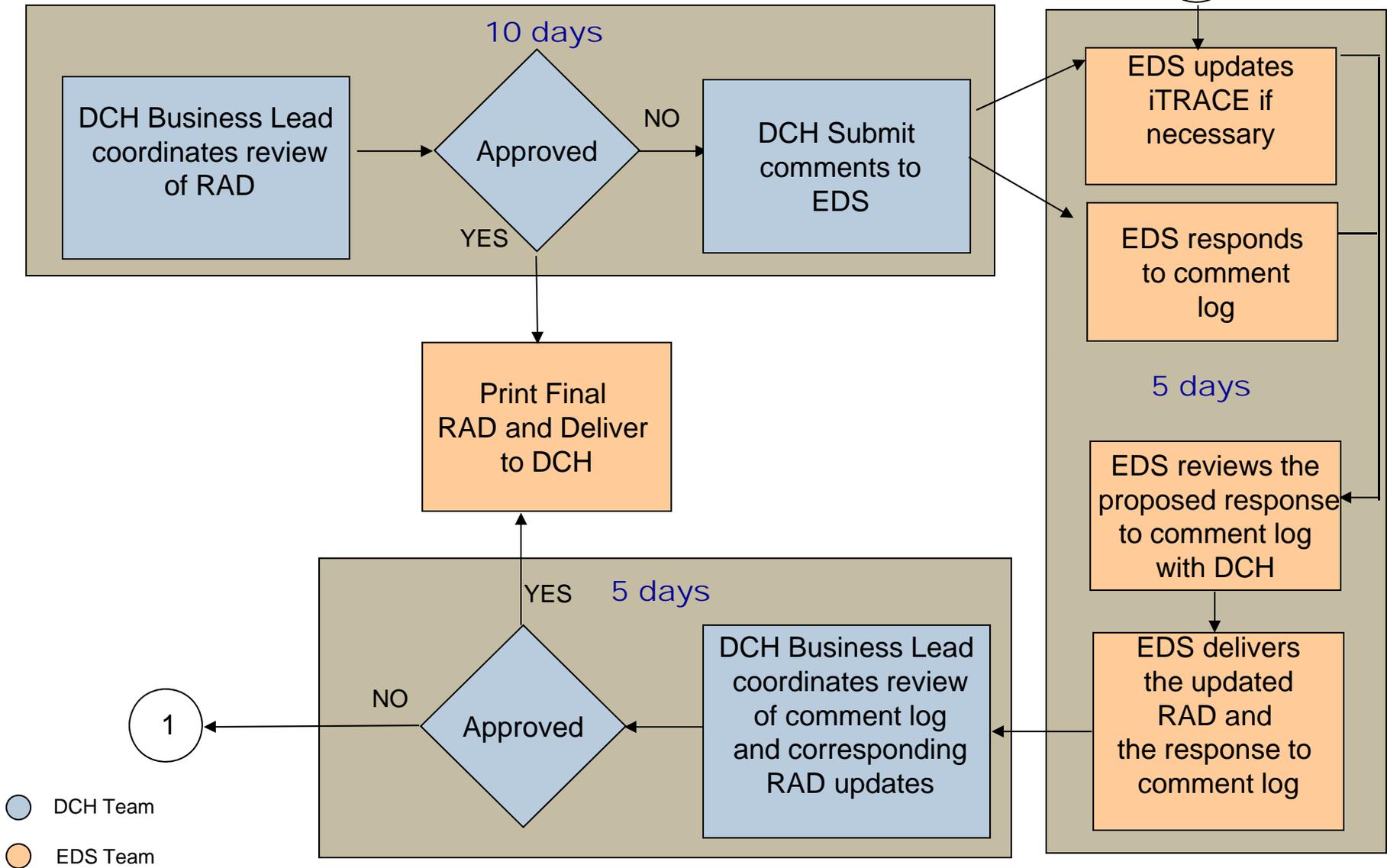
# RAD Production Process

Attachment A



# Document Review Period Process

Attachment A



# *What Does It Mean To Approve The RAD*

Attachment A

- DCH should focus on reviewing the requirement with the associated clarifications. This should match what you printed and signed in the RV sessions
- DCH is agreeing that the RAD contains the requirement clarifications discussed on each of the requirements to date as documented in iTRACE from Analysis session (KTT, RV, work sessions and RAD comment log)
- DCH is agreeing that EDS understands the DCH business requirement
- From this point forward requirements with status codes of RAD Ready, Informational, State, Interim RV Sign off or CCB/Deferred will be included in the RAD
- Change Orders and updated System Objects are approved in the Technical Design Document

# *When is Requirements Analysis Phase Complete?*

Attachment A

- One on One sessions conducted
- Kick the Tire sessions conducted
- Requirements Validation sessions conducted
- iTRACE requirements are in a status of RAD Ready, Informational, State, interim RV Sign off or CCB/Deferred
- Requirements Analysis Documents are approved

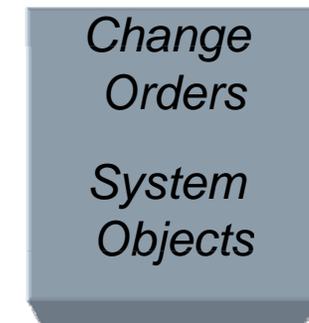
# How Does The RAD Fit Into The Design

Attachment A

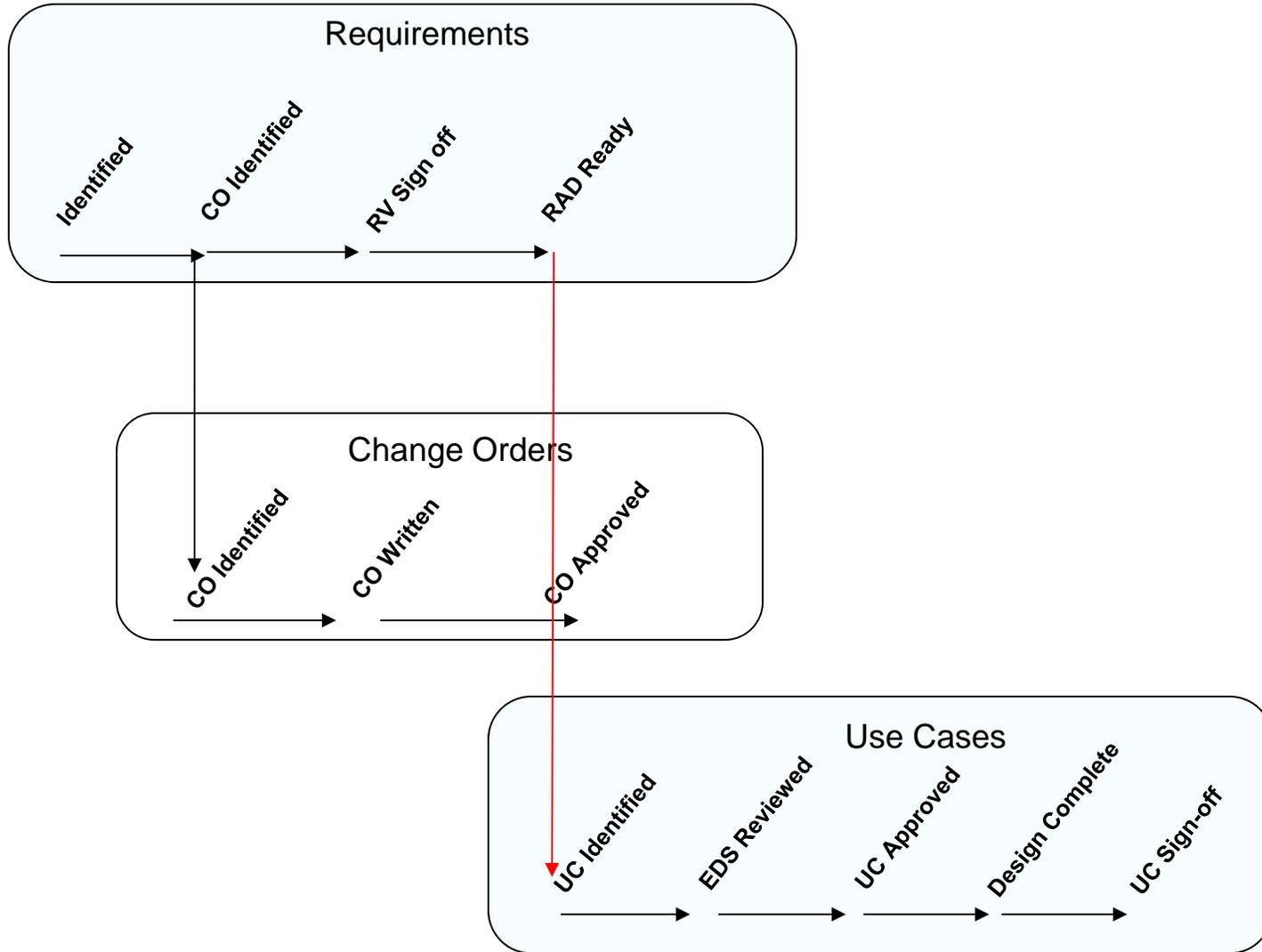
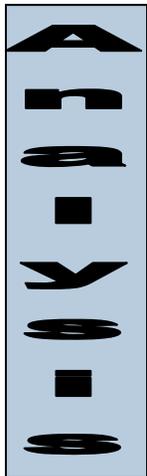
## WHAT



## HOW



# Next Steps



# Walk a Requirement through to Design

Attachment A

- Review requirement 5.4.3.1.2 in the Provider RAD
- Review Change Order 85
- Review the 'License Expiration Report' System Object
- Review the 'Notify Provider when License is Expiring' Use Case

Refer to Handout for discussion

# *Questions and Answers*

GA MMIS DDI Project – Requirements Analysis Activities

August 28, 2008



GEORGIA DEPARTMENT OF  
COMMUNITY HEALTH



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## Drug Utilization Review Board

Motions - Votes

New Drugs

December 11, 2012 - Attachment B

New Drug Review		Enzyme Replacement					
Drug Name	PDL Status	Motion - Recommendations					
Elelyso™ (Intraven)	P/PA	P/PA					
Cerezyme™ (Intraven)	P/PA	P/PA					
Vpriv™ (Intraven)	P/PA	P/PA					
Board Members - Present		Motion Maker (v)	Seconded By (v)	VOTES			
				YES (v)	NO (v)	ABSTAIN (v)	RECUSE (v)
1	Ashworth, Laurel E. Pharm.D. - Chair	N/A					
2	Bona, Joseph R. M.D. - Co-Chair	✓		✓			
3	Boyce, Paul D., M.D.			✓			
4	Carter, Karen L., M.D.			✓			
5	Damon, Ann R., Pharm.D.			✓			
6	Ellis, Carl, R.Ph.			✓			
7	Fincher, Deborah W., M.S., R.Ph.			✓			
8	Gore, Thomas B., M.D.			✓			
9	Greeson, John D., M.D., MBA			✓			
10	Jones, Edwina L., Pharm.D., MBA			✓			
11	Lorys, Robyn Pharm.D.			✓			
12	May, J. Russell, Pharm.D.			✓			
13	Miller, Osgood (Drew) A. R.Ph.		✓	✓			
14	Paul, Donald A., M.D.			✓			
15	Perri, III, Matthew, R,Ph., Ph.D.			✓			
16	White, Sandra L., M.D., MBA, FACR			✓			
17	Yates, Mary Virginia "Ginny", Pharm.D.			✓			
		27	<b>TOTAL</b>	<b>16</b>	<b>0</b>	<b>0</b>	<b>0</b>

## Drug Utilization Review Board

Motions - Votes

New Drugs

December 11, 2012 - Attachment B

New Drug Review		Hormone Modifier					
#	Drug Name	PDL Status	Motion - Recommendations	VOTES			
				YES (v)	NO (v)	ABSTAIN (v)	RECUSE (v)
	Korlym (Oral)™	P/PA	P/PA				
	Ketoconazole (off label)	P	P				
	<b>Board Members - Present</b>	<b>Motion Maker (v)</b>	<b>Seconded By (v)</b>				
1	Ashworth, Laurel E. Pharm.D. - Chair	N/A					
2	Bona, Joseph R. M.D. - Co-Chair			✓			
3	Boyce, Paul D., M.D.			✓			
4	Carter, Karen L., M.D.			✓			
5	Damon, Ann R., Pharm.D.			✓			
6	Ellis, Carl, R.Ph.			✓			
7	Fincher, Deborah W., M.S., R.Ph.			✓			
8	Gore, Thomas B., M.D.			✓			
9	Greeson, John D., M.D., MBA		✓	✓			
10	Jones, Edwina L., Pharm.D., MBA			✓			
11	Lorys, Robyn Pharm.D.	✓		✓			
12	May, J. Russell, Pharm.D.			✓			
13	Miller, Osgood (Drew) A. R.Ph.			✓			
14	Paul, Donald A., M.D.			✓			
15	Perri, III, Matthew, R.Ph., Ph.D.			✓			
16	White, Sandra L., M.D., MBA, FACR			✓			
17	Yates, Mary Virginia "Ginny", Pharm.D.			✓			
<b>28 TOTAL</b>				<b>16</b>	<b>0</b>	<b>0</b>	<b>0</b>

## Drug Utilization Review Board

Motions - Votes

New Drugs

December 11, 2012 - Attachment B

New Drug Review		Anticonvulsant				
Drug Name	PDL Status	Motion - Recommendations	Drug Name	PDL Status	Motion - Recommendations	
Gabapentin Caps(Oral)	P	P	Levetiracetam Solution(Oral)	P	P	
Gabapentin Solution (Oral)	NP/PA	NP/PA	Lyrica Sol (Oral)	NP/PA	NP/PA	
Gabapentin Tabs (Oral)	NP/PA	NP/PA	Lyrica Caps (Oral)	P	P	
Keppra	NP	NP	Neurontin	NP	NP	
Keppra XR	NP/PA	NP/PA	Oxcarbazepine	P	P	
Lamictal	NP	NP	Potiga (Oral) <sup>™</sup>	NP/PA	NP/PA	
Lamictal ODT	NP/PA	NP/PA	Trileptal	NP	NP	
Lamictal XR	NP/PA	NP/PA	Vimpat (Oral)	P/PA	P/PA	
Lamotrigine	P	P	Zonegran	NP	NP	
Levetiracetam IR (Oral)	P	P	Zonisamide (Oral)	P	P	
Levetiracetam ER (Oral)	NP/PA	NP/PA				
Board Members - Present	Motion Maker (v)	Seconded By (v)	VOTES			
			YES (v)	NO (v)	ABSTAIN (v)	RECUSE (v)
1 Ashworth, Laurel E. Pharm.D. - Chair	N/A					
2 Bona, Joseph R. M.D. - Co-Chair	✓		✓			
3 Boyce, Paul D., M.D.			✓			
4 Carter, Karen L., M.D.			✓			
5 Damon, Ann R., Pharm.D.			✓			
6 Ellis, Carl, R.Ph.			✓			
7 Fincher, Deborah W., M.S., R.Ph.			✓			
8 Gore, Thomas B., M.D.			✓			
9 Greeson, John D., M.D., MBA			✓			
10 Jones, Edwina L., Pharm.D., MBA		✓	✓			
11 Lorys, Robyn Pharm.D.			✓			
12 May, J. Russell, Pharm.D.			✓			
13 Miller, Osgood (Drew) A. R.Ph.			✓			
14 Paul, Donald A., M.D.			✓			
15 Perri, III, Matthew, R.Ph., Ph.D.			✓			
16 White, Sandra L., M.D., MBA, FACR			✓			
17 Yates, Mary Virginia "Ginny", Pharm.D.			✓			
29 TOTAL			16	0	0	0

**Drug Utilization Review Board**  
 Motions Votes - Clinical Utilization Review  
 December 11, 2012 - Attachment B

**Class Review**

**Antiretrovirals for Human Immunodeficiency Virus**

Drug Name	PDL Status	Motion - Recommendations	Drug Name	PDL Status	Motion - Recommendations	
Abacavir (Oral)	NP/PA	NP/PA	Norvir Tabs (Oral)	NP/PA	NP/PA	
Aptivus (Oral)	P/PA	P/PA	Prezista (Oral)	P/PA	P/PA	
Atripla (Oral)	P	P	Rescriptor (Oral)	P	P	
Combivir	P	P	Retrovir (Oral)	NP	NP	
Complera (Oral)	P/PA	P/PA	Reyataz (Oral)	P	P	
Crixivan (Oral)	P	P	Selzentry (Oral)	P/PA	P/PA	
Didanosine (Oral)	P	P	Stavudine (Oral)	P	P	
Edurant (Oral)	P/PA	P/PA	Stribild (Oral)	P/PA	P/PA	
Emtriva (Oral)	P	P	Sustiva (oral)	P	P	
EpiVir (Oral)	P	P	Trizivir (Oral)	P	P	
Epzicom (Oral)	P	P	Truvada (Oral)	P	P	
Intelence (Oral)	P/PA	P/PA	Videx (oral)	P	P	
Invirase (Oral)	P	P	Videx EC (Oral)	NP	NP	
Isentress (Oral)	P/PA	P/PA	Viracept (Oral)	P	P	
Kaletra (Oral)	P	P	Viramune Susp (Oral)	P	P	
Lamivudine (Oral)	NP/PA	NP/PA	Viramune Tabs (Oral)	NP	NP	
Lamivudine-Zidovudine (Oral)	NP/PA	NP/PA	Viramune XR (Oral)	NP/PA	NP/PA	
Lexiva (Oral)	P	P	Viread (Oral)	P	P	
Nevirapine (Oral)	P	P	Zerit	NP	NP	
Nevirapine Susp(Oral)	NP/PA	NP/PA	Ziagen (Oral)	P	P	
Norvir Caps (Oral)	NP/PA	NP/PA	Zidovudine (Oral)	P	P	
Norvir Sol (Oral)	P	P				
Board Members - Present <i>(Strike out when absent)</i>	Motion Maker (v)	Seconded By (v)	VOTES			
			YES (v)	NO (v)	ABSTAIN (v)	RECUSE (v)
1 Ashworth, Laurel E. Pharm.D. - Chair	N/A					
2 Bona, Joseph R. M.D. - Co-Chair			✓			
3 Boyce, Paul D., M.D.		✓	✓			
4 Carter, Karen L., M.D.			✓			
5 Damon, Ann R., Pharm.D.			✓			
6 Ellis, Carl, R.Ph.			✓			
7 Fincher, Deborah W., M.S., R.Ph.			✓			
8 Gore, Thomas B., M.D.			✓			
9 Greeson, John D., M.D., MBA			✓			
10 Jones, Edwina L., Pharm.D., MBA			✓			
11 Lorys, Robyn Pharm.D.			✓			
12 May, J. Russell, Pharm.D.			✓			
13 Miller, Osgood (Drew) A. R.Ph.			✓			
14 Paul, Donald A., M.D.					✓	
15 Perri, III, Matthew, R.Ph., Ph.D.	✓		✓			
16 White, Sandra L., M.D., MBA, FACR			✓			
17 Yates, Mary Virginia "Ginny", Pharm.D.			✓			
30	<b>TOTAL</b>		<b>15</b>	<b>0</b>	<b>1</b>	<b>0</b>

## **Manufacturers' Forum Manufacturer Presentations**

**Dates:** February 7 and 12, 2013

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

### **Attendees**

#### *Department of Community Health*

Linda Wiant, PharmD, Pharmacy Director, Pharmacy Services  
Gilletta Gray, RPh, Clinical Manager, 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  
Nekia Austin, PharmD, JD, Director, Program Compliance  
Amy Baker, PharmD, Pharmacist

#### *Catamaran Health Solutions*

Talmahjia "Tami" Sweat, PharmD, Clinical Systems Product Manager

### **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 that were either new drugs, drugs not previously presented or existing drugs with new information since last presented, 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. AbbVie**

Sharon N. Hoffman, PharmD, Clinical Executive, Clinical Evidence & Outcomes  
Phil Hecht, MBA, Managed Care Area Manager  
Cammy Hill, Group Practice Account Executive

#### **Humira® (adalimumab)**

Humira is a fully human monoclonal antibody directed specifically against tumor necrosis factor (TNF) alpha, a pro-inflammatory cytokine that plays an important role in inflammation. Humira is indicated in rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease and chronic plaque psoriasis and newly indicated for ulcerative colitis.

#### **New Indication and Usage**

- Humira has a new indication for inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to immunosuppressants (IMMs) such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP).
- The effectiveness of Humira has not been established in patients who have lost response to or were intolerant to TNF blockers in UC.
- The recommended initial dose for patients with UC is 160 mg at Day 1 (administered as 4 injections on day one or as 2 injections/day for 2 consecutive days), then 80 mg at Day 15 then at Day 29, start 40 mg every other week (eow).

#### **New Efficacy**

- ULTRA 1: a randomized, double-blind, placebo-controlled trial of patients with moderately to severely active UC who had failed corticosteroids and/or IMMs, patients treated with Humira 160/80 mg achieved clinical remission

(Mayo Score <2 with no individual subscore >1) more frequently compared to placebo-treated patients (18.5% vs. 9.2%, p<0.031, respectively; n=130 in each arm) at week 8.

- ULTRA 2: a randomized, double-blind, placebo-controlled trial, evaluated clinical remission at week 8 and week 52 in patients with moderately to severely active UC who had failed corticosteroids and/or IMMs. ULTRA 2 allowed enrollment of patients with previous anti-TNF use (representing 40% of the ITT population). Patients treated with Humira 160/80 mg induction followed by 40 mg eow maintenance (n=248) achieved clinical remission more often than placebo-treated patients (n=246) at week 8 (16.5% vs. 9.3%, p=0.019) and week 52 (17.3% vs. 8.5%, p=0.04).
- Poster: Data from ULTRA 1 and ULTRA 2 was assessed for hospitalization and colectomy rates in patients using adalimumab (ADA) for UC. A 31% reduction in the percentage of patients hospitalized for any reason and a 32% reduction in the number of all-cause hospitalizations were observed for ADA vs. placebo (p<0.05). When UC-related hospitalizations were compared, the reductions for hospitalization rate (45%) and number of hospitalizations (48%) were statistically significant. Rates of colectomy were numerically lower in the ADA group compared with the placebo group, representing a 22% reduction.

### **New Safety**

- ULTRA 1: Serious adverse events occurred in 7.6%, 3.8% and 4.0% of patients in the placebo, ADA 80/40, and ADA160/80 groups, respectively. There were two malignancies in the placebo group, none in the ADA groups. There were no cases of tuberculosis and no deaths.
- ULTRA 2: Serious adverse events occurred in 12% of patients given adalimumab or placebo. Serious infections developed in 1.6% of patients given adalimumab and 1.9% given placebo. In the group given adalimumab, 1 patient developed squamous cell carcinoma and 1 developed gastric cancer.

### **Questions and Answers**

Q: Did any new safety concerns result from the ulcerative colitis trials?

A: No.

Q: What other studies are being explored or conducted?

A: Treatment-naïve in ulcerative colitis, uveitis, pediatric Crohn's disease and spinal arthropathies.

Q: When does the patent expire?

A: 2015-2018.

Q: Do you know of any plans managing this class?

A: No plans as of yet as class is usually protected due to importance of individual patient needs and treatment.

## **II. Bausch & Lomb**

Deanine Grace Halliman, PhD, Sr Medical Science Liaison

Kevin Cowles, Regional Account Manager

### **Besivance® (besifloxacin 0.6% ophthalmic suspension)**

Besivance is a chloro-fluoroquinolone, not previously commercialized as a systemic antibiotic, for the treatment of bacterial conjunctivitis with broad spectrum activity.

### **New Indication**

- In 2012, Besivance expanded its already broad spectrum of activity to include *Pseudomonas aeruginosa*, *Moraxella catarrhalis*, *Staphylococcus warneri*, and *Aerococcus viridians*.
- Besivance was recently approved to treat *Pseudomonas aeruginosa* involved in bacterial conjunctivitis and has the lowest minimal inhibitory concentrations (MICs) of any fluoroquinolone to MRSA and MRSE exhibiting fluoroquinolone-resistance.
- The potency of besifloxacin against *P. aeruginosa* was demonstrated in Phase III Bacterial Conjunctivitis trials where the MIC<sub>90</sub> of clinical isolates ranged from 1 – 4 µg/mL and all isolates were 100% eradicated by the end of treatment.

### **Questions and Answers**

Q: How many days supply is 1 bottle?

A: 21 days supply (3 courses) for bilateral treatment in case the patient loses drops, etc.

Q: When do physicians usually switch to another antibiotic if first product does not clear the bacterial conjunctivitis?

A: Usually after 1 course of the first antibiotic.

Q: Has any resistance been reported?

A: No resistance in phase III or phase IV trials yet; besifloxacin is the newest antibiotic for bacterial conjunctivitis and is not available in a systemic formulation, which helps to prevent resistance.

### **Lotemax<sup>®</sup> Gel (loteprednol etabonate 0.05% ophthalmic gel) – New Formulation**

Lotemax<sup>®</sup> Gel 0.5% was introduced in 2013 and is an ophthalmic corticosteroid indicated for the treatment of post-operative inflammation and pain. The ophthalmic gel represents advancement over Lotemax<sup>®</sup> (loteprednol etabonate ophthalmic suspension) as indicated in the formulation attributes detailed below.

#### **Unique Qualities to Lotemax<sup>®</sup> Ophthalmic Gel**

- 1) **Efficacy:** In two, double-blinded, randomized, placebo-controlled Phase III studies in patients undergoing routine cataract surgery, patients were treated with Lotemax<sup>®</sup> Gel QID for 14 days post-surgery. Patients in the Lotemax<sup>®</sup> Gel arm had complete resolution of Anterior Chamber Cells (30.5% and 31.1%, study 1 and 2, respectively) which was statistically significantly higher compared to ACC resolution in patients in the placebo group (16.3% and 1.9%, study 1 and 2, respectively). These results are similar to those seen in the Phase III studies for Lotemax<sup>®</sup> suspension and Lotemax<sup>®</sup> ointment.
- 2) **Resolution of Pain:** Patients in the Phase III studies also had complete resolution of Pain (Grade 0 = No Pain) in the Lotemax<sup>®</sup> Gel group (72.9% and 75.7%, study 1 and 2, respectively) that was statistically significantly higher than the placebo group (41.9% and 45.8%, study 1 and 2 respectively).
- 3) **Non-Shaking Formulation:** Lotemax<sup>®</sup> suspension (0.5%) is a low viscosity agent containing povidone and glycerin, agents found in OTC dry eye relief products. Lotemax<sup>®</sup> Gel had the povidone ingredient removed and replaced with polycarbophil, a high molecular weight polymer, which acts as a suspending agent for the loteprednol etabonate molecule and affords the non-settling properties of Lotemax<sup>®</sup> Gel.  
In sedimentation experiments, Lotemax<sup>®</sup> Suspension and Lotemax<sup>®</sup> Gel were centrifuged for 120x g for 24 hours. Within 20 minutes, the loteprednol etabonate molecules in Lotemax<sup>®</sup> Suspension settled to the bottom of the tube, whereas after 24h Lotemax<sup>®</sup> Gel did not demonstrate any settling. Lotemax<sup>®</sup> Suspension requires that the patient shake 20 – 30 times before instillation. Lotemax<sup>®</sup> Gel does not require any shaking, which will improve patient compliance while ensuring adequate dosing of the drug in every drop.
- 4) **Adaptive Viscosity:** Lotemax<sup>®</sup> Gel was formulated so that it is a gel at rest, however when placed under pressure, thins out and begins to flow as a liquid. When a bottle of Lotemax Gel is tipped and squeezed, the gel is able to flow like a liquid and be expressed as a drop. There is minimal blurring when instilled in the eye as the gel thins out due to pressure during blinking as well as the electrolytes in tears which aid in thinning the product even more. The incidence of drug-related blurred vision in the Phase III studies was 0% in the Lotemax<sup>®</sup> Gel arm and 0.5% in the vehicle control group.
- 5) **Patient Comfort:** A proprietary combination of moisturizing agents has been added to Lotemax<sup>®</sup> Gel – glycerin and propylene glycol. These two demulcents are known to bind water at the highest levels seen for all demulcents used in ophthalmic drops. In addition the pH of Lotemax Gel has been buffered closer to that of human tears.
- 6) **Less Preservative:** Lotemax<sup>®</sup> Gel has 70% less BAK preservative than Lotemax<sup>®</sup> suspension.
- 7) **Safety:** The inclusion of polycarbophil in Lotemax<sup>®</sup> Gel optimizes the retention of loteprednol etabonate molecules on the ocular surface. This does not compromise the safety of Lotemax<sup>®</sup> Gel as the incidence of IOP elevation was similar in Phase 3 clinical trials for both Lotemax<sup>®</sup> Gel and Placebo (0.5% in each arm).

#### **Questions and Answers**

Q: When do the patents on each formulation expire?

A: The suspension expired in 2012 but there is not yet a generic, the ointment expires in 2014 and the gel expires in 2015.

Q: Are any additional indications being sought?

A: No.

### **III. Pfizer**

Tom Heard, Associate Director, Medical Outcomes Specialist

Cathy Preiser, Specialty Account Manager

Doug Hurley, Account Manager

### **Lyrica® (pregabalin)**

Lyrica is an alpha-2-delta ligand that has analgesic and antiseizure activity, and a novel mechanism of action. Lyrica is indicated in partial onset seizures, neuropathic pain associated with diabetic peripheral neuropathy and post-herpetic neuropathy, fibromyalgia and newly indicated for neuropathic pain associated with spinal cord injury (SCI).

#### **New Indication and Usage**

- Lyrica is newly indicated for neuropathic pain associated with SCI with a recommended dose range of 150 to 600 mg/day. The recommended starting dose is 75 mg two times a day. The may be increased to 150 mg two times a day within 1 week based on efficacy and tolerability. Patients who do not experience sufficient pain relief after 2 to 3 weeks of treatment with 150 mg two times a day and who tolerate Lyrica may be treated with up to 300 mg two times a day.

#### **New Efficacy**

- The efficacy of pregabalin for the management of neuropathic pain associated with spinal cord injury was established in two randomized, double-blind, placebo-controlled, multicenter studies.
- Pain was significantly improved in patients taking pregabalin 150-600 mg/day as compared to those in the placebo group and the onset of pain relief was rapid, with significant efficacy observed in the pregabalin group at Week 1.
- The mean baseline pain score was 6.54 in the pregabalin group and 6.73 in the placebo group. The mean endpoint pain score was lower in the pregabalin group (4.62) than the placebo group (6.27;  $p < 0.001$ ), with efficacy observed as early as week 1 and maintained for the duration of the study. The average pregabalin dose after the 3-week stabilization phase was 460 mg/day. Pregabalin was significantly superior to placebo in endpoint assessments on the SF-MPQ. The  $\geq 30\%$  and  $\geq 50\%$  pain responder rates were higher with pregabalin than placebo ( $p < 0.05$ ). Pregabalin was associated with improvements in disturbed sleep ( $p < 0.001$ ) and anxiety ( $p < 0.05$ ), and more patients reported global improvement at endpoint in the pregabalin group ( $p < 0.001$ ).

#### **New Safety**

- Mild or moderate, typically transient, somnolence and dizziness were the most common adverse events.

#### **Questions and Answers**

Q: Did any new safety concerns result from the SCI trials?

A: No.

Q: When does the patent expire?

A: June 2019.

### **Genotropin® (somatotropin [rDNA origin] injection)**

Genotropin is a growth hormone indicated in pediatric growth hormone deficiency, Prader-Willi syndrome, pediatric patients born small for gestational age, Turner syndrome, idiopathic short stature and adult growth hormone deficiency.

#### **New Switching Data**

*Published article on the consequences of brand switches during the course of pediatric growth hormone treatment*

- Objective: To explore the effects of insurance-mandated brand switches during the course of pediatric recombinant human growth hormone (rhGH) treatment on clinical practice.
- Methods: We e-mailed a 9-question, anonymous, Internet-based survey to active members of the Pediatric Endocrine Society. The survey consisted of multiple-choice and yes/no answers. Free-text comments were solicited for further explanation of responses. Quantitative answers were tabulated. Each investigator independently coded the free-text responses; themes based on codes identified by all 3 investigators in a minimum of 5 different respondents' comments were compiled and organized.
- Results: Of the 812 active members of the Pediatric Endocrine Society who were e-mailed the survey, 231 responded. Two hundred eight respondents reported switching a patient's regimen from one rhGH product to another, and of these, 50% experienced repeated switches. Switches occurred for each commercially available rhGH brand. Frequent concerns noted by respondents involved dosing errors and treatment lapses from having to learn a new device and impaired adherence related to patient-family frustration and anxiety. Anti-GH antibodies, measured by only 3 endocrinologists when switching a patient's regimen from one brand to another, were negative before and after the product switch. When a patient switched rhGH brands, the most frequently reported time involvement for endocrine office staff was 2 hours for paperwork, 1 hour for device instruction, and 1 hour for "other" (mostly related to telephone reassurance).
- Conclusion: GH brand switches may adversely affect patient care and burden pediatric endocrinology practices.

## Questions and Answers

Q: Are any additional indications being sought?

A: No.

### **Pristiq® (desvenlafaxine)**

Pristiq is a novel molecular indicated for the treatment of major depressive disorder (MDD) in adults. Desvenlafaxine is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI).

#### **New Drug-Drug Interaction Data**

- Poster presentation study found desvenlafaxine did not affect 2D6 and thus did not interact with aripiprazole (Abilify) which can be helpful in patients that need to take both agents for MDD.
- Poster presentation study found desvenlafaxine did not affect 2D6 and thus did not affect tamoxifen levels which can be helpful in patients with breast cancer who have depression.

## Questions and Answers

Q: Does venlafaxine affect 2D6?

A: Venlafaxine is a weak inhibitor of 2D6.

## IV. Sunovion

Lizbeth Delgado, PharmD, Senior Area Medical Specialist

John G. Karafilidis, PharmD, Senior Director Medical Affairs

Danny Van Deventer, Account Director

### **Latuda® (lurasidone)**

Latuda is benzoisothiazol atypical antipsychotic indicated in the treatment of schizophrenia in adults.

#### **New Efficacy and Safety Data**

- In Study D1050290, patients continued with the same dose of lurasidone taken at study endpoint in the 6-week McEvoy et al. study. As in the last four weeks of the McEvoy study, dosing was flexible between 40 and 120 mg/day.
- A total of 149 patients completed the core phase study and elected to continue in the extension study.
  - A total of 98 patients (65.8%) completed the 6-month study.
  - A total of 34.2% discontinued from the study due to patient decision to withdraw (12.1%); adverse event (11.4%), of which 6% was due to underlying disease exacerbation; lost to follow-up (6.0%); insufficient clinical response (1.3%); protocol violation (1.3%); failed to meet entry criteria (0.7%); noncompliance with study drug (0.7%); and administrative reasons (0.7%).
- The most commonly reported treatment-emergent adverse events (TEAEs) considered related to the study drug were akathisia (8.1%), nausea (8.8%), insomnia (8.8%), and anxiety (6.1%).
- Sixteen patients in the safety population (n=148) had at least one TEAE leading to discontinuation from the study.
- There were small changes from core phase baseline in prolactin over the course of the study. The median change in prolactin at Month 6 was -0.4 ng/mL. Both male patients (-0.4 ng/mL) and female patients (-0.4 ng/mL) had small median changes in prolactin at Month 6.
- Slight decreases from core phase baseline were observed in median total cholesterol (-1.0 mg/dL) and LDL cholesterol (-5.5 mg/dL) at Month 6. There was a slight median increase for glucose (2.0 mg/dL) and triglycerides (2.0 mg/dL), and no change for HDL cholesterol.
- The mean weight change from core phase baseline to Month 6 was -0.4 kg [(SD 5.1 kg) (last observation carried forward population)]. Relative to the core phase baseline, 27 patients (18.8%) had a markedly abnormal decrease in body weight and 23 patients (16.0%) had a markedly abnormal increase in body weight.
- There were no notable changes in the Simpson-Angus Scale (SAS), Barnes Akathisia Scale (BAS), Abnormal Involuntary Movement Scale (AIMS) scores or Columbia Suicide Severity Rating Scale (C-SSRS).

#### **New Health Economic Outcomes Research Data**

- The committee has also previously reviewed data from a 12-month, double-blind, randomized clinical study that compared the efficacy of lurasidone to that of quetiapine XR for prevention of relapse and relapse related hospitalization. This study was a double-blind continuation of the fifth pivotal trial listed in Table 8 of the package insert. Using a model based on the data of the 12-month continuation study, the lower risk of relapse and hospitalizations due to relapse with lurasidone compared to quetiapine XR was estimated to result in lower annual direct mental health care costs for patients treated with lurasidone compared to quetiapine XR.

- Observed relapse-related hospitalization rates at 12 months for all patients receiving lurasidone were 7.3%, n=151 and for all patients receiving quetiapine XR were 17.6%, n=85.
- Observed relapse rates at 12 months for all patients receiving lurasidone were 19.9%, n=151 and for all patients receiving quetiapine XR were 28.2%, n=85.
- Total direct mental health care costs were calculated for categories including psychiatric hospitalizations, emergency services, medication management, and outpatient individual therapy using the findings of Ascher-Svanum, et al. 2010.
- The model then estimated the annual cost saving based upon the difference in relapse rates between the groups. The estimated annual cost savings associated with the use of lurasidone compared to quetiapine XR was \$2702. Lurasidone was estimated to cost \$24,567 PPPY while quetiapine XR was estimated to cost \$27,269 PPPY.
- The model then estimated the annual cost saving based upon the difference in relapse-related hospitalizations between the groups. The estimated annual cost savings associated with the use of lurasidone compared to quetiapine XR was \$3277. Lurasidone was estimated to cost \$21,025 PPPY while quetiapine XR was estimated to cost \$24,301 PPPY.

### Questions and Answers

Q: Are any other indications being sought?

A: Have filed for treatment in bipolar disorder.

### Zetonna® (ciclesonide) – New Formulation

Zetonna is a corticosteroid, new 37mcg/actuation nasal aerosol formulation of ciclesonide, indicated for the treatment of symptoms associated with seasonal (ocular and nasal) and perennial allergic rhinitis (nasal only) in adults and adolescents ≥12 years of age. The recommended total daily dosage of Zetonna nasal aerosol is 74 mcg administered as 1 actuation (37-mcg) per nostril once daily.

### Product Attributes

- Zetonna nasal aerosol provides a 50 mL spray actuation and provides 60 sprays after initial priming.
- It has a dose indicator with a remaining-dose color indicator that changes from green to yellow to red to show how much is left.
- There's no need to shake the device before use however, patients will need to prime Zetonna before using for the first time (by spraying 3 actuations) or when not used for 10 consecutive days.

### Pivotal Trial Summary

- The clinical development program for ciclesonide nasal aerosol consisted of several clinical evaluations including three randomized, double blind, parallel-group, multi-center (United States), placebo-controlled short-term clinical trials (2 to 6 weeks duration) in 2,488 adolescents and adults with seasonal and perennial allergic rhinitis. Among these patients, 761 received the 74 mcg once-daily dose.
- In three clinical trials in seasonal and perennial allergic rhinitis (SAR/PAR), patients treated with once daily ciclesonide nasal aerosol 74 mcg exhibited statistically significantly greater improvements in reflective TNSS (rTNSS) scores, the primary endpoint, than vehicle placebo-treated patients.
- In the 2 pivotal SAR trials, patients also demonstrated clinically and statistically significant improvements in quality of life on the Rhinitis Quality of Life Questionnaire (RQLQ, a validated questionnaire) as well as clinically and statistically significant improvements in reflective TOSS (rTOSS) scores, a secondary endpoint, than vehicle placebo-treated patients.
- Adverse events occurring with a frequency of ≥2.0% and greater than placebo from trials 2 to 6 weeks in duration in the ciclesonide nasal aerosol 74 mcg group included nasal discomfort (3.2%), headache (3.1%) and epistaxis/blood-tinged mucus (2.9%) compared to placebo (1.8%, 1.2%, and 2.7% respectively). A total of 2 out of 2335 patients treated with Zetonna reported nasal septal perforations compared with none of 892 patients treated with placebo, with both nasal septal perforations being reported within the 2-week SAR trials. There were no reports of nasal septal perforation for patients treated with ciclesonide nasal aerosol 74 mcg in the 6-month double-blind perennial allergic rhinitis (PAR) clinical trial.

### Scintigraphy

- In two open-label, single-dose, single-site, randomized trials evaluating radiolabelled solution of ciclesonide deposition in the nasal cavity (Study 1 [N=10] healthy patients and Study 2 [N=14] patients with symptomatic PAR or SAR), scintigraphy data showed administration of radiolabelled solution of ciclesonide delivered high local retention of radioactivity in the nasal cavity (≥98%).

**Patient Reported Satisfaction**

- In a 2-week, randomized, multicenter, two-period, study in patients aged ≥12 years with PAR, patients reported high levels of satisfaction for ZETONNA, with a satisfaction score of 84 out of 100 after 2 weeks of treatment with ZETONNA (based on a primary satisfaction composite score endpoint), compared to a baseline score of 68 out of 100 (for their prior nasal spray taken within 6 months prior to trial start).

**Questions and Answers**

Q: What is the onset of effect?

A: Peak effect is in 2-4 weeks but relief is provided within 24 hours.

Q: Is a pediatric indication being sought?

A: Yes, being studied in 6-11 years of age.

Q: When do the patents on Omnaris (ciclesonide 50mcg/actuation nasal aerosol) and Zetonna expire?

A: Both in 2017.

Q: What are the differences Zetonna over Omnaris?

A: Zetonna is a dry nasal aerosol (Omnaris is aqueous), is a lower strength/actuation (37mcg vs. 50mcg per actuation) and is only 1 actuation (Omnaris is 2 actuations) per nostril once daily.

**V. Amgen**

Ann Lyons, PharmD, BCPS, Principal Regional Medical Liaison

Janet K. Gusmerotti, Corporate Account Manager

**Enbrel® (etanercept)**

Enbrel is indicated for the treatment of moderately to severely active rheumatoid arthritis (RA), chronic moderate to severe plaque psoriasis (PsO) in adults (≥ 18 years) who are candidates for systemic therapy or phototherapy, psoriatic arthritis (PsA), active ankylosing spondylitis (AS), and moderately to severely active polyarticular juvenile idiopathic arthritis (JIA). Enbrel binds to tumor necrosis factor (TNF) reversibly. Cell lysis in vitro due to the presence of Enbrel has not been reported. Neutralizing antibody formation in the presence of Enbrel has not been reported.

**New Clinical Data**

- The Agency for Healthcare Research and Quality (AHRQ) recently conducted a comparative review of 30 studies and found that RA patients demonstrated greater improvement in disease activity (American College of Rheumatology 50% improvement [ACR 50]) with etanercept compared with abatacept, adalimumab, anakinra, infliximab, rituximab, and tocilizumab (Figure).

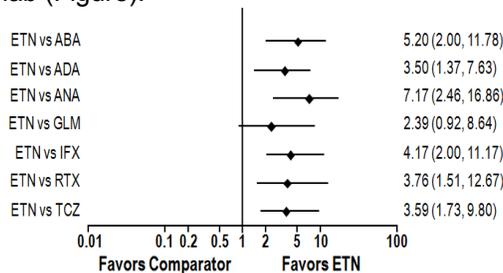


Figure. Relative treatment effect for ACR 50 response in AHRQ.4  
 ABA = abatacept; ADA = adalimumab; ANA = anakinra; GLM = golimumab;  
 IFX = infliximab; RTX = rituximab; TCZ = tocilizumab

- In a drug class review conducted by Oregon Health and Science University, researchers concluded that etanercept was more efficacious than infliximab for RA based on ACR response rates when 2 trials and 5 observational studies were analyzed. When indirect comparisons of randomized, placebo-controlled trials were analyzed, etanercept was found to be significantly more efficacious than adalimumab, anakinra, infliximab, and tocilizumab. In plaque PsO, the authors found good evidence that demonstrated the efficacy of adalimumab, alefacept, etanercept, infliximab, and ustekinumab in achieving Psoriasis Area and Severity Index 75% improvement (PASI 75) scores.
- A comparative effectiveness analysis of 2,242 RA patients in the Consortium of Rheumatology Researchers of North America (CORRONA) database who were biologically naïve or switched anti-TNFs suggests that similar response and remission rates were achieved across patients treated with adalimumab, infliximab, and etanercept, with more robust effectiveness consistently observed for those who were biologically naïve versus patients who switched therapies (Table).

	Biologically Naïve Patients					
	6 Months			12 Months		
	IFX (n = 230)	ADA (n = 235)	ETN (n = 222)	IFX (n = 182)	ADA (n = 190)	ETN (n = 178)
mACR 50 Responders, %	14.3%	19.6%	26.6%	20.3%	17.4%	20.8%
Adjusted OR	1.00	1.03 (0.62, 2.01)	1.75 (0.99, 3.09)	1.00	0.72 (0.46, 1.13)	1.03 (0.62, 1.70)
	IFX (n = 103)	ADA (n = 107)	ETN (n = 116)	IFX (n = 71)	ADA (n = 75)	ETN (n = 72)
DAS28 Remission, %	28.2%	25.2%	28.4%	33.8%	33.3%	37.5%
Adjusted OR	1.00	0.72 (0.48, 1.08)	0.95 (0.43, 2.08)	1.00	0.89 (0.39, 2.00)	1.01 (0.47, 2.12)

Table. Comparative effectiveness in biologically naïve and switched RA patients in CORRONA.

DAS28 = 28-joint count Disease Activity Score; mACR = modified ACR;  
OR = odds ratio.

- A comparative review recently conducted by AHRQ for PsO suggested that etanercept improved PASI compared with acitretin, with moderate strength of evidence. The report concluded that there is insufficient evidence to describe the comparative effectiveness of biologic and nonbiologic treatments in PsO.
- A recent update to ACR recommendations for treatment of RA provides guidance for adding or switching biologic therapy, use of biologics in patients with comorbid conditions, considerations with regard to vaccinations, and TB screening. The update recommends that etanercept may be used in RA patients infected with hepatitis C, but no biologic treatment is recommended for patients with untreated hepatitis B. Also, anti-TNFs should not be used to treat patients with New York Heart Association Class III/IV congestive heart failure with an ejection fraction of 50% or less.

## Questions and Answers

Q: Is an ulcerative colitis or any other indications being sought?

A: Not at this time.

## VI. Sanofi

Maria del Pilar Martin, PhD, Deputy Director, Medical Science Liaison

Mary Kate Reeves-Hoche, PhD, APRN, ANP-BC, Senior Director, Medical Science Liaison

Liz Cirri, Associate Vice President, Government Reimbursement

### Sklice® (ivermectin 0.05% lotion) – New Drug

Sklice (ivermectin) Lotion, 0.5%, approved by the FDA in February 2012, is a pediculicide indicated for the topical treatment of head lice infestations in patients 6 months of age and older. The active ingredient of Sklice lotion is ivermectin, a member of the avermectin class, causes death of parasites, primarily through binding selectively and with high affinity to glutamate-gated chloride channels, which occur in invertebrate nerve and muscle cells. This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, resulting in paralysis and death of the parasite. The oral form of ivermectin has been used safely in humans for over 30 years to treat African River blindness.

### Scientific and Clinical Data Summary

- Using the pyrethrin resistant SF-HL louse strain in an in vitro rearing system Strycharz demonstrated ivermectin formulations were 100% effective at killing lice using 1, 0.5, and 0.25% ivermectin concentrations after a single 10-min exposure. In evaluating the effect of ivermectin on SF-HL louse eggs and emerging nymphs, the percent of hatched lice from treated eggs that took a blood meal significantly decreased (80-95%) compared with lice that hatched from untreated eggs. All treated eggs that hatched, the lice died within 48 hrs of hatching – thus never reaching maturity to mate and lay eggs.
- A pediatric pharmacokinetics study in children 6 months to 3 years of age (n=20) reported minimal systemic absorption from a single 10-minute application, levels much lower than other studies have shown for absorption of a typical therapeutic oral dose of ivermectin used in treating strongyloidiasis.
- An adult repeat insult patch test for cumulative dermal irritation and contact sensitization test in 265 adults (F = 164, M = 101) tested 4 patches each of which were: 0.5% ivermectin lotion, vehicle control (lotion sans ivermectin), normal saline (negative control), and 0.1% sodium dodecyl sulfate (positive control) demonstrated that Sklice lotion had lower cumulative scores as compared to normal saline. These results suggest that repeated treatments, if needed, should not be irritating nor result in sensitization.
- Two identical Phase 3 multi-center, randomized, double-blind, vehicle-controlled studies were conducted in subjects 6 months of age and older with head lice infestation (N=780). All subjects received a single application of

either Sklice Lotion or vehicle control with instructions not to use a nit comb. For the evaluation of efficacy, the youngest subject from each household was considered to be the index subject of the household (n=289). Other enrolled infested household members received the same treatment as the youngest subject and were evaluated for all safety parameters. The primary efficacy was assessed as the proportion of index subjects who were free of live lice at day 2 and through day 8 to the final evaluation 14 (+2) days following a single application. Significantly more patients in the ivermectin group than in the vehicle-control group were louse-free on day 2 (131 of 138 [94.9%] vs. 46 of 147 [31.3%]) and day 8 (115 of 135 [85.2%] vs. 30 of 144 [20.8%]) and remained louse-free through day 15 (104 of 141 [73.8%] vs. 26 of 148 [17.6%]) (P<0.001 for each day).

### Safety Summary

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

### Questions and Answers

Q: Does the hair have to be wet or dry?

A: Dry and this is in the patient education leaflet.

Q: How much of the lotion needs to be used?

A: Use enough to cover the scalp and hair.

Q: Does treatment need to be repeated?

A: No.

Q: Is there any resistance yet?

A: No.

Q: Are the pivotal trials published and were all studies conducted presented today?

A: Yes.

Q: What are considered the advantages over other products for lice?

A: Indicated in patients as young as 6 months old, only requires a single, 10-minute treatment regardless of hair length, combing is not required, safe with minimal adverse reactions, no resistance, minimal absorption and no dermal or contact sensitization.

## VII. Vertex

Michelle Mattox, PharmD, Managed Care Liaison II

Dan Petty, PharmD, MBA, Regional Account Manager

### Incivek® (telaprevir)

Incivek is a protease inhibitor that, in combination with peginterferon alfa and ribavirin, is indicated for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease, including cirrhosis, who are treatment-naïve or who have previously been treated with interferon-based treatment, including prior null responders, partial responders, and relapsers. The following points should be considered when initiating treatment with Incivek:

- Incivek must not be administered as monotherapy and must only be prescribed with both peginterferon alfa and ribavirin.
- A high proportion of previous null responders (particularly those with cirrhosis) did not achieve a Sustained Virologic Response (SVR) and had telaprevir resistance-associated substitutions emerge on treatment with Incivek combination treatment.
- Incivek efficacy has not been established for patients who have previously failed therapy with a treatment regimen that includes INCIVEK or other HCV NS3/4A protease inhibitors.

### New Safety

*IMPORTANT DRUG WARNING: Serious Skin Reactions*

- Serious skin reactions including fatal outcome reported with Incivek (telaprevir) combination treatment
- New risk information regarding serious skin reactions with fatal outcome have been reported in post-marketing experience. The Incivek US Prescribing Information has been updated with a new **Boxed Warning** and risk information to highlight this safety issue and to emphasize discontinuation of treatment in the event of serious skin reactions.

- **BLACK BOX WARNING: SERIOUS SKIN REACTIONS** Fatal and non-fatal serious skin reactions, including Stevens Johnson Syndrome (SJS), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), and Toxic Epidermal Necrolysis (TEN), have been reported in patients treated with Incivek combination treatment [see Warnings and Precautions]. Fatal cases have been reported in patients with progressive rash and systemic symptoms who continued to receive Incivek combination treatment after a serious skin reaction was identified. For serious skin reactions, including rash with systemic symptoms or a progressive severe rash, Incivek, peginterferon alfa, and ribavirin must be discontinued immediately. Discontinuing other medications known to be associated with serious skin reactions should be considered. Patients should be promptly referred for urgent medical care.
- Additional information on serious skin reactions from the Prescribing Information: In clinical trials, serious skin reactions, including DRESS and SJS were reported in less than 1% of subjects who received Incivek combination treatment compared to none who received peginterferon alfa and ribavirin alone. These serious skin reactions required hospitalization, and all subjects recovered. The presenting signs of DRESS may include rash, fever, facial edema, and evidence of internal organ involvement (e.g., hepatitis, nephritis). Eosinophilia may or may not be present. The presenting signs of SJS may include fever, target lesions, and mucosal erosions or ulcerations (e.g., conjunctivae, lips). TEN and Erythema Multiforme (EM) have been observed in post-marketing experience. Patients should be instructed to contact their health care provider immediately if they experience any skin changes. Sometimes these skin rashes and other skin reactions can become serious, require treatment in a hospital and may result in death.

**WARNINGS AND PRECAUTIONS: Anemia**

- In clinical trials, the median time to onset of hemoglobin less than or equal to 10 g/dL was faster among subjects treated with Incivek combination treatment compared to those who received peginterferon alfa and ribavirin: 56 days (range 8-365 days) versus 63 days (range 13-341 days), respectively.
- Anemia requiring ribavirin dose reduction, blood transfusion, and/or erythropoiesis stimulating agent (ESA) has been reported to occur as soon as 10 days following initiation of Incivek combination treatment.
- Hemoglobin should be monitored prior to and at least at weeks 2, 4, 8 and 12 during Incivek combination treatment and as clinically appropriate. Earlier and more frequent monitoring for some patients should be considered.

**Questions and Answers**

Q: How many fatalities due to a serious skin reaction?

A: 2 fatalities worldwide (US and Japan); 1 patient experienced TENS and the other patients experienced DRESS.

Q: Is the FDA requiring a new REMS program or study due to the new black box warning for serious skin reactions?

A: No.

Q: What is the percentage of patients that experience anemia?

A: 32% in phase III trials.

Q: Are any supplemental new drug applications (sNDA) being sought?

A: Yes, a sNDA has been filed for twice daily dosing (same number of pills) and a decision is expected in March or April.

**VIII. GlaxoSmithKline**

Amber Coleman, PharmD, BCPS, Health Outcomes Liaison

Vivian Lee Ryan, Account Manager

**Advair® (fluticasone propionate and salmeterol)**

Advair is a combination of inhaled corticosteroid and long-acting beta-agonist indicated in the treatment of asthma and chronic obstructive pulmonary disease (COPD).

**New Clinical Data**

- A retrospective observational study compared physician prescribing of a low/moderate dose *Advair* with moderate/high dose *Flovent* using medical and pharmacy claims from a managed care organization and linked medical records. The study included 32,189 adult patients without a claims history of ICS use within 3 years of first initiating *Advair* or *Flovent*. Baseline pre-index claims showed patients prescribed *Advair* were more likely to use systemic corticosteroids or have a respiratory-related inpatient or emergency department (ED) visit ( $P < 0.001$ ) compared with *Flovent*. However, the cohorts were similar in baseline rates of asthma-related inpatient or ED visits. In the chart sample (n=460) the proportion of patients reporting asthma symptoms and the types of asthma symptoms were similar between groups.

- A retrospective, observational study compared rehospitalization rates between a cohort of COPD patients initiated on *Advair Diskus* 250/50 or initiated or continued on anticholinergics within 30 days of a COPD-related hospitalization or ED visit. The study included 1,936 patients who were matched using propensity scores. The cohort receiving *Advair Diskus* had a significantly lower proportion of rehospitalized patients compared with the anticholinergic cohort, 3.1% versus 4.6% ( $P = 0.047$ ).
- A retrospective, observational study compared exacerbation rates between a cohort of COPD patients who initiated *Advair Diskus* 250/50 or anticholinergics following a moderate COPD exacerbation. The study included a total of 2,849 patients. After adjusting for differences in baseline characteristics, the cohort receiving *Advair* had a lower risk of a COPD exacerbation compared with the anticholinergic cohort (HR = 0.58; 95% CI: 0.38, 0.91).
- Effect of combination fluticasone propionate and salmeterol or inhaled corticosteroids on asthma-related outcomes in a Medicare-eligible population showed better outcomes in patients that initiated with combination therapy vs. inhaled corticosteroid alone.
- Observational study on the impact of initiating tiotropium alone versus tiotropium with fluticasone propionate/salmeterol combination therapy on outcomes and costs in chronic obstructive pulmonary disease showed patients who initiate triple therapy had better outcomes.

### Questions and Answers

There were no questions.

### **Flovent® (fluticasone propionate)**

Flovent is an inhaled corticosteroid indicated in the treatment of asthma.

### New Clinical Data

- A retrospective observational study compared physician prescribing of a low/moderate dose *Advair* with moderate/high dose *Flovent* using medical and pharmacy claims from a managed care organization and linked medical records. The study included 32,189 adult patients without a claims history of ICS use within 3 years of first initiating *Advair* or *Flovent*. Baseline pre-index claims showed patients prescribed *Advair* were more likely to use systemic corticosteroids or have a respiratory-related inpatient or emergency department (ED) visit ( $P < 0.001$ ) compared with *Flovent*. However, the cohorts were similar in baseline rates of asthma-related inpatient or ED visits. In the chart sample ( $n=460$ ) the proportion of patients reporting asthma symptoms and the types of asthma symptoms were similar between groups.
- A retrospective, observational study utilized medical and pharmacy claims data to compare asthma-related outcomes in children 4-11 years of age with asthma who were newly initiated on *Flovent* 44 mcg or montelukast (any dose). The study included 6,636 patients who were matched 1:2 (*Flovent*:montelukast) using propensity scores. Results showed patients in the cohort receiving *Flovent* had a lower risk of an asthma-related ED visit compared with montelukast (HR 0.71; 95% CI (0.52, 0.96)) and a lower risk of asthma-related ED/hospitalization (HR 0.75; 95% CI (0.57, 0.99)).

### Questions and Answers

There were no questions.

## IX. Biogen

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

Glenn G. Tropf, Regional Account Manager

### **Avonex® (interferon beta-1a)**

Avonex is an FDA approved therapy indicated to treat relapsing forms of Multiple Sclerosis (RRMS). Avonex is a 166 amino acid glycoprotein produced by recombinant DNA technology using genetically engineered Chinese Hamster Ovary cells into which the human interferon beta gene has been introduced. The amino acid sequence is identical to that of natural human interferon beta.

### New Dosing and Delivery Enhancements

- Flu-like symptoms (FLS) are common with interferon-beta product and may present barrier to initiation of therapy or maintaining treatment.
  - Study was conducted to characterize the effects of Avonex dose titration on FLS with regards to incidence and severity.
  - Results of dose titration split over 4 weeks, ( Week 1: ¼ (7.5µg), Week 2: ½ (15µg), Week 3: ¾ (22.5µg) and Weeks 4-8: 30µg full dose), and full dose provided for another 4 wks, reduced FLS by 76% at 4-6 hrs. post-injection and 37% at the 12-15 hrs. post-injection versus no titration (30ug given weekly).

- Avostartgrip™ is available to be used with Avonex prefilled syringes.
- Avonex Pen™ is the first single dose, IM autoinjector with a 5/8" needle, available for long term use for treatment of patients with RRMS.
  - An open-label, 4 week study to evaluate effective use, safety, and patient preference of Avonex Pen was conducted in patients who were stabilized on prefilled syringes.
  - Overall success rate in utilizing Avonex Pen was 89%. Failures (11%) were defined as failure in any of the 14 steps in the procedure for using Avonex Pen. 88% (7/8) of failures due to removal of needle cover before extending injector shield. No patient harm or device failures occurred. Safety data collected were comparable to known safety profile of Avonex prefilled syringe and consistent with post marketing data.
  - Mean pain score was 1.7 (0 no pain-10 extremely painful) following injection with Avonex prefilled syringe, and 0.7 by week 3 with Avonex Pen. 94% of patients preferred autoinjector over prefilled manual injection.

### Questions and Answers

Q: When does the patent expire?

A: 2016.

Q: So portion of medication has to be wasted during titration dosing since single-use that may cost approximately \$1,100?

A: Anecdotal reports indicated wasting was occurring previously anyway, but faster titration is better to do.

Q: Is the new pen at price parity?

A: Yes.

Q: How is the Avostartgrip obtained?

A: It is free through physician offices.

Q: Is Biogen discontinuing vials?

A: No.

Q: How is the new pen packaged?

A: Package of 4 pens.

## X. Novartis

Julia Compton, PharmD, Regional Account Scientific Director

### **Exelon® Patch (rivastigmine transdermal system)**

Exelon Patch is a dopamine agonist indicated for the treatment of mild to moderate dementia of the Alzheimer's type and is the only dopamine agonist indicated for treatment of mild to moderate dementia associated with Parkinson's disease.

#### **New Strength**

- Exelon Patch 13.3 mg/24 hours

#### **New Efficacy**

- The International 48-Week Study of Exelon Patch in Dementia of the Alzheimer's Type was a randomized, double-blind clinical investigation in patients with Alzheimer's disease (diagnosed by NINCDS-ADRDA and DSM-IV criteria, MMSE score  $\geq 10$  and  $\leq 24$ ). Approximately 27% of patients were taking memantine throughout the entire duration of the study. Patients who received 24-48 weeks of open-label treatment with Exelon Patch 9.5 mg/24 hours and demonstrated functional and cognitive decline were randomized to either Exelon Patch 9.5 mg/24 hours or Exelon Patch 13.3 mg/24 hours in a 48-week double-blind treatment phase. Functional decline was assessed by the investigator and cognitive decline was defined as a decrease in the MMSE score of  $\geq 2$  points from the previous visit or a decrease of  $\geq 3$  points from baseline. The co-primary endpoints were the change from baseline at Week 48 on the ADAS-Cog to assess cognitive performance, and change from baseline on the ADCS-IADL to assess overall function. Out of a total of 1584 patients enrolled in the initial open-label phase of the study, 567 patients were classified as decliners and were randomized into the double-blind phase. Exelon Patch 13.3 mg/24 hours demonstrated significantly less decline on ADCS-IADL compared to Exelon Patch 9.5 mg/24 hours at Weeks 16, 24, 32, and 48. Exelon Patch 13.3 mg/24 hours demonstrated nominally statistically significant less cognitive decline on ADAS-Cog compared to Exelon Patch 9.5 mg/24 hours at Week 24 ( $p=0.027$ ), but not at Week 48 ( $p=0.227$ ).

## New Safety

- In the 48-week active comparator controlled trial, the most commonly observed adverse reaction ( $\geq 3\%$  in any treatment group) in the Exelon Patch 13.3 mg/24h group was nausea, followed by vomiting, fall, weight decreased, application site erythema, decreased appetite, diarrhea and urinary tract infection. The percentage of patients with these events was higher in the 13.3 mg/24 h group than the 9.5 mg/24 h group. The most common adverse reactions ( $>1\%$  at any dose) leading to discontinuation were vomiting, application site pruritus, and aggression. The most commonly reported skin irritation events for both treatment groups in the 48-week active comparator controlled trial were application site erythema and application site pruritus, while skin reactions reported in the 24-week placebo-controlled trial were application site reactions, application site dermatitis, and application site irritation.

## New Dosage and Administration

- Exelon Patch is for transdermal administration. The effective dosage is 9.5 mg/24h or 13.3 mg/24h administered once per day; replace with a new patch every 24 hours.
- Initiate treatment with one 4.6 mg/24 hours Exelon Patch applied to the skin once daily. Increase the dose only after a minimum of 4 weeks at the previous dose, and only if the previous dose has been well tolerated. Continue the recommended effective dose of 9.5 mg/24 hours for as long as therapeutic benefit persists. Patients can then be increased to the maximum effective dose of Exelon Patch 13.3 mg/24 hours dose.
- Doses higher than 13.3 mg/24 hours confer no appreciable additional benefit, and are associated with an increase in the incidence of adverse reactions.

## Questions and Answers

Q: Are any other studies being conducted?

A: There are ongoing studies evaluating efficacy in patients with severe Alzheimer's.

## Fanapt® (iloperidone)

Fanapt is an atypical antipsychotic indicated for the treatment of schizophrenia in adults. In choosing among treatments, prescribers should consider the ability of FANAPT to prolong the QT interval and the use of other drugs first. Prescribers should also consider the need to titrate FANAPT slowly to avoid orthostatic hypotension, due to its alpha adrenergic properties, which may lead to delayed effectiveness compared to some other drugs that do not require similar titration. It is proposed that the efficacy of FANAPT is mediated through a combination of dopamine type 2 (D2) and serotonin type 2 (5-HT2) antagonisms.

## New Information

The data below is not new but Novartis released the drugs used as the active controls in the following studies:

### *6-Week Placebo-Controlled and Active Controlled Trial (n=706)*

- Two dose ranges of Fanapt (12-16 mg/day or 20-24 mg/day) were compared to placebo and an active control (risperidone).
- Titration of Fanapt started at 1 mg twice daily on days 1 and 2 and increasing to 2, 4, 6, 8, 10 and 12 mg twice daily on days 3, 4, 5, 6, and 7, as needed.
- The primary endpoint was change from baseline on the BPRS total score at the end of treatment (Day 42). Both the 12-16 mg/day and the 20-24 mg/day dose ranges of Fanapt were superior to placebo on the BPRS total score.
- The active control antipsychotic drug appeared to be superior to Fanapt in this trial within the first 2 weeks, a finding that may in part be explained by the more rapid titration that was possible for that drug.
- In patients in this study who remained on treatment for at least two weeks, iloperidone appeared to have had comparable efficacy to the active control.

### *4-Week Placebo-Controlled and Active-Controlled Trial (n=604)*

- One fixed dose of Fanapt (24 mg/day) compared to placebo and an active control (ziprasidone). Titration of FANAPT starting at 1 mg twice daily on day 1 and increasing to 2, 4, 6, 8, 10 and 12 mg twice daily on days 2 through 7. The primary endpoint was change from baseline on the PANSS total score at the end of treatment (Day 28).
- The 24 mg/day FANAPT dose was superior to placebo in the PANSS total score. Fanapt appeared to have similar efficacy to the active control drug which also needed a slow titration to the target dose.

## Questions and Answers

There were no questions.

## **Gilenya® (fingolimod)**

Gilenya is the 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. Gilenya has a novel mode of action (sphingosine 1-phosphate receptor modulator) that has the potential to fulfill unmet needs for an effective treatment for MS in an oral formulation. Gilenya has established efficacy and safety in placebo-controlled and active-controlled 1- and 2 year trials. Gilenya provided significant efficacy in reducing relapse frequency compared with intramuscular (IM) interferon-beta (IFN $\beta$ -1a) and demonstrated a significant effect in delaying confirmed disability progression versus placebo.

### **New Contraindications**

- Myocardial infarction
- Unstable angina
- Stroke
- Transient ischemic attack
- Decompensated heart failure requiring hospitalization or Class III/IV heart failure

### **New Pre-Dose Screening – All patients**

- Consult prescribing physician of drugs that slow the heart rate or atrioventricular conduction to evaluate the possibility to switch to drugs that do not slow the heart rate or atrioventricular conduction (overnight continuous ECG monitoring recommended in patients who cannot switch)
- Cardiac evaluation for patients with pre-existing cardiac conditions\* (overnight continuous ECG monitoring recommended)

### **New First Dose Observation – All patients**

- Administer in a setting in which resources to appropriately manage symptomatic bradycardia are available
- ECG prior to dosing and at the end of the six-hour observation period
- Hourly pulse and blood pressure

### **New Additional First Dose Observation – Until finding is resolved – Some patients**

- Heart rate at six hours post-dose <45 beats per minute
- Heart rate at six hours post-dose is lowest value
- ECG 6 hours post-dose shows new onset second degree or higher AV block
- Symptomatic bradycardia – initiate appropriate management with continuous ECG monitoring until symptoms resolve

### **Overnight Continuous ECG Monitoring in a Medical Facility – Some patients:**

- Pharmacologic intervention required for symptomatic bradycardia and repeat observation procedures with 2nd dose
- Pre-existing cardiac conditions
- Prolonged QTc (@ baseline or during observation period)
  - QTc > 450 ms for males, >470 ms for females before dosing or during six-hour observation period
  - At additional risk for QT prolongation (e.g. hypokalemia, hypomagnesemia, congenital long QT syndrome)
  - On concurrent therapy with QT-prolonging drugs with a known risk of Torsades de pointes (e.g. citalopram, chlorpromazine, haloperidol, methadone, erythromycin)
- Concurrent medications that slow heart rate or atrioventricular conduction (beta-blockers, diltiazem, verapamil, digoxin)

### **New Additional Recent Major Changes**

- Re-initiation of therapy following discontinuation:
  - Within the first two weeks of treatment, first dose procedures are recommended after interruption of one day or more
  - During week 3 and 4 of treatment, first dose procedures are recommended after interruption of 7 days or more
  - After one month of treatment, first dose procedures are recommended after interruption of more than 14 days
- In MS clinical trials, patients treated with Gilenya 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 1 month of treatment initiation, and persisting with continued treatment.

## **Questions and Answers**

Q: Were the recent label updates due to additional safety concerns?

A: No, the recent label updates were to make the patient selection more clear.

Q: Are prescribing physicians still concerned with safety issues?

A: Physicians are becoming more comfortable with safety concerns and prescribing.

Q: Is there any head-to-head data?

A: Yes, The TRANSFORMS study. In TRANSFORMS, oral Gilenya 0.5 mg significantly reduced the mean number of new or newly enlarging lesions on T<sub>2</sub>-weighted images compared with IM IFN $\beta$ -1a (1.6 vs 2.6 lesions;  $P=0.002$ ). The mean number of T<sub>1</sub> Gd enhancing lesions at 12 months was 0.2 vs 0.5;  $P<0.001$ .

## XI. Janssen

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

### Xarelto® (rivaroxaban)

Xarelto is an oral factor Xa inhibitor indicated in the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), reduction in risk of recurrence of DVT and of PE following initial 6 months treatment for DVT and/or PE and reduction in risk of stroke in patients with nonvalvular atrial fibrillation (AF). Routine monitoring of coagulation parameters is not required because of the predictable pharmacokinetic (PK) and pharmacodynamic (PD) profile of Xarelto.

#### **New Clinical Data**

- Background: A fixed-dose regimen of rivaroxaban, an oral factor Xa inhibitor, has been shown to be as effective as standard anticoagulant therapy for the treatment of deep-vein thrombosis, without the need for laboratory monitoring. This approach may also simplify the treatment of pulmonary embolism.
- Methods: In a randomized, open-label, event-driven, noninferiority trial involving 4832 patients who had acute symptomatic pulmonary embolism with or without deep-vein thrombosis, we compared rivaroxaban (15 mg twice daily for 3 weeks, followed by 20 mg once daily) with standard therapy with enoxaparin followed by an adjusted-dose vitamin K antagonist for 3, 6, or 12 months. The primary efficacy outcome was symptomatic recurrent venous thromboembolism. The principal safety outcome was major or clinically relevant nonmajor bleeding.
- Results: Rivaroxaban was noninferior to standard therapy (noninferiority margin, 2.0;  $P=0.003$ ) for the primary efficacy outcome, with 50 events in the rivaroxaban group (2.1%) versus 44 events in the standard-therapy group (1.8%) (hazard ratio, 1.12; 95% confidence interval [CI], 0.75 to 1.68). The principal safety outcome occurred in 10.3% of patients in the rivaroxaban group and 11.4% of those in the standard-therapy group (hazard ratio, 0.90; 95% CI, 0.76 to 1.07;  $P=0.23$ ). Major bleeding was observed in 26 patients (1.1%) in the rivaroxaban group and 52 patients (2.2%) in the standard-therapy group (hazard ratio, 0.49; 95% CI, 0.31 to 0.79;  $P=0.003$ ). Rates of other adverse events were similar in the two groups.
- Conclusions: A fixed-dose regimen of rivaroxaban alone was noninferior to standard therapy for the initial and long-term treatment of pulmonary embolism and had a potentially improved benefit-risk profile.

#### **Questions and Answers**

Q: Is there an antidote in progress?

A: Yes, in phase III clinical trial and co-factors can be used.

Q: Are other indications being sought?

A: Indication in ACS has been submitted, Janssen responded to FDA and further response from FDA is expected in 1<sup>st</sup> Quarter 2013. Indication in stent thrombosis prophylaxis is also under review by the FDA and a response is expected in 1<sup>st</sup> Quarter 2013.

### Invega® Sustenna® (paliperidone palmitate extended-release injectable suspension)

Invega Sustenna is an atypical antipsychotic extended-release injection indicated for the treatment of schizophrenia in adults. Clinical trials have demonstrated efficacy in *acute* symptom management and *delaying time to relapse* in adult patients with schizophrenia.

#### **New Dosing**

- Dosing: *Initiation*: The recommended initiation regimen of INVEGA SUSTENNA is with a dose of 234 mg on treatment Day 1 and 156 mg one week later, both administered in the deltoid muscle without the need for oral supplementation. *Maintenance*: The recommended monthly maintenance dose is 117 mg, administered in either the gluteal or deltoid muscle; some patients may benefit from lower or higher maintenance doses within the additional available strengths (39 mg, 78 mg, 156 mg, and 234 mg).

- *August 2012 PI Revision for Dosing:* The second initiation dose (Day 8) may be administered within  $\pm 4$  days (Days 4-12) to help avoid a missed dose (revised from  $\pm 2$  days). Additionally, information was added to reinstate Invega Sustenna in patients who may have missed the second initiation dose (Day 8).

### Questions and Answers

There were no questions.

Q: Does the Baker Act have any impact on obtaining additional doses?

A: In states with Baker Act, 2<sup>nd</sup> dose can be obtained before leaving facility.

## XII. AstraZeneca

Tim A. Briscoe, PharmD, CDE, Senior Regional Scientific Manager

Negelle Green, LCSW, Integrated Markets Director

Dan McCall, Corporate Account Director

### **Brilinta® (ticagrelor)**

Brilinta is a cyclo-pentyl-triazolo-pyrimidine (CPTP) that reversibly inhibits platelet P2Y<sub>12</sub> receptor indicated to reduce the rate of thrombotic cardiovascular (CV) events in patients with acute coronary syndrome (ACS) (unstable angina [UA], non-ST elevation myocardial infarction [NSTEMI], or ST elevation myocardial infarction [STEMI]). Brilinta has been shown to reduce the rate of a combined endpoint of CV death, MI or stroke compared to clopidogrel. The difference between treatments was driven by CV death and MI with no difference in stroke. In patients treated with percutaneous coronary intervention (PCI), it also reduces the rate of stent thrombosis. Brilinta is the first and only oral antiplatelet agent FDA approved to demonstrate significant reductions in CV death versus clopidogrel (21% RRR;  $p < 0.001$ ). The overall rate of PLATO-defined total major bleeding was similar between the Brilinta and clopidogrel groups; there was a higher rate of non-CABG related bleeding with ticagrelor. Ticagrelor offers a rapid inhibition of platelet aggregation (IPA). A pharmacodynamic study that compared IPA following a loading dose of ticagrelor 180 mg versus clopidogrel 600 mg showed that the maximum IPA for ticagrelor was reached around 2 hours (ticagrelor IPA 88% vs clopidogrel IPA 38%), was maintained for at least 8 hours, and was higher than the IPA for clopidogrel at all time points on day 1. Brilinta should not be used with doses of aspirin (ASA) above 100mg daily.

### US Clinical Guidelines Update

- Four US clinical guidelines (STEMI, NSTEMI/UA, PCI, and Secondary Prevention and Risk Reduction) were updated to include Brilinta as a Class 1 recommendation for the management of patients with ACS undergoing PCI with stent placement. The NSTEMI/UA and Secondary Prevention and Risk Reduction guidelines also include Brilinta as a Class 1 recommendation for the management of ACS in patients not undergoing PCI.
- The 2012 ACCP *Chest* guidelines for Antithrombotic Therapy and Prevention of Thrombosis recommend Brilinta plus low-dose ASA (75 mg to 100 mg) as a treatment option during the first year following an ACS event (with or without PCI; Grade 1B). The guidelines suggest the use of Brilinta over clopidogrel (Grade 2B).

### Questions and Answers

Q: How many patients are eligible for therapy?

A: A small % of patients.

Q: Are any additional indications being sought?

A: Use in secondary peripheral artery disease is being studied.

Q: How are insurers covering?

A: Approximately 60% of commercial, 40% of Medicare and 6% of Medicaid have as preferred on formularies. Hospitals have on formulary.

Q: How are some other Medicaid plans covering?

A: Indiana, Nevada, Texas and Pennsylvania have as preferred without prior authorization.

## XIII. United Therapeutics

Ron Rideman, PharmD, Senior Medical Science Liaison

Don Nopper, MBA, Government Account Manager

### **Adcirca® (tadalafil)**

Adcirca is a once-daily oral phosphodiesterase-5 (PDE5) inhibitor approved for the treatment of WHO Group I pulmonary arterial hypertension (PAH) to improve exercise capacity. PDE-5 inhibitors are important for the treatment of PAH, not only because of their vasodilatory effects, but also for their antiproliferative effects.

#### **New Clinical Data**

- A long-term open-label study of Adcirca (median exposure 356 days) reported a 96.5% survival rate, as well as sustained improvements in exercise ability at the approved dose of 40 mg once daily, as well as a statistically significant reduction in time to clinical worsening vs a 20 mg daily dose.
- Recent data presented at CHEST 2011 examined the adherence profile of PDE-5 inhibitors in patients with PAH. A significantly higher proportion of patients receiving Adcirca once-daily (61%) were more adherent than those receiving Revatio 3 times a day (44%).

#### **Questions and Answers**

Q: What was the age range the pivotal clinical trials were conducted in?

A: 18-75 years of age.

Q: Is there any pediatric data?

A: There are publications, data and reports on use in pediatrics but an indication is not being sought at this time.

Q: What are considered the advantages?

A: Once daily dosing so helps with compliance and delays worsening.

Q: When does the patent expire?

A: 2015.

### **Tyvaso® (inhaled treprostinil)**

Treprostinil is a stable prostacyclin analogue, with the longest half life of any commercially-available prostanoid, and is available in intravenous, subcutaneous and now, inhaled routes of administration. The reduction of prostacyclin plays a key role in the pathogenesis of PAH since endogenous prostacyclin promotes vascular health due to important vasodilatory, antiproliferative, and antithrombotic properties. Tyvaso is indicated for the treatment of World Health Organization Group 1 PAH to improve exercise ability. Studies establishing effectiveness included predominately patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases. Nearly all controlled clinical experience with Tyvaso has been on a background therapy of bosentan (endothelin receptor antagonist [ERA]) or sildenafil (PDE5).

#### **New Clinical Data**

- Data from the two year open label extension study demonstrated an overall lack of clinical worsening, sustained improvements in 6MW distance and overall favorable survival over two years.
- In a study of patients switched from inhaled iloprost to inhaled treprostinil the time spent on daily treatment activities was reduced by 1.4 hours each day. Improvements were also observed in 6-minute walk distance, NT pro-BNP and the Cambridge Pulmonary Hypertension Outcome Review.

#### **Questions and Answers**

Q: Is a supplemental rebate being offered?

A: No.

Q: When does the patent expire?

A: 2017-2019.

Q: What are considered the advantages?

A: Is the only inhaled prostanoid dosed less frequently at four times a day (vs. 6-9 times a day); compliance; improves 6-minute walking distance and quality of life; does not require special inhalation technique; is the only inhaled prostanoid in a large scale, randomized clinical trial that has been shown to increase exercise ability at both peak and trough time intervals used in combination with an ERA or a PDE5 inhibitor; and use of use since treatment only involves once a day set up and treatment times of 2 to 3 minutes per session.

#### **XIV. Merck**

Vicki L. Star, MD, FACR, Senior Regional Medical Director

Kerry Edwards, MD, Senior Regional Medical Director

Lisa Bishop, Senior Regional Account Executive

#### **Cosopt® PF (dorzolamide hydrochloride-timolol maleate ophthalmic solution) – New Formulation**

- **INDICATION:** COSOPT PF (preservative-free) is a carbonic anhydrase inhibitor with a beta-adrenergic receptor blocking agent indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to beta-blockers (failed to achieve target IOP determined after multiple measurements over time). The IOP-lowering of COSOPT administered twice a day was slightly less than that seen with the concomitant administration of 0.5% timolol administered twice a day and 2% dorzolamide administered 3 times a day.
- **CONTRAINDICATIONS:** COSOPT PF is contraindicated in patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second or third degree atrioventricular block, overt cardiac failure, cardiogenic shock, or hypersensitivity to any component of this product.
- **DOSAGE AND ADMINISTRATION:** The dose is one drop of COSOPT PF in the affected eye(s) two times daily. The solution from one individual unit is to be used immediately after opening for administration to one or both eyes. Since sterility cannot be maintained after the individual unit is opened, the remaining contents should be discarded immediately after administration.
- **WARNINGS AND PRECAUTIONS:** **Potential of Respiratory Reactions Including Asthma:** Severe respiratory reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate; **Cardiac Failure:** Sympathetic stimulation may be essential for support of the circulation in individuals with diminished myocardial contractility, and its inhibition by beta-adrenergic receptor blockade may precipitate more severe failure. In patients without a history of cardiac failure, continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of cardiac failure, COSOPT PF should be discontinued; **Sulfonamide Hypersensitivity:** COSOPT PF contains dorzolamide, a sulfonamide; and although administered topically, it is absorbed systemically. Therefore, the same types of adverse reactions that are attributable to sulfonamides may occur with topical administration of COSOPT PF. Fatalities have occurred, although rarely, due to severe reactions to sulfonamides, including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias; **Obstructive Pulmonary Disease:** Patients with chronic obstructive pulmonary disease (eg, chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease (other than bronchial asthma or a history of bronchial asthma, in which COSOPT PF is contraindicated) should, in general, not receive beta- blocking agents, including COSOPT PF; **Increased Reactivity to Allergens:** While taking beta-blockers, patients may be more reactive to allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions; **Potential of Muscle Weakness:** Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (eg, diplopia, ptosis, and generalized weakness); **Masking of Hypoglycemic Symptoms in Patients with Diabetes Mellitus:** Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta- adrenergic receptor blocking agents may mask the signs and symptoms of acute hypoglycemia; **Masking of Thyrotoxicosis:** Beta-adrenergic blocking agents may also mask certain clinical signs (eg, tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents that might precipitate a thyroid storm; **Renal and Hepatic Impairment:** Because dorzolamide and its metabolite are excreted predominantly by the kidney, COSOPT PF is not recommended in patients with severe renal impairment (CrCl <30 mL/min). Dorzolamide should be used with caution in patients with hepatic impairment; **Impairment of Beta-Adrenergically Mediated Reflexes During Surgery:** Some patients receiving beta-adrenergic receptor blocking agents have experienced protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients undergoing elective surgery, some authorities recommend gradual withdrawal of beta-adrenergic receptor blocking agents; **Corneal Endothelium:** There is an increased potential for developing corneal edema in patients with low endothelial cell counts. Caution should be used when prescribing COSOPT PF to this group of patients.
- **MECHANISM OF ACTION:** COSOPT PF decreases elevated intraocular pressure by reducing aqueous humor secretion. Dorzolamide hydrochloride is an inhibitor of human carbonic anhydrase II. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. Timolol maleate is a beta<sub>1</sub> and beta<sub>2</sub> (non-selective) adrenergic receptor blocking agent that does not have significant intrinsic sympathomimetic, direct myocardial depressant, or local anesthetic (membrane stabilizing) activity.

- **CLINICAL STUDIES (EFFICACY):** COSOPT: clinical studies of 3 to 15 months duration were conducted to compare the IOP-lowering effect over the course of the day of COSOPT twice daily (dosed morning and bedtime) to individually and concomitantly administered 0.5% timolol twice daily and 2.0% dorzolamide twice and three times daily. The IOP-lowering effect of COSOPT twice daily was greater (1-3 mmHg) than that of monotherapy with either 2.0% dorzolamide three times daily or 0.5% timolol twice daily. The IOP-lowering effect of COSOPT twice daily was approximately 1 mmHg less than that of concomitant therapy with 2.0% dorzolamide three times daily and 0.5% timolol twice daily. Open-label extensions of two studies were conducted for up to 12 months. During this period, the IOP-lowering effect of COSOPT twice daily was consistent during the 12-month follow-up period. COSOPT PF: In an active-treatment controlled, parallel, double-masked study in 261 patients with elevated intraocular pressure  $\geq 22$  mmHg in one or both eyes, COSOPT PF had an IOP-lowering effect equivalent to that of COSOPT.
- **SELECTED TOLERABILITY INFORMATION:** In clinical trials evaluating COSOPT and COSOPT PF, approximately 5% of all patients discontinued therapy because of adverse reactions. The most frequently reported adverse reactions occurring in up to 30% of patients were taste perversion (bitter, sour, or unusual taste) or ocular burning and/or stinging. The following adverse reactions were reported in 5% to 15% of patients: conjunctival hyperemia, blurred vision, superficial punctate keratitis, or eye itching.

### Questions and Answers

Q: Why was a preservative-free formulation developed?

A: Preservatives cause dry eyes, can cause sensitivity/immunologic reactions, can affect tear formation and the EU has asked for development of preservative-free ophthalmics.

Q: Are there any head-to-head studies vs. Cosopt with preservatives?

A: No, but switching studies and survey studies have shown less adverse events with PF and retinologists use PF after surgery.

### **Januvia® (sitagliptin)**

Januvia is a dipeptidyl peptidase-4 (DPP-4) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus. Januvia should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Januvia has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk of developing pancreatitis while taking Januvia.

### New Safety Information

- Hypersensitivity reactions: There have been postmarketing reports of serious hypersensitivity reactions in patients treated with Januvia. These reactions include anaphylaxis, angioedema, and exfoliative skin conditions including Stevens-Johnson syndrome. Onset of these reactions occurred within the first 3 months after initiation of treatment with Januvia, with some reports occurring after the first dose. If a hypersensitivity reaction is suspected, discontinue Januvia, assess for other potential causes for the event, and institute alternative treatment for diabetes. Angioedema has also been reported with other DPP-4 inhibitors. Use caution in a patient with a history of angioedema with another DPP-4 inhibitor because it is unknown whether such patients will be predisposed to angioedema with Januvia.
- Medication Guide was updated to educate that patients should swallow tablet whole and not break, crush or cut tablets.

### Questions and Answers

Q: What are considered the advantages?

A: Market leader, robust data, combination products available, long-term safety and tolerability, broad indications as monotherapy and combination therapy, published elderly data that shows safe and efficacious, no major drug-drug interactions, renal function monitoring that has to be conducted is not an issue since needs to be performed in this patient population anyway, no product has shown improvement in macrovascular outcomes and a long-term cardiovascular study is underway per FDA post-approval requirement.

### **Victrelis® (boceprevir)**

Victrelis is a protease inhibitor indicated for the treatment of chronic hepatitis C virus (HCV) genotype 1 (G1) infection, in combination with peginterferon alfa and ribavirin (PR), in adult patients (18 years and older) with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous interferon and ribavirin therapy. The following points should be considered when initiating Victrelis for treatment of chronic hepatitis C infection:

- Victrelis must not be used as monotherapy and should only be used in combination with peginterferon alfa and ribavirin.
- Victrelis efficacy has not been studied in patients who have previously failed therapy with a treatment regimen that includes Victrelis or other hepatitis C virus (HCV) NS3/4A protease inhibitors.

- Victrelis in combination with peginterferon alfa and ribavirin has not been studied in patients documented to be historical null responders (less than a 2- $\log_{10}$  HCV-RNA decline by treatment week 12) during prior therapy with peginterferon alfa and ribavirin. The clinical studies included subjects who were poorly interferon responsive. Subjects with less than 0.5- $\log_{10}$  HCV-RNA decline in viral load at Treatment Week 4 with peginterferon alfa plus ribavirin alone are predicted to have a null response (< 2- $\log_{10}$  viral load decline at Treatment Week 12) to peginterferon alfa and ribavirin therapy.
- Poorly interferon responsive patients who were treated with Victrelis in combination with peginterferon alfa and ribavirin have a lower likelihood of achieving a sustained virologic response (SVR), and a higher rate of detection of resistance-associated substitutions upon treatment failure, compared to patients with a greater response to peginterferon alfa and ribavirin.

#### **New Safety Information**

- Hypersensitivity: Serious acute hypersensitivity reactions (e.g., urticaria, angioedema) have been observed during combination therapy with Victrelis, peginterferon alfa, and ribavirin. If such an acute reaction occurs, combination therapy should be discontinued and appropriate medical therapy immediately instituted.

#### **Questions and Answers**

Q: Has there been any incidences of TENS or DRESS?

A: No, so there is no black box warning for hypersensitivity reactions.

#### **XV. Teva**

Tanisha Hill, MPH, Medical Science Liaison

#### **ProAir® HFA (albuterol sulfate) with Dose Counter – New Formulation**

On March 7, 2012, the U.S. Food and Drug Administration (FDA) approved the New Drug Application (NDA) for ProAir HFA with Dose Counter. The dose counter counts in increments of two and is designed to help patients, as well as their caregivers, keep track of the number of doses remaining in the inhaler. ProAir® HFA with Dose Counter has a 24-month expiration, can be carried or stored in any position, and features a warm, soft plume of long duration. ProAir HFA with Dose Counter was distributed to pharmacies in December 2012.

#### **Indication and Usage**

- ProAir HFA (albuterol sulfate) Inhalation Aerosol is a beta2-adrenergic agonist indicated in patients 4 years of age and older for the treatment or prevention of bronchospasm with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm.

#### **Dosage and Strength**

- 2 inhalations every 4 to 6 hours for the treatment or prevention of bronchospasm in adults and children 4 years of age and older. In some patients, one inhalation every 4 hours may be sufficient.
- 2 inhalations 15 to 30 minutes before exercise for the prevention of exercise-induced bronchospasm in adults and children 4 years of age and older.

#### **Important Safety Information**

- Adverse Events: The most common adverse reactions ( $\geq 3.0\%$  and  $>$ placebo) are headache, tachycardia pain, dizziness, pharyngitis, and rhinitis.
- Warnings and Precautions:
  - Inhaled albuterol sulfate can produce paradoxical bronchospasm that may be life-threatening. It should be recognized that paradoxical bronchospasm, when associated with inhaled formulations, frequently occurs with the first use of a new canister.
  - Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs in patients with asthma.
  - ProAir® HFA, as with all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders (especially coronary insufficiency, cardiac arrhythmias, and hypertension), convulsive disorders, hyperthyroidism, and diabetes.
  - Potential drug interactions can occur with beta-blockers, diuretics, digoxin, or monoamine oxidase inhibitors, and tricyclic antidepressants.
  - Do not exceed the recommended dose.
  - Adverse events, which occurred at an incidence rate of at least 3% with ProAir HFA, include headache, tachycardia, pain, dizziness, pharyngitis, and rhinitis.

## Questions and Answers

Q: Is the new formulation with dose counter at price parity?

A: Yes.

Q: Is the new formulation with dose counter replacing inhaler without dose counter?

A: Yes.

## **Qnasl® (beclomethasone dipropionate nasal aerosol) – New Formulation**

### **Indication and Usage**

- Qnasl is indicated for the treatment of the symptoms of seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) in adults and adolescent patients 12 years of age and older.

### **Dosage and Strength**

- The recommended dose of Qnasl Nasal Aerosol is 320 mcg per day administered as 2 nasal aerosol sprays in each nostril once daily (maximum total daily dose of 4 nasal aerosol sprays per day).

### **Efficacy and Safety**

- Qnasl Nasal Aerosol has been evaluated in randomized, double-blind, parallel-group, multicenter, placebo-controlled clinical trials in adult and adolescent patients 12 years of age and older with symptoms of SAR or PAR including a 2-week SAR dose-ranging trial, a 2-week SAR efficacy trial, and a 6-week PAR trial, totaling collectively 1049 patients receiving Qnasl Nasal Aerosol. Of these patients, 521 received the 320 mcg once daily dose of Qnasl administered as 2 sprays in each nostril. Additionally, a 52-week, long-term, randomized, double-blind, placebo-controlled safety trial with a total of 415 PAR patients receiving Qnasl Nasal Aerosol at 320 mcg once daily was conducted. Of note, a Phase 3 hypothalamic-pituitary-adrenal (HPA)-axis trial also evaluated the safety of Qnasl Nasal Aerosol, but was not used to assess clinical benefit.
- Highlights from the Qnasl Nasal Aerosol clinical trials include:
  - Qnasl Nasal Aerosol 320 mcg once daily resulted in statistically significant and clinically meaningful improvements in nasal symptoms vs. placebo in the short-term (2 to 6 week) SAR and PAR studies as well as the long-term (52-week) PAR study
  - The 320 mcg per day dose of Qnasl Nasal Aerosol also demonstrated greater improvement in morning nasal symptoms vs. placebo, indicating that the therapeutic effect was maintained over the entire 24 hour dosing interval in all four clinical trials.
  - In the Phase 3, long-term PAR trial, improvements in nasal symptoms were maintained for up to 52 weeks of repeat-dose treatment, thus demonstrating the long-term efficacy of once daily treatment with Qnasl Nasal Aerosol.
  - In the Phase 3, 2-week SAR trial, improvements in nasal symptoms were seen as early as 1 day following the start of treatment and significant improvements in ocular symptom scores met the clinically meaningful criterion.
  - In the Phase 3, 6-week PAR trial, improvements in nasal symptoms were seen as early as 2 days following the start of treatment and statistically significant, clinically meaningful improvements in the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) were observed.
  - Qnasl Nasal Aerosol 320 mcg/day was generally well-tolerated with mild to moderate nasal discomfort (5.2% vs. 4.8%), epistaxis (1.9% vs. 1.2%), and headache (2.3% vs. 1.6%) being the most commonly observed adverse events (AEs) vs. placebo in the 2 to 6 week studies.
  - In the long-term, 52-week PAR trial, most AEs were similar in type and rate between the treatment groups; however, epistaxis occurred more frequently in the Qnasl Nasal Aerosol group compared with the placebo group (≈11% vs. 2%, respectively).

### **Warnings and Precautions**

- Although class labeling for all INs available in the US, including Qnasl, contains warnings about hypercorticism and adrenal suppression, HPA-axis suppression has not been associated with Qnasl when used at the recommended dose relative to placebo in adult and adolescent patients with PAR.

## Questions and Answers

Q: Is a pediatric indication being sought in patients younger than 12 years of age?

A: Yes, phase III trials in patients 4-11 are underway and submission is expected in 2014.

Q: Are there any head-to-head studies?

A: No.

Q: Are all studies published?

A: There are 2 deposition studies not yet published that showed 99% of drug stays in the nose, adolescent data for ocular symptoms and safety has been presented as poster but not yet published and long-term data is to be published and presented at upcoming AAAAI meeting.

Q: Are any additional indications being sought?

A: No, this requires additional studies and company is comfortable with the data that is available.

Q: What are considered the advantages?

A: Compared to aqueous products, drug stays in nasal cavity longer and some patients prefer dry products, adherence is higher with dry products, has indication in both SAR and PAR, has not caused nasal perforation and there are phase IV studies being conducted to evaluate efficacy and satisfaction.

## **XVI. UCB**

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Melanie Beckemeyer, PharmD, CNS Medical Science Liaison II

Cindy Harper, Regional Account Executive

### **Neupro® (rotigotine transdermal system) – New Drug**

#### **Indication and Usage**

- Neupro is indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease and moderate-to-severe primary Restless Legs Syndrome (or RLS).
- Neupro is the first and only dopamine agonist transdermal patch that provides continuous drug delivery over a 24-hour period; therefore, we ask that you provide unrestricted formulary access to this therapy.
- Neupro is contraindicated for individuals with a history of hypersensitivity to rotigotine or components of the transdermal patch.

#### **Safety**

- The most common adverse reactions ( $\geq 5\%$  greater than placebo) for the highest recommended doses of Neupro for treatment of Parkinson's disease are nausea, vomiting, somnolence, application site reactions, dizziness, anorexia, hyperhidrosis, insomnia, peripheral edema, and dyskinesias.
- The most common adverse reactions ( $\geq 5\%$  greater than placebo) for the highest recommended dose of Neupro for treatment of Restless Legs Syndrome are application site reactions, nausea, somnolence, and headache.

#### **Conclusion**

- In conclusion, Neupro has demonstrated efficacy for patients with early- and advanced-stage Parkinson's disease and moderate-to-severe primary Restless Legs Syndrome. Its innovative transdermal delivery provides continuous, stable plasma concentrations.

#### **Questions and Answers**

Q: Are all studies published and were all studies presented today?

A: Yes.

Q: How was the previous issue with the patch pulled from the market addressed with this new patch?

A: The new patch uses a more stable polymorph that has not yet formed crystals. Study evaluated stability for two years.

Q: How are other insurers covering?

A: 80-90% of commercial have as Tier 2, Medicare D is more restrictive. Use for Parkinson's is not as severely restricted as is use for RLS.

Q: Did the FDA use EU data for US approval?

A: Yes.

## **Cimzia® (certolizumab)**

Cimzia is a TNF blocker indicated in the treatment of rheumatoid arthritis and Crohn's disease.

### **New Clinical Information**

#### ***USE IN SPECIAL POPULATIONS***

- **8.1 Pregnancy:** Pregnancy Category B
  - **Risk Summary:** Adequate and well-controlled studies with Cimzia have not been conducted in pregnant women. Certolizumab pegol plasma concentrations obtained from 10 women treated with Cimzia during pregnancy and their newborn infants demonstrated low placental transfer of certolizumab pegol. Cimzia may be eliminated at a slower rate in exposed infants than in adult patients. No fetal harm was observed in animal reproduction studies. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Cimzia during pregnancy. To enroll, healthcare providers or patients can call 1-877-311-8972.
  - **Human Data:** In an independent clinical study conducted in 10 pregnant women with Crohn's disease treated with Cimzia, certolizumab pegol concentrations were measured in maternal blood as well as in cord and infant blood (n=12) at the day of birth. The last dose of Cimzia (400 mg for every mother) was given on average 19 days prior to delivery (range 5-42 days). Plasma certolizumab pegol concentrations were <0.41 –1.66 µg/mL in cord blood, <0.41 – 1.58 µg/mL in infant blood, and 1.87–59.57 µg/mL in maternal blood. Plasma certolizumab pegol concentrations were lower (by at least 75%) in the infants than in mothers, suggesting low placental transfer of certolizumab pegol. In one infant, the plasma certolizumab pegol concentration declined from 1.02 to 0.84 µg/mL over 4 weeks suggesting that Cimzia may be eliminated at a slower rate in infants than adults.
  - **Animal Data:** Because certolizumab pegol does not cross-react with mouse or rat TNFα, reproduction studies were performed in rats using a rodent anti-murine TNFα pegylated Fab' fragment (cTN3 PF) similar to certolizumab pegol. Reproduction studies have been performed in rats at doses up to 100 mg/kg and have revealed no evidence of impaired fertility or harm to the fetus due to cTN3 PF.
- **8.3 Nursing Mothers:** It is not known whether certolizumab pegol is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Cimzia, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.
- **8.4 Pediatric Use:** Safety and effectiveness in pediatric patients have not been established. Due to its inhibition of TNFα, Cimzia administered during pregnancy could affect immune responses in the *in utero* exposed newborn and infant.

### **Questions and Answers**

Q: Have there been any IgG issues?

A: No.

Q: Are there any anecdotal issues related to low placental transfer of drug?

A: No, but there is a pregnancy registry to follow outcomes data.

## **XVII. Bristol-Myers Squibb**

Russ Rainwater, PharmD, MBA, Medical Affairs

Tim Carr, RPh, PAHM, Sr Account Executive

Negelle Green, LCSW, Integrated Markets Director

## **Bydureon® (exenatide extended-release for injectable suspension) – New Formulation**

### **Indication and Important Limitations of Use**

- Bydureon is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus in multiple clinical settings.
- Because of the uncertain relevance of the rat thyroid C-cell tumor findings to humans, prescribe only to patients for whom potential benefits are considered to outweigh potential risk.
- Not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.
- Not a substitute for insulin, should not be used in patients with type 1 diabetes or diabetic ketoacidosis, and cannot be recommended for use with insulin.
- Bydureon and Byetta (exenatide) injection both contain the same active ingredient, exenatide, and should not be used together.

- Exenatide has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, based on postmarketing data. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Bydureon; consider other antidiabetic therapies for these patients.

#### **BOXED WARNING: RISK OF THYROID C-CELL TUMORS**

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

#### **Warnings and Precautions**

- **Pancreatitis:** Based on postmarketing data, exenatide has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. After initiation of Bydureon, observe patients carefully for pancreatitis (persistent severe abdominal pain, sometimes radiating to the back, with or without vomiting). If pancreatitis is suspected, Bydureon should be discontinued promptly and should not be restarted if pancreatitis is confirmed.

#### **Clinical Trial Efficacy**

- **Comparator-Controlled Study-A** 24-week, randomized, open label trial was conducted to compare exenatide once weekly (ExQW) to exenatide twice daily (ExBID) in T2DM patients with inadequate glycemic control on diet and exercise alone or with metformin (MET), a sulfonylurea (SU), a thiazolidinedione (TZD), or a combination of two of those therapies. The mean A1C was 8.4%. Patients received ExQW (n=129) or ExBID 10 mcg (n=123).
- ExQW provided significant improvements in mean change from baseline in A1C and FPG compared to ExBID: A1C (-1.6% vs. -0.9%, respectively; P<0.001); FPG (-25mg/dL vs. -5 mg/dL, respectively; P<0.001). Proportion achieving A1C<7% was 58% and 30% (P<0.001), respectively. Reduction in body weight was observed in both the ExQW group (-2.3 kg) and the ExBID group (-1.4 kg).

#### **Clinical Trial Safety**

- **Most Common Adverse Reactions (≥5%)**
  - **Bydureon vs. Byetta:** 24-week trial: nausea (14% vs. 35%), diarrhea (9.3% vs. 4.1%), injection-site erythema (5.4% vs. 2.4%) 30-week trial: nausea (27% vs. 33.8%), diarrhea (16.2% vs. 12.4%), vomiting (10.8% vs. 18.6%), injection-site pruritus (18.2% vs. 1.4%), constipation (10.1% vs. 6.2%), gastroenteritis viral (8.8% vs. 5.5%), gastroesophageal reflux disease (7.4% vs. 4.1%), dyspepsia (7.4% vs. 2.1%), injection-site erythema (7.4% vs. 0.0%), fatigue (6.1% vs. 3.4%), headache (6.1% vs. 4.8%), injection-site hematoma (5.4% vs. 11.0%).
  - **Bydureon vs. titrated insulin glargine:** nausea (12.9% vs. 1.3%), headache (9.9% vs. 7.6%), diarrhea (9.4% vs. 4.0%), injection-site nodule (6.0% vs. 0.0%).
  - **Combination trial vs. sitagliptin and pioglitazone:** nausea (24.4% vs. 9.6% and 4.8%), diarrhea (20.0% vs. 9.6% and 7.3%), vomiting (11.3% vs. 2.4% and 3.0%), headache (9.4% vs. 9.0% and 5.5%), constipation (6.3% vs. 3.6% and 1.2%), fatigue (5.6% vs. 0.6% and 3.0%), dyspepsia (5.0% vs. 3.6% and 2.4%), decreased appetite (5.0% vs. 1.2% and 0.0%), injection-site pruritus (5.0% vs. 4.8% and 1.2%).
  - **Monotherapy trial vs. sitagliptin, pioglitazone, and metformin:** nausea (11.3% vs. 3.7%, 4.3%, and 6.9%), diarrhea (10.9% vs. 5.5%, 3.7%, and 12.6%), injection-site nodule (10.5% vs. 6.7%, 3.7%, and 10.2%), constipation (8.5% vs. 2.5%, 1.8%, and 3.3%), headache (8.1% vs. 9.2%, 8.0%, and 12.2%), dyspepsia (7.3% vs. 1.8%, 4.9%, and 3.3%).
- **Hypoglycemia**
  - No major hypoglycemia was reported for Bydureon- or comparator-treated patients in five 24- to 30-week trials. Minor† hypoglycemia incidences for Bydureon vs. comparator-treated patients were as follows: 24-week trial vs. Byetta: with SU, 12.5% vs. 11.8%; without SU, 0.0% for both; 30-week trial vs. Byetta: with SU, 14.5% vs. 15.4%; without SU, 0.0% vs. 1.1%; monotherapy trial vs. sitagliptin, pioglitazone, and metformin: 2.0% vs. 0.0% (all comparators); combination trial vs. sitagliptin and pioglitazone: 1.3% vs. 3.0% and 1.2%; vs. titrated insulin glargine, with SU, 20.0% vs. 43.9%; without SU, 3.7% vs. 19.1%.

#### **Questions and Answers**

Q: Is a supplemental rebate being offered?

A: Not at this time due to transition of marketing of product.

Q: Are there any studies evaluating macrovascular outcomes?

A: Signal suggests benefit, but there is no data available yet. Data is in progress due to FDA requirement.

Q: Is the comparative trial vs. liraglutide going to be published?

A: Believe so.

Q: When does patent expire on Byetta?

A: Will get back with us.

Q: Did Bydureon receive extension on patent?

A: Will get back to us but Bydureon is not a line extension due to difference in pharmacokinetics (PK) compared to Byetta.

Q: Is there any compliance data?

A: A study showed patients that switched from Byetta to Bydureon were 25% more compliant.

Q: What are considered the advantages?

A: Superior A1c lowering, better PK profile, improved compliance and ease of use.

## **XVIII. Novo Nordisk**

Cheryl Pryor, PharmD, Director, Managed Markets Medical Liaisons

Joe Spano, Account Executive II

### **Norditropin® (somatropin [rDNA origin] injection)**

Norditropin is a growth hormone indicated for treatment of children with growth failure due to growth hormone deficiency (GHD), short stature associated with Noonan syndrome, short stature associated with Turner syndrome and short stature born with no catch-up growth by age 2 to 4 years and in adults for treatment of adults with either adult onset or childhood onset GHD.

### **Norditropin Delivery Devices**

Norditropin® Flexpro® - Approved in March 2010, FlexPro offers enhanced features that support dosing accuracy, such as an easy-to-push dose button and an end-of-dose signal when the entire dose has left the pen. Summary of key features of Norditropin Flexpro:

- Pre-loaded: No mixing, loading or changes of cartridges necessary
- Ergonomic design
- Easy to read numbers - black on white background
- Different dialing sounds depending on the direction; can potentially avoid dosing errors
- End-of-dose click which indicates that the medication has left the pen
- Small dosing increments: The FlexPro 5 mg/1.5 mL pen has a dosing increment of 0.025 mg. Physicians have greater flexibility in selecting an optimal dose based on the patient's weight, thus potentially reducing product wastage and generating cost savings.
- Storage Flexibility: After initial injection, FlexPro 5 mg and 10 mg pens can be stored at room temperature (up to 77F) for 3 weeks or in the refrigerator (36-46F) for 4 weeks. This is convenient when patients have to travel with their medication and it can also reduce product wastage if they forget to return the pens back into the refrigerator after use. FlexPro 15 mg must be refrigerated at all times while in use. All FlexPro pens must be refrigerated prior to initial use.
- Overfill: FlexPro has demonstrated overfill to optimize the deliverable doses in each pen and helping to ensure patients receive the full labeled volume in each pen.
- Fuchs et al evaluated the usability and acceptability of Norditropin Flexpro: 10 mg pen for the administration of growth hormone in pediatric patients with GH deficiency. This open-label, uncontrolled study included 70 patients between the ages of 10 to <18 years, who completed a 21-item questionnaire on the acceptability and usability of the device. All of the patients reported that learning to use the FlexPro pen device was very easy or quite easy. FlexPro pen was reported by 90% of the patients (n=63) to be a lot better in term of the stability of the device as compared to their currently used device. Overall, 45 patients (64%) preferred FlexPro over the current one, 14 patients were uncertain and 11 patients preferred their current device over FlexPro pen.

### **GH Budget Impact Model**

Share with the committee members a new health economic model evaluating costs to a payor associated with the top four growth hormone market leaders, Genotropin®, Humatrope®, Nutropin®, and Norditropin®. Costs drivers in the

model are: WAC, dosing increments of the pen delivery devices, and wastage due to storage and reconstitution requirements.

- Shift of 60% use to Norditropin results in decrease drug spend by \$166K due to other products requires manipulation of product, refrigeration, waste, dosing increments, storage and/or reconstitution.

### Questions and Answers

Q: How long can a parent wait to give a child a dose if the child does not want if dose is already dialed?

A: Since syringe is prefilled, this is not an issue.

Q: Has the model been validated?

A: Pharmacoeconomist showed the model was sound.

## XIX. Forest

Carla McSpadden, RPh, CGP, Senior Managed Care Specialist

Bill Everage, Regional Account Manager

### Daliresp® (roflumilast)

Daliresp is phosphodiesterase-4 (PDE4) inhibitor indicated as a treatment to reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. It is not a bronchodilator and should not be used for the relief of acute bronchospasm.

### New Information – Updated GOLD Guidelines

- The Global Initiative for Chronic Obstructive Lung Disease (GOLD) is an international group that has established guidelines for the diagnosis, management and prevention of COPD. The GOLD Guidelines have identified exacerbation prevention as a goal of COPD treatment. The recently updated GOLD Guidelines recommend assessing patients to determine severity and guide therapy. Assessment of disease severity should incorporate severity of airflow limitation (i.e., spirometry), impact of disease on patient's health status, and history of COPD exacerbations. These factors combined are used to classify patients into four groups, which are then used to guide therapy.
  - Group A = Low Risk, Less Symptoms
  - Group B = Low Risk, More Symptoms
  - Group C = High Risk, Less Symptoms
  - Group D = High Risk, More Symptoms
- The GOLD Guidelines state that Daliresp may be used to reduce the risk of exacerbations in patients with severe or very severe COPD, chronic bronchitis, and frequent exacerbations that are not adequately controlled by long-acting bronchodilators. Daliresp is listed as a treatment option for patients classified in Group C and Group D.

### Questions and Answers

There were no questions but the presenter requested that DCH consider accepting spirometry, exacerbations or symptoms in the prior authorization criteria.

## XX. Otsuka

Bradford Loo, PharmD, Senior Medical Science Liaison

Diana Sedgwick, CMR, Senior Account Executive

Tim Carr, RPh, PAHM, Senior Account Executive

### Abilify® (aripiprazole)

Abilify is an atypical antipsychotic indicated in the treatment of schizophrenia, bipolar disorder, irritability associated with autism and as adjunct therapy in MDD.

### Practice Guidelines for Major Depressive Disorder: an Evidence-Based Assessment of Adjunctive Therapy

- American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder. 3rd ed. Arlington, VA: American Psychiatric Association; 2010.
  - After an inadequate response to initial pharmacotherapy, APA guidelines recommend optimizing the dose of the current medication, or switching or augmenting with another agent or psychotherapy. These parameters of practice should be considered guidelines only and not standard of medical care.
  - Augmentation options for an inadequate response include adjunctive use of an atypical antipsychotic

- Some agents within the atypical antipsychotic class are indicated for the adjunctive treatment of adults with MDD who have had an inadequate response to antidepressant therapy.
- Canadian Network for Mood and Anxiety Treatments (CANMAT) Guidelines: Recommendations for Nonresponse or Incomplete Response to Initial Antidepressant Therapy.

**First-line (Level 1 or Level 2 evidence, plus clinical support†)**

Switch to an agent with evidence for superiority  
 -SSRIs [Level 1]  
 -SNRIs [Level 1-2]  
 -Noradrenergic-serotonin modulator [Level 2]  
 Add on another agent  
 -Mood stabilizer [Level 1]  
 -Atypical antipsychotics [Level 1-2]

**Second-line (Level 3 evidence or higher, plus clinical support†)**

Add on another agent  
 -DNRI [Level 2]  
 -Noradrenergic-serotonin modulator [Level 2]  
 -Atypical antipsychotic [Level 2]  
 -Thyroid hormone [Level 2]  
 -Other antidepressants [Level 3]  
 Switch to an agent with evidence for superiority, but with side effect limitations  
 -TCAs [Level 2]  
 -MAO inhibitors [Level 2]

**Third-line (Level 4 evidence or higher, plus clinical support†)**

Add on another agent  
 -Serotonin 5-HT1A receptor partial agonist [Level 2]  
 -Psychostimulant [Level 2]  
 -Stimulants [Level 3]  
 -Atypical antipsychotic [Level 3]

Level of Evidence Criteria per Above: 1=At least two RCTs with adequate sample sizes, preferably placebo controlled, and/or meta-analysis with narrow confidence intervals. 2=At least one RCT with adequate sample size and/or meta-analysis with wide confidence intervals. 3=Nonrandomized, controlled prospective studies or case series or high quality retrospective studies. 4=Expert opinion/consensus.

†Treatments with higher Levels of Evidence may be downgraded to lower Lines of Treatment due to clinical issues such as side effect or safety profile.

- International Consensus Statement on Optimizing Antidepressant Therapy.
  - Reasonable treatment options for partial or lack of efficacy include: Modifying the antidepressant dose, Switching to a different antidepressant, Switching to augmentation/combination strategies. Augmentation or combination strategies include, but are not limited to: mood stabilizers, atypical antipsychotics, thyroid hormone, NaSSA, or DNRI‡.
    - ‡Not all products in the therapeutic categories listed are indicated for adjunctive treatment in adult patients with MDD with an inadequate response to antidepressant therapy.
- Discuss strategies and evidence-basis for adjunctive therapy:
  - STAR\*D (Sequenced Treatment Alternatives to Relieve Depression)
  - Combining Medications to Enhance Depression Outcomes (CO-MED) Study
- Review Abilify (aripiprazole) as an adjunctive option for treatment of adults with MDD who have had an inadequate response to an antidepressant.

**Questions and Answers**

There were no questions but a statement from an audience member was made that generally non-US guidelines are not used when there are US guidelines available.

**XXI. Actelion**

Michele Cole, PharmD, Medical Science Liaison  
 Brad Burris, MBA/MHA, National Account Executive

**Tracleer® (bosentan)**

Tracleer is an endothelin receptor antagonist (ERA) indicated for use in pulmonary arterial hypertension in patients with WHO Class II-IV symptoms.

**New Clinical Data**

- COMPASS 2 study showed bosentan can be safely and effectively be added to sildenafil therapy.
- COMPASS 3 study showed sildenafil can be safely and effectively be added to bosentan therapy.

**Questions and Answers**

Q: When does the patent on Tracleer expire?

A: November 2015.

Q: What are considered the advantages of Tracleer?

A: Robust data, improves 6-minute walking distance >30 meters which is clinically and statistically significant (>25-30 meters is clinically significant) and antagonizes endothelin receptors A and B so may be associated with less edema.

Q: Are you offering a supplemental rebate on your Ventavis or Veletri products?

A: No.

Q: What are considered the advantages of Ventavis?

A: Superior efficacy, breath activated so ease of use and device has software to map inhalations with dates so that physician can use for counseling, etc.

Q: What are considered the advantages of Veletri?

A: Can be stored at room temperature and is financially just slightly higher than generic when comparing WAC or AWP.

## **XXII. Ferring**

Lisa Young, PhD, Medical Science Liaison

Patricia Boseman, Corporate Accounts Manager, Government Accounts

### **Prepopik® (sodium picosulfate, magnesium oxide, and anhydrous citric acid for oral solution) – New Drug**

#### **Current colonoscopy screening rates**

- CRC is highly preventable and Colonoscopy is the gold standard for CRC screening
  - 5-year survival rate over 90% after removal of localized polyps
  - Diagnostic and treatment applications
  - Allows for visualization and removal of polyps
- Recommended by American College of Gastroenterology every 10 years in adults over 50

#### **Inadequate bowel prep is a persistent problem**

- As many as 25% of patients undergoing colonoscopy are inadequately prepped, resulting in longer procedure times and substantial numbers of missed lesions (among inadequately prepped patients, 34% had 1 or more missed adenoma during rescreening).

#### **Prepopik product profile**

- Dosage forms and strength: Available in a carton that contains a dosing cup and 2 packets, each holding 16.1 g of powder for oral solution. Each packet contains: 10.0 mg sodium picosulfate, 3.5 g magnesium oxide, and 12.0 g anhydrous citric acid.
- Dual mechanism of action: sodium picosulfate is converted into an active metabolite, BHPM, to stimulate colonic peristalsis; magnesium oxide and anhydrous citric acid react in water to create magnesium citrate, which produces osmotic water retention. Offers 2 dosing options and a flexible hydration schedule.

#### **SEE CLEAR I and II: Study Design**

- Phase 3 randomized, assessor-blinded, multicenter studies, 1195 adult patients
- SEE CLEAR I—split-dose regimen (N=601)
- SEE CLEAR II—day-before dose regimen (N=594)
- Primary objective: To demonstrate noninferiority of PREPOPIK (sodium picosulfate, magnesium oxide, and anhydrous citric acid) to 2L PEG with electrolytes (PEG+E) plus 2x 5 mg bisacodyl tablets in overall colon cleansing in preparation for colonoscopy based on the Aronchick scale.
- Secondary objectives: (1) To demonstrate noninferiority of PREPOPIK to 2L PEG with electrolytes (PEG+E) plus 2x 5 mg bisacodyl tablets with respect to the efficacy of ascending colon cleansing based on the Ottawa scale. (2) To determine tolerability and satisfaction of the preparation as assessed by a standardized subject questionnaire administered at the study site before colonoscopy. (3) To evaluate safety and tolerability through the collection of adverse events, clinical laboratory tests, and physical examination.

#### **Clinical Trial Results**

- SEE CLEAR I: Prepopik achieved a statistically superior level of “excellent” or “good” cleansing vs 2L PEG+E plus 2x 5 mg bisacodyl tablet (84% [256/304] vs 74% [221/297], respectively;  $P<0.05$ )\*; and additionally achieved superiority in each section of the bowel (Ottawa Scale)
- SEE CLEAR II: PREPOPIK achieved the primary endpoint of non-inferiority to 2L PEG+E plus 2x 5 mg bisacodyl tablets, with similar levels of “excellent” or “good” cleansing (83% [244/294] vs 80% [239/300], respectively;

$P=0.34$ )\*. When evaluated by segment via the Ottawa Scale, PREPOPIK achieved “excellent” or “good” cleansing consistently throughout the colon, including the ascending, mid, and rectosigmoid sections.

- In both trials (I and II), Prepopik demonstrates efficacy and safety in the elderly (Patients 65 or older). Treatment-Emergent Adverse Reactions Observed in at Least (>1%) of Patients Using the Split-Dose Regimen and Day-Before Regimen in were nausea headache and vomiting (3% or less for Prepopik, 5% or less for 2L PEG with electrolytes (PEG+E) plus 2x 5 mg bisacodyl tablets
- Subjects were instructed to complete a standardized questionnaire prior to contact with the Investigator (and prior to sedation for colonoscopy): Proportion of patients who reported being able to consume the entire prep as instructed = 575/596 (96.5%) of PREPOPIK group vs 541/594 (91%) of 2L PEG+E + Bis group. Additionally, proportion of patients who would ask their doctor for the prep again if they need another colonoscopy = 563/595 (94.5%) of PREPOPIK group vs 339/594 (57.0%) of 2L PEG+E + Bis group.

### **Important Safety Information**

- Contraindications: Patients with severely reduced renal function (creatinine clearance less than 30 mL/minute) which may result in accumulation of magnesium, Gastrointestinal obstruction or ileus, Bowel perforation, Toxic colitis or toxic megacolon, Gastric retention, An allergy to any of the ingredients in Prepopik
- Warnings and precautions: Serious fluid and serum chemistry abnormalities, Seizures, Use in patients with renal impairment, Cardiac arrhythmias, Colonic mucosal ulceration, ischemic colitis and ulcerative colitis, Use in patients with significant gastrointestinal disease, Aspiration, Not for direct ingestion

### **Summary**

- Prepopik is the lowest volume of active prep solution and a flexible hydration schedule. It has demonstrated non-inferiority, with both split-dose and day-before regimen and demonstrated superior cleansing efficacy with ACG-recommended split-dose vs day-before regimen comparator. Prepopik is a dual mechanism that stimulates peristalsis and produces osmotic water retention and post-marketing ex-US experience based on over 30 years of use in 28 million patients.

### **Questions and Answers**

Q: Which dosing regimen do the guidelines generally recommend?

A: A split dose for excellent colonoscopy.

Q: What are considered the advantages?

A: Lowest volume bowel prep, showed non-inferiority and superiority (SEE CLEAR I) over market leader at that time, 2 dosing options available, is the market leader in Canada and can drink any liquid.

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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 Catamaran, announces the Manufacturers' Forum occurring on Thursday, May 2, 2013.

**Date:** Thursday, May 2, 2013 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 – 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](mailto:GAMedicaid@nhc-llc.com). **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.**

**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.
- **An electronic one-page summary of the presentation should be provided one week prior to the presentation via email to [GAMedicaid@nhc-llc.com](mailto: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](mailto:GAMedicaid@nhc-llc.com).
- Manufacturers with comments or inquiries related to Georgia Medicaid FFS **supplemental rebates** should submit these in writing to [GAMedicaid@nhc-llc.com](mailto:GAMedicaid@nhc-llc.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:

Catamaran, Inc.  
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 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 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](mailto: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](mailto: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> under Providers – Pharmacy – Drug Utilization Review Board – Meeting Information.

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

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2013

## Upcoming Meetings

### Drug Utilization Review Board Meeting

2 Peachtree Street, N.W.

5<sup>th</sup> Floor Board Room

Atlanta, Georgia 30303

Thursday, June 6, 2013:	10:00am – 2:00pm
Thursday, September 19, 2013:	10:00am – 2:00pm
Tuesday, December 10, 2013:	10:00am – 2:00pm

### Manufacturers' Forum

NorthStar HealthCare Consulting

1121 Alderman Drive

Suite 112

Alpharetta, Georgia 30005

Thursday, May 2, 2013:	9:00am – 5:00pm
Thursday, August 1, 2013:	9:00am – 5:00pm
Thursday, November 7, 2013:	9:00am – 5:00pm