



## **AGENDA**

### **State and Public School Life and Health Insurance Board Drug Utilization and Evaluation Committee**

**April 04, 2016**

**1:00 p.m.**

**EBD Board Room – 501 Building, Suite 500**

- I. Call to Order..... Dr. Hank Simmons, Chairman***
- II. Approval of February 1, 2016 Minutes ..... Dr. Hank Simmons, Chairman***
- III. Delivery Coordination Workgroup..... Dr. Geri Bemberg, UAMS***
- IV. 2<sup>nd</sup> Review of Drugs.....Dr. Geri Bemberg, Dr. Jill Johnson, UAMS***
- V. New Drugs.....Dr. Jill Johnson, UAMS***
- VI. Insulin Class Review for Rebate Contracting..... Dr. Rachael McCaleb, UAMS***
- VII. EBD Report ..... Dr. Geri Bemberg, UAMS***

#### ***Upcoming Meetings***

***August 1, 2016***

***November 7, 2016***

***NOTE: All material for this meeting will be available by electronic means only asepse-board@dfa.arkansas.gov***

***Notice: Silence your cell phones. Keep your personal conversations to a minimum. Observe restrictions designating areas as "Members and Staff only"***

**State and Public School Life and Health Insurance Board  
Clinical and Fiscal Drug Utilization and Evaluation Committee Minutes  
April 4, 2016**

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday April 4, 2016 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Little Rock, AR.

**Voting Members present:**

Mike Boyd (Proxy for Larry Dickerson)  
Dr. Kat Neill – Vice-Chairman  
Leonie Declerk (Proxy for Melodee Harris)  
Dr. Hank Simmons Chairman  
Dr. Appathurai Balamurugan  
Dr. John Kirtley

**Non-Voting Members present:**

Dr. Jill Johnson  
Connie Bennett  
Dr. Geri Bemberg

**Members absent:**

Dr. Melodee Harris  
Dr. Scott Pace  
Larry Dickerson  
Dr. William Golden

Lori Eden, Deputy Executive Director, Employee Benefits Division

**OTHERS PRESENT**

David Keisner, UAMS College of Pharmacy; Sherry Bryant, Ethel Whittaker, Janis Harrison, Shay Burleson, EBD; Marc Watts, ASEA; Charlene Kaiser, Amgen; Takisha Sanders, Health Advantage; Mary Abels, AHTD; Jennifer Smith, ASU; Arlene Chan-Mouton, Leah Ramirez, ACHI; Jon McGuire, Eric Brumleve, Cameron James, GSK; Bridgett Johnson, Pfizer; Takisha Sanders, Jessica Akins, Health Advantage; Jim Chapman, ABBVIE; Connie Bennett, Optum Rx; Marck Adkison, Allcare Specialty; Treg Long, ACS; Karyn Langley. Qualchoice; Kelli Heathman, Biogen; Janie Huff, Takeda; Frances Bauman, Nova Nordisk; Sean Teague, Merck; Dr. Creshelle Nash, ABCBS

**CALL TO ORDER**

Meeting was called to order by Dr. Hank Simmons, Chairman.

**APPROVAL OF MINUTES**

The request was made by Dr. Simmons to approve the February 1, 2016 minutes. Dr. Kirtley made the motion to approve. Dr. Neill seconded. All were in favor.

**Minutes Approved.**

## I. Recommended Changes to Current Coverage

### A. Delivery Coordination Workgroup Report: *by Dr. Geri Bemberg, UAMS*

Drugs used in the treatment of cancers and non-cancer drugs were reviewed by the DCWG and a report made to the DUEC on April 4th. Recommendations from this report are outlined below.

	Current Coverage	Proposed Coverage
Pulmonary Hypertension		
Selexipag (Uptravi)	Excluded (New Drug)	T4-PA, QL 2/1
Tadalafil (Adcirca)	Excluded	T4-PA
<u>Multiple Myeloma</u> Carfilzomib (Kyprolis)	Covered, no utilizers	Exclude pharmacy & medical
<u>Basal Cell Carcinoma</u> Vismodegib (Erivedge)	Exclude	Exclude
<u>ALK +Non-Small Cell Lung Cancer</u>		
Crizotinib (Xalkori)	Exclude	T4-PA
Alectinib (Alecensa)	Exclude (New Drug)	Exclude

**Dr. Neill motioned to approve the proposed coverage for section A. Dr. Kirtley seconded. All were in favor.**

**Motion Approved.**

### B. 2nd Review of Drugs *by Drs. Geri Bemberg and Jill Johnson, UAMS*

#### 1. Oral Mesalamine Products:

Brand	Strength/Formula	Cost/Month (UC Maint)	Current 4/4/16 Coverage	Proposed Coverage
Apriso	0.375mg ER Capsule 24 hour Therapy Pack	\$500.40	Excluded	Tier 4
Pentasa	250mg, 500mg Controlled Release Capsule	\$674.40/\$1348.80	Excluded	Tier 4
Delzicol	400mg	\$427.20	Tier 2	Tier 2
Asacol HD	800mg EC Tablet	\$776.70/\$1553.40	Excluded	Excluded
Lialda	1.2g EC Tablet	\$567.26	Excluded	Tier 4

**Dr. Neill motioned to approve the proposed modified coverage for section B, 1. Dr. Kirtley seconded. All were in favor.**

**Motion Approved.**

2. Rifaximin (Xifaxan) – Miscellaneous Antibiotic; FDA Labeled Indications: Traveler’s diarrhea, Irritable bowel syndrome with diarrhea, and Hepatic encephalopathy.

**The committee recommended PA for all indications of Xifaxan, and a move to T4. Currently, it is T3 with 59 utilizers in Q42015. All 59 were using 550mg. PA for IBS-diarrhea would be good for #126/365 days. All utilizers will be lettered and given 90 days notice about the PA requirement.**

**Dr. Neill motioned to approve the recommendations. Dr. Kirtley seconded. All were in favor.**

**Motion Approved.**

3. Pioglitazone (Actos) – Currently, there is a PA on pioglitazone.  
**The committee recommends removing the PA requirement due to an improvement in outcomes when the drug is used after ischemic stroke.**

**Dr. Kirtley motioned to approve the recommendations. Dr. Bala seconded. All were in favor.**

**Motion Approved.**

4. Afatinib (Gilotrif) – **The committee recommended; 1) Adding afatinib (Gilotrif) to coverage for the full labeled indication with T4PA. 2) Continuing exclusion of gefitinib.**

**Dr. Kirtley motioned to approve the recommendations. Dr. Neill seconded. All were in favor.**

**Motion Approved.**

## II. NEW DRUGS

Dr. Johnson reported on new drugs. The review covered products released from October 12, 2015 – January 4, 2016. The Committee’s recommendations follow:

### A. Recommended Additions

#### 1. Specialty medications-proposed additions

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	DUEC VOTE
Upravi tabs	Selexipag tabs	\$17,400/60-1600mcg tabs	Treatment of pulmonary hypertension to delay disease progression and reduce risk of hospitalization.		Cover, T4PA, QL
Zepatier tab 50-100mg	Elbasvir-grazoprevir tab 50-100mg	\$780/tab	Chronic Hepatitis C	All other Hep C treatments T4PA	Cover, T4PA Seek rebate opportunities

### B. Recommended Exclusions

#### 1. Nonspecialty medications-proposed exclusions

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	EXCLUSION CODE
Enstilar Aerosol	Calcipotriene/betamethasone dipropionate foam 0.005%/0.064%	\$997.16/60g (foam)	Psoriasis	Tier1-betamethasone dipropionate cream 0.05% \$81/45gm. Calcipotriene cream 0.005%/\$840/120gm	Exclude, use each product separately
Dyanavel XR	Amphetamine extended release suspension 2.5mg/ml	\$1094.998/454ml (\$2,35991/ml)	ADHD	Extended release amphetamine products tiered for children, Reference prices to \$2.50/unit	Exclude code 13
Quillichew ER	Methylphenidate HCl Chew Tab Extended Release 20mg, 30mg, 40mg	\$10.80/tablet	ADHD	Extended release amphetamine products tiered for children. Reference priced to \$2.50/unit	Excluded, code 13

## 2. Specialty Medications – proposed exclusions

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	EXCLUSION CODE
Viberzi Tabs	Eluxadine	\$1,152/60-100mg tabs. Dose=200mg/day	Treatment of irritable bowel syndrome wit diarrhea		Exclude code 13

Dr. Neill motioned to approve the recommendations for nonspecialty exclusions. Dr. Kirtley seconded. All were in favor.  
Motion approved.

Dr. Kirtley motioned to approve the recommendations for Specialty drugs and exclusions. Dr. Bala seconded. All were in favor.  
Motion approved.

### **III. Insulin Class Review for Rebate Contracting: *By Dr. Rachael McCaleb, UAMS***

Dr. McCaleb reported that insulin products are Food and Drug Administration (FDA) approved to improve glycemic control in patients with type I diabetes mellitus and summarized the available insulin products below.

<u>Generic Name</u>	<u>Trade Name/Manufacturer</u>	<u>Vial</u>	<u>Prefilled Disposable Pen</u>
<b><u>Rapid-acting insulins</u></b>			
Insulin lispro	HumaLOG/Lilly	Yes	Yes
Insulin aspart	NovoLOG/ Novo Nordisk Inc	Yes	Yes
Insulin glulisine	Apidra/Sanoi Avnetis US	Yes	Yes
<b><u>Short-acting insulin</u></b>			
Insulin regular	NovoLIN/ Novo Nordisk Inc HumuLIN/Lilly	Yes	No
<b><u>Intermediate-acting insulin</u></b>			
Insulin NPH (isophane suspension)	NovoLIN/ Novo Nordisk Inc HumuLIN/Lilly	Yes	Yes
<b><u>Long-acting insulins</u></b>			
Insulin glargine	Lantus/Sanoi Avnetis US Toujeo/Sanoi Avnetis US	Yes No	Yes Yes
Insulin detemir	Levemir/Novo Nordisk Inc	Yes	Yes
Insulin degludec	Tresiba/Novo Nordisk Inc	No	Yes
<b><u>Combination Products</u></b>			
Insulin degludec/insulin aspart	Ryzodeg 70/30 Novo Nordisk Inc	No	Yes
Insulin aspart protamine suspension/insulin aspart	NovoLOG Mix 70/30 Novo Nordisk Inc	Yes	Yes
Insulin lispro protamine/insulin lispro	HumaLOG Mix 75/25/Lilly HumaLOG Mix 50/50/Lilly	Yes	Yes
Insulin NPH suspension/insulin regular solution	NovoLIN 70/30 Novo Nordisk Inc HumuLIN 70/30/Lilly	Yes	Yes (HumuLIN only)

Dr. McCaleb recommended:

- Maintain Humulin or Novolin as preferred but move to T1 copay
  - o Coverage for vials and pens
- Include one rapid-acting and one long-acting insulin analogue as preferred as a T2 copay
  - o Coverage for vials and pens
  - o Remaining rapid-acting and long-acting insulin analogues will be excluded from plan
  - o All current members on an excluded analogue will NOT be grandfathered and will be given a 90 day grace period following the implementation of the contract to switch to a preferred analogue
- Required price protection for the life of the contract

**Dr. Kirtley motioned to accept the recommendations as presented. Dr. Bala seconded. All were in favor.**

**Motion approved.**

#### **IV. EBD REPORT: *by Dr. Geri Bemberg, UAMS***

Dr. Bemberg requested the committee to suggest new drugs for possible rebates. She also reported the plan is currently working on TIMs, Hepatitis C agents, and Insulins. Dr. Kirtley recommended inhalers for rebate.

Dr. Bemberg reported that the new pharmacy vendor, MedImpact will begin service July 1, 2016. Members will have minimum disruption and new cards will not be issued. The mail order members will be notified and assistance will be provided for the transfer process. There are less than 50 members affected by this change.

Currently, some members are using Briova Rx as their specialty pharmacy. Those members will be required to switch to a new pharmacy, as Briova will no longer be in-network since it is owned by Catamaran/Optum. No more than a one-month supply for specialty drugs and mail order drugs will be issued. There are 450 members affected by this change.

Dr. Bennett recommended communicating with those Pharmacies that are in the plan's network regarding the new Pharmacy Benefit Manager. Dr. Bemberg reported that those discussions had already taken place with the new PBM and that decisions have been made about when to notify pharmacies.

**Dr. Kirtley motioned to adjourn. Dr. Neill seconded. All were in favor.**

**Meeting adjourned.**

**\*New Drug Code Key:**

1	Lacks meaningful clinical endpoint data; has shown efficacy for surrogate endpoints only.
2	Drug's best support is from single arm trial data
3	No information in recognized information sources (PubMed or Drug Facts & Comparisons or Lexicomp)
4	<b>Convenience Kit Policy</b> - As new drugs are released to the market through Medispan, those drugs described as "kits will not be considered for inclusion in the plan and will therefore be excluded products unless the product is available solely as a kit. Kits typically contain, in addition to a pre-packaged quantity of the featured drug(s), items that may be associated with the administration of the drug (rubber gloves, sponges, etc.) and/or additional convenience items (lotion, skin cleanser, etc.). In most cases, the cost of the "kit" is greater than the individual items purchased separately.
5	<b>Medical Food Policy</b> - Medical foods will be excluded from the plan unless two sources of peer-reviewed, published medical literature supports the use in reducing a medically necessary clinical endpoint. A medical food is defined below: A medical food, as defined in section 5(b)(3) of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)), is "a food which is formulated to be consumed or administered eternally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." FDA considers the statutory definition of medical foods to narrowly constrain the types of products that fit within this category of food. Medical foods are distinguished from the broader category of foods for special dietary use and from foods that make health claims by the requirement that medical foods be intended to meet distinctive nutritional requirements of a disease or condition, used under medical supervision, and intended for the specific dietary management of a disease or condition. Medical foods are not those simply recommended by a physician as part of an overall diet to manage the symptoms or reduce the risk of a disease or condition, and all foods fed to sick patients are not medical foods. Instead, medical foods are foods that are specially formulated and processed (as opposed to a naturally occurring foodstuff used in a natural state) for a patient who is seriously ill or who requires use of the product as a major component of a disease or condition's specific dietary management.
6	<b>Cough &amp; Cold Policy</b> - As new cough and cold products enter the market, they are often simply re-formulations or new combinations of existing products already in the marketplace. Many of these existing products are available in generic form and are relatively inexpensive. The new cough and cold products are branded products and are generally considerably more expensive than existing products. The policy of the ASE/PSE prescription drug program will be to default all new cough and cold products to "excluded" unless the DUEC determines the product offers a distinct advantage over existing products. If so determined, the product will be reviewed at the next regularly scheduled DUEC meeting.
7	<b>Multivitamin Policy</b> - As new vitamin products enter the market, they are often simply re-formulations or new combinations of vitamins/multivitamins in similar amounts already in the marketplace. Many of these existing products are available in generic form and are relatively inexpensive. The new vitamins are branded products and are generally considerably more expensive than existing products. The policy of the ASE/PSE prescription drug program will be to default all new vitamin/multivitamin products to "excluded" unless the DUEC determines the product offers a distinct advantage over existing products. If so determined, the product will be reviewed at the next regularly scheduled DUEC meeting.
8	Drug has limited medical benefit &/or lack of overall survival data or has overall survival data showing minimal benefit
9	Not medically necessary
10	Peer -reviewed, published cost effectiveness studies support the drug lacks value to the plan.
11	<b>Oral Contraceptives Policy</b> - OCs which are new to the market may be covered by the plan with a zero dollar, tier 1, 2, or 3 copay, or may be excluded. If a new-to-market OC provides an alternative product not similarly achieved by other OCs currently covered by the plan, the DUEC will consider it as a new drug. IF the drug does not offer a novel alternative or offers only the advantage of convenience, it may not be considered for inclusion in the plan.
12	Other

13	Insufficient clinical benefit OR alternative agent(s) available
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**Delivery Coordination Workgroup Report**

Members

Geri Bemberg, PharmD – EBRx  
 David Keisner, PharmD – EBRx  
 Jill Johnson, PharmD – EBRx  
 Andrew Mullings-Lewis, PharmD – EBRx Managed Care Resident  
 Henry Simmons, MD, PhD – Medical Director Arkansas Poison Control  
 Sidney Keisner, PharmD – Board Certified Oncology Pharmacist, VA Little Rock  
 Kati Beth Lewis, PharmD – Clinical Pharmacist BCBS/Wendy See, PharmD  
 Stephen Sorsby, MD – Medical Director, Qualchoice/Barry Fielder, PharmD

	<u>Current Coverage</u>	<u>Proposed Coverage</u>
<u>Pulmonary Hypertension</u>		
Selexipag (Uptravi)	Excluded (New Drug)	T4 PA, QL 2/1
Tadalafil (Adcirca)	Excluded	T4 PA
<u>Multiple Myeloma</u>		
Carfilzomib (Kyprolis)	Covered, no utilizers	Exclude pharmacy & medical
<u>Basal Cell Carcinoma</u>		
Vismodegib (Erivedge)	Exclude	Exclude
<u>ALK+ Non-Small Cell Lung Cancer</u>		
Crizotinib (Xalkori)	Exclude	T4PA
Alectinib (Alecensa)	Excluded (New Drug)	Exclude

**Oral Mesalamine Products**

Brand	Strength/ Formulation	Dosing*						Area of the GI Tract	Cost/ Month (UC Maint)	Current 4/4/16 Coverage	Proposed Coverage
		UC Active	UC Maint	Crohn's Active	Crohn's Maint	Crohn's ileitis Active	Crohn's ileitis Maint				
Apriso	0.375mg ER Capsule 24 Hour Therapy Pack	1.5-3g	1.5g	ID	ID	ID	ID	Release occurs at pH ≥6, then prolonged throughout colon	\$500.40	Excluded	Tier 3
Pentasa	250mg, 500mg Controlled Release Capsule	4g	2-4g	4g	2-4g	4g	2-4g	Prolonged release throughout duodenum, jejunum, ileum, & colon. 50% released in small bowel	\$674.40 - 1348.80	Excluded	Tier 4
Delzicol	400mg Delayed Release Capsule	1.2- 2.4g	1.6g					Release occurs in the terminal ileum & beyond	\$427.20	Tier 2	Tier 2
Asacol HD	800mg EC Tablet	2.4- 4.8g	2.4- 4.8g	2.4-4.8g	2.4- 4.8g	2.4-4.8g	2.4- 4.8g	Release is delayed until terminal ileum & cecum, then releases as bolus in right colon.	\$776.70 - 1553.40	Excluded	Excluded
Lialda	1.2g EC Tablet	2.4- 4.8g	2.4g	ID	ID	ID	ID	Release is delayed until terminal ileum, then designed to release throughout colon, including sigmoid colon & rectum.	\$567.26	Excluded	Tier 3

\* Dosing from Up to Date, ID: Insufficient data; Maint: maintenance

**References:**

1. Steinhart AH, Forbes A, Mills EC, et al. Systematic Review: the potential influence of mesalazine formulation on maintenance of remission in Crohn's disease. *Ailment Pharmacol Ther* 25,13989-1399.
2. Aminosaliclylate derivative dosages for active disease and remission maintenance in ulcerative colitis and Crohn's disease. Up to Date 2014.
3. PL Detail-Document, Treatments for Ulcerative Colitis. Pharmacist's Letter/Prescriber's Letter. March 2013.

**Rifaximin (Xifaxan)**  
**200mg & 550mg tablets**  
Miscellaneous Antibiotic

**FDA Labeled Indications:**

- \* Traveler’s diarrhea
- \* Hepatic encephalopathy
- \* Irritable bowel syndrome with diarrhea (IBS-D) (May 2015 Indication)

	Traveler’s Diarrhea	Hepatic Encephalopathy*	Irritable Bowel Syndrome-Diarrhea
<b>Strength</b>	200mg	550mg	550mg
<b>Dose</b>	200mg TID	550mg BID	550mg TID
<b>Duration of Treatment</b>	3 days	Indefinitely	14 days, may be retreated 2 times
<b>Price/month or treatment</b>	\$173.05	\$2,199.01 (Bottle of 60)	\$1,539.31 (Bottle of 42)

\*Dosing for reduction of overt hepatic encephalopathy recurrence.

Date	Cost/Unit	Time Since Last Increase	Percent Increase
4/26/2010	\$22.40400		
3/31/2011	\$23.52417	11 months	5%
5/17/2012	\$24.70033	13.5 months	5%
5/10/2013	\$26.42933	12 months	7%
6/3/2014	\$28.28400	13 months	7.02%
1/31/2015	\$30.84000	7 months	9.04%
3/25/2015	\$33.62400	2 months	9.03%
1/15/2016	\$36.65017	9 months	9%

Valeant acquired Salix Pharmaceuticals, the manufacturer of Xifaxan, on April 1, 2015 for \$11 billion.

**Evidence**

*Pimentel M, Lembo A, Chey WD, et al. Rifaximin Therapy for Patients with Irritable Bowel Syndrome without Constipation. N Engl J Med 2011;364:22-32.*

Two identical phase 3, DB, PC trials (TARGET 1 & TARGET 2) in patients w/ IBS w/o constipation. Eligible patients: at least 18 yrs old, had a colonoscopy within the prev 2 yrs, had a dx of & current sx of IBS-D (as defined by Rome II criteria) in particular sx of abdominal pain & discomfort; did not have adequate relief of global IBS sx & of IBS-related bloating at both the time of screening & the time of randomization. Patients were allowed to take antidepressant agents of the SSRI & TCA classes, provided that they had been taking a stable dose for at least 6 weeks.

Pts were assigned to either Rifaximin 550mg TID x 14 days or placebo, and were followed for an additional 10 wks. The primary end point was the proportion of pts who had adequate relief of global IBS sx for at least 2 of the 4 weeks (threshold for clinical relevance) during primary evaluation period. Endpoint was determined by responding yes or no to: “In regard to all your symptoms of IBS, as

compared with the way you felt before you started the study medication, have you, in the past 7 days, had adequate relief of your IBS symptoms?”. Secondary endpoints included the proportion of patients who had adequate relief of IBS-related bloating during the primary eval period, the proportion of patients who had relief of IBS symptoms, and the consistency of stool.

1260 patients were randomized, 623 in TARGET 1 and 637 in TARGET 2. At baseline, patients had an avg daily score of  $3.4 \pm 0.7$  for global IBS symptoms and  $3.3 \pm 0.8$  for IBS-related bloating on a scale from 0 to 6, with 0 = not at all and 6 = a very great deal. For the primary endpoint, adequate relief of global IBS sx for at least 2 of the 1<sup>st</sup> 4 weeks after tx, the results were: 40.8% vs. 31.2%, P=0.01 in TARGET 1, 40.6% vs. 32.2%, P=0.03 in TARGET 2, and 40.7% vs 31.7%, P >0.001 in the two studies combined.

*Li J, Zhu W, Liu W, et al. Rifaximin for Irritable Bowel Syndrome A Meta-Analysis of Randomized Placebo-Controlled Trials. Medicine 95(4):e2534. January 2016.*

A meta-analysis of studies of Rifaximin treatment for IBS was performed. 108 original studies were identified, and utilizing pre-specified inclusion and exclusion criteria, 4 eligible studies were identified, which included 1803 participants ranging in age from 18 to 45.

The primary outcome was the overall relief of IBS sx. The fixed effects model showed that at the end of the treatment period, the remission of overall IBS sx was significantly greater in patients treated with Rifaximin. OR = 1.19, 95% CI: 1.08-1.32. There was no difference in adverse effects between Rifaximin and placebo.

#### **Recommendation:**

PA all indications of Xifaxan, and move to T4. Currently T3 with 59 utilizers in Q42015. All 59 were using 550mg. PA for IBS-D would include: 1) Dx of IBS-D 2) At least 18 years of age 3) Tried and failed 60 days (each) of: dietary modifications (FODMAP diet), loperamide, bile acid sequestrants, antispasmodics (hyoscyamine, dicyclomine), and tricyclic antidepressants. PA would be good for **#126/365 days**.

- a) “Modified grandfathering” – grandfather everyone using Xifaxan for 6 months
- b) “Indication-specific grandfathering” – grandfather those getting qty #42 for 90 days, and those getting qty #60 for 6 months – 1 year.

**Delivery Coordination Workgroup Report**

Members

- Geri Bemberg, PharmD – EBRx
- David Keisner, PharmD – EBRx
- Jill Johnson, PharmD – EBRx
- Andrew Mullings-Lewis, PharmD – EBRx Managed Care Resident
- Henry Simmons, MD, PhD – Medical Director Arkansas Poison Control
- Sidney Keisner, PharmD – Board Certified Oncology Pharmacist, VA Little Rock
- Kati Beth Lewis, PharmD – Clinical Pharmacist BCBS/Wendy See, PharmD
- Stephen Sorsby, MD – Medical Director, Quaichoice/Barry Fielder, PharmD

	<u>Current Coverage</u>	<u>Proposed Coverage</u>
<u>Pulmonary Hypertension</u>		
Selexipag (Uptravi)	Excluded (New Drug)	T4 PA, QL 2/1
Tadalafil (Adcirca)	Excluded	T4 PA
<u>Multiple Myeloma</u>		
Carfilzomib (Kyprolis)	Covered, no utilizers	Exclude pharmacy & medical
<u>Basal Cell Carcinoma</u>		
Vismodegib (Erivedge)	Exclude	Exclude
<u>ALK+ Non-Small Cell Lung Cancer</u>		
Crizotinib (Xalkori)	Exclude	T4PA
Alectinib (Alecensa)	Excluded (New Drug)	Exclude

## Pioglitazone (Actos)

Jill Johnson, Pharm.D.

4/4/16

Currently: We have a PA on pioglitazone.

1. Patient must have the diagnosis of type 2 diabetes mellitus.
2. Patient must have a documented HbA1C in the previous 3 months >7.0%.
3. Patient must be receiving metformin at 1000mg twice daily<sup>b</sup> (or near the max dose; not just the starting dose) for the past 4 of 5 months. Pharmacist must look back to be sure this occurred. OR the patient must have a contraindication to metformin that must be documented by the pharmacist.
4. Patients with a metformin contraindication must be taking a sulfonylurea for previous 4 of 5 months.
5. Pioglitazone should be denied if it is being used as monotherapy.<sup>a</sup>

<sup>a</sup>This allows access to pioglitazone prior to requiring basal insulin as the guidelines suggest. Use of pioglitazone is considered a less well-validated therapy than basal insulin.

<sup>b</sup>Metformin must be taken at the maximally tolerated dose. Metformin use without titrating the dose slowly upwards is known to cause gastrointestinal side effects. Metformin 500mg twice daily is a starting dose. Many will require 1000mg twice daily.

### PROPOSAL: Remove PA requirement due to both reasons below.

1. Kernan, Walter N., et al. "Pioglitazone after ischemic stroke or transient ischemic attack." *New England Journal of Medicine* (2016).

This MC, DB trial that randomized 3876 patients who had had recent ischemic stroke or TIA to either pioglitazone or placebo. Eligible pts did not have diabetes but did have insulin resistance on the basis of a score of more than 3 on the homeostasis model assessment of insulin resistance index. The 1<sup>st</sup> endpt was fatal or NF stroke or MI. Results:

Outcome	Pioglitazone (N=1939) no. of patients (%)	Placebo (N=1937) no. of patients (%)	Hazard Ratio (95% CI) <sup>a</sup>	Adjusted P Value <sup>†</sup>
<b>Primary outcome</b>				
Stroke or myocardial infarction <sup>‡</sup>	175 (9.0)	228 (11.8)	0.76 (0.62–0.93)	0.007
Stroke	123 (6.3)	150 (7.7)		
Fatal	9 (0.5)	13 (0.7)		
Nonfatal	114 (5.9)	137 (7.1)		
Myocardial infarction	52 (2.7)	78 (4.0)		
Fatal	7 (0.4)	14 (0.7)		
Nonfatal	45 (2.3)	64 (3.3)		
<b>Secondary outcome<sup>§</sup></b>				
Stroke	127 (6.5)	154 (8.0)	0.82 (0.61–1.10)	0.19
Acute coronary syndrome: myocardial infarction or unstable angina	96 (5.0)	128 (6.6)	0.75 (0.52–1.07)	0.11
Stroke, myocardial infarction, or serious heart failure <sup>¶</sup>	206 (10.6)	249 (12.9)	0.82 (0.65–1.05)	0.11
Diabetes mellitus	73 (3.8)	149 (7.7)	0.48 (0.33–0.69)	<0.001
Death from any cause	136 (7.0)	146 (7.5)	0.93 (0.73–1.17)	0.52

2. Pioglitazone is a MACd medication.

<sup>a</sup> Hazard ratios were calculated by means of a Cox regression model with corresponding 95% confidence intervals. The confidence interval for the primary outcome was adjusted for interim monitoring; confidence intervals for the secondary outcomes were adjusted for multiple comparisons.

<sup>†</sup> The P value for the primary outcome was adjusted for interim monitoring. P values for the five secondary outcomes were adjusted for multiple comparisons by the Hochberg procedure using an overall familywise type I error of 5%.

<sup>‡</sup> Only the first event, stroke or myocardial infarction, was counted for each patient.

<sup>§</sup> In the composite categories, only the first event was counted for each patient (e.g., a patient with myocardial infarction followed by unstable angina would be counted only as having a myocardial infarction in the category for acute coronary syndrome). More strokes are listed as occurring as a secondary outcome than a primary outcome because the secondary outcome included strokes occurring after myocardial infarction.

<sup>¶</sup> Serious heart failure was defined as an episode resulting in hospitalization or death.

**Afatinib (Gilotrif)**  
**Andrew Mullings, PharmD**  
**2/24/2016**

**Current Coverage:** Erlotinib is currently covered with a PA for EGFR mutations. Afatinib and gefitinib are currently excluded.

**Policy Change Recommendation:**

- Add afatinib to coverage for the full labeled indication.

**Non-small cell lung cancer, metastatic:** First-line treatment of metastatic non-small cell lung cancer (NSCLC) in patients whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an approved test.

**Limitations of use:** Safety and efficacy have not been established in patients whose tumors express EGFR mutations other than exon 19 deletion or exon 21 (L858R) substitution.

- Continue exclusion of gefitinib.

**FDA approval:** 1<sup>st</sup> line treatment of metastatic NSCLC in pts whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an approved test.

**Limitations of use:** Safety and efficacy have not been established in pts whose tumors express EGFR mutations other than exon 19 deletion or exon 21 (L858R) substitution.

*Kuan, Feng-Che, et al. "Overall survival (OS) benefits of first-line EGFR tyrosine kinase inhibitors in EGFR-mutated non-small-cell lung cancers: a systematic review and meta-analysis." British journal of cancer (2015).*

**Design:** Systematic review and meta-analysis of RCTs comparing TKIs with conventional chemotherapy was performed. Eight trials of 1498 pts and five trials of 1279 pts w/ either exon 19 deletions or L858R were included.

**Results:** TKI treatment demonstrated PFS benefit in pts w/ exon 19 deletions (HR 0.27, 95%CI 0.21–0.35) and L858R (HR 0.45, 95% CI: 0.35–0.58). **Pts w/ exon 19 deletions had significant OS benefit w/ TKI.** (HR 0.72, 95% CI: 0.60–0.88).

**Subgroup analyses showed that irreversible TKIs, but not reversible TKIs, had statistically significant OS benefit in these pts (irreversible TKIs, HR: 0.59, 95% CI: 0.47–0.73; reversible TKIs, HR: 0.84, 95% CI: 0.69–1.02). Pts w/ L858R demonstrated no OS benefit under first-line TKI use (HR: 1.15, 95% CI: 0.95–1.39).**

**Discussion Points:** The OS in the meta-analysis above is confounded by the high proportion of pts crossing over to the alternative treatment and was underpowered for assessment of such effect. 39%–95% of the pts allocated to CTX arms of the phase III trials for gefitinib or erlotinib were crossed over to either gefitinib or erlotinib<sup>6-8</sup>. 53%–74% of the pts allocated to CTX arms of the phase III trials for afatinib were crossed over to a TKI<sup>9</sup>. It is also important to consider that all three of these agents are associated with either an increase in QoL or decreased rate of severe toxicities compared to standard CTX<sup>10</sup>. Additionally, EGFR TKI maintenance therapy improves OS and PFS in unselected metastatic NSCLC patients. A larger benefit is observed, however, in EGFR mut patients<sup>1</sup>

**Data suggesting superiority of afatinib to gefitinib exists concerning outcomes of PFS. Data for overall survival for gefitinib, as with the other TKIs, did not demonstrate a survival benefit but is likely secondary to high rates of crossover in the trial<sup>11</sup>. Data has failed to demonstrate superiority of erlotinib to gefitinib in terms of PFS and OS<sup>12-13</sup>. Data In the open-label study, the 18-month PFS rates were 27% versus 15%, for afatinib and gefitinib, respectively. At 24 months, 18% of those in the afatinib arm remained alive and progression-free compared with 8% in the gefitinib group. The time to treatment failure was 13.7 versus 11.5 months and the objective response rates were 70% compared with 56% for afatinib and gefitinib, respectively (P = .0083). Serious AEs-related to treatment were more frequent with**

afatinib (10.6%) versus gefitinib (4.4%). AEs resulting in dose reductions occurred in 41.9% of patients treated with afatinib versus 1.9% with gefitinib; however, treatment discontinuation due to AEs was the same in each arm, at 6.3%.<sup>2-3</sup>

Agent	Type TKI	Cost of a 1 Month Supply
Afatinib 40mg	IRReversible	\$8389.68
Erlotinib 150mg	Reversible	\$8694.85
Gefitinib 250mg	Reversible	\$8683.20

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Oral Mesalamine Products

Brand	Strength/ Formulation	Dosing*						Area of the GI Tract	Cost/ Month (UC Maint)	Current 4/4/16 Coverage	Proposed Coverage
		UC Active	UC Maint	Crohn's Active	Crohn's Maint	Crohn's ileitis Active	Crohn's ileitis Maint				
Apriso	0.375mg ER Capsule 24 Hour Therapy Pack	1.5-3g	1.5g	ID	ID	ID	ID	Release occurs at pH ≥6, then prolonged throughout colon	\$500.40	Excluded	Tier 3
Pentasa	250mg, 500mg Controlled Release Capsule	4g	2-4g	4g	2-4g	4g	2-4g	Prolonged release throughout duodenum, jejunum, ileum, & colon. 50% released in small bowel	\$674.40 - 1348.80	Excluded	Tier 4
Delzicol	400mg Delayed Release Capsule	1.2- 2.4g	1.6g					Release occurs in the terminal ileum & beyond	\$427.20	Tier 2	Tier 2
Asacol HD	800mg EC Tablet	2.4- 4.8g	2.4- 4.8g	2.4-4.8g	2.4- 4.8g	2.4-4.8g	2.4- 4.8g	Release is delayed until terminal ileum & cecum, then releases as bolus in right colon.	\$776.70 - 1553.40	Excluded	Excluded
Lialda	1.2g EC Tablet	2.4- 4.8g	2.4g	ID	ID	ID	ID	Release is delayed until terminal ileum, then designed to release throughout colon, including sigmoid colon & rectum.	\$567.26	Excluded	Tier 3

\* Dosing from Up to Date, ID: Insufficient data; Maint: maintenance

**References:**

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**Rifaximin (Xifaxan)**  
**200mg & 550mg tablets**  
Miscellaneous Antibiotic

**FDA Labeled Indications:**

- \* Traveler's diarrhea
- \* Hepatic encephalopathy
- \* Irritable bowel syndrome with diarrhea (IBS-D) (May 2015 Indication)

	Traveler's Diarrhea	Hepatic Encephalopathy*	Irritable Bowel Syndrome-Diarrhea
<b>Strength</b>	200mg	550mg	550mg
<b>Dose</b>	200mg TID	550mg BID	550mg TID
<b>Duration of Treatment</b>	3 days	Indefinitely	14 days, may be retreated 2 times
<b>Price/month or treatment</b>	\$173.05	\$2,199.01 (Bottle of 60)	\$1,539.31 (Bottle of 42)

\*Dosing for reduction of overt hepatic encephalopathy recurrence.

Date	Cost/Unit	Time Since Last Increase	Percent Increase
4/26/2010	\$22.40400		
3/31/2011	\$23.52417	11 months	5%
5/17/2012	\$24.70033	13.5 months	5%
5/10/2013	\$26.42933	12 months	7%
6/3/2014	\$28.28400	13 months	7.02%
1/31/2015	\$30.84000	7 months	9.04%
3/25/2015	\$33.62400	2 months	9.03%
1/15/2016	\$36.65017	9 months	9%

Valeant acquired Salix Pharmaceuticals, the manufacturer of Xifaxan, on April 1, 2015 for \$11 billion.

**Evidence**

*Pimentel M, Lembo A, Chey WD, et al. Rifaximin Therapy for Patients with Irritable Bowel Syndrome without Constipation. N Engl J Med 2011;364:22-32.*

Two identical phase 3, DB, PC trials (TARGET 1 & TARGET 2) in patients w/ IBS w/o constipation. Eligible patients: at least 18 yrs old, had a colonoscopy within the prev 2 yrs, had a dx of & current sx of IBS-D (as defined by Rome II criteria) in particular sx of abdominal pain & discomfort; did not have adequate relief of global IBS sx & of IBS-related bloating at both the time of screening & the time of randomization.

Patients were allowed to take antidepressant agents of the SSRI & TCA classes, provided that they had been taking a stable dose for at least 6 weeks.

Pts were assigned to either Rifaximin 550mg TID x 14 days or placebo, and were followed for an additional 10 wks. The primary end point was the proportion of pts who had adequate relief of global IBS sx for at least 2 of the 4 weeks (threshold for clinical relevance) during primary evaluation period. Endpoint was determined by responding yes or no to: "In regard to all your symptoms of IBS, as

compared with the way you felt before you started the study medication, have you, in the past 7 days, had adequate relief of your IBS symptoms?”. Secondary endpoints included the proportion of patients who had adequate relief of IBS-related bloating during the primary eval period, the proportion of patients who had relief of IBS symptoms, and the consistency of stool.

1260 patients were randomized, 623 in TARGET 1 and 637 in TARGET 2. At baseline, patients had an avg daily score of  $3.4 \pm 0.7$  for global IBS symptoms and  $3.3 \pm 0.8$  for IBS-related bloating on a scale from 0 to 6, with 0 = not at all and 6 = a very great deal. For the primary endpoint, adequate relief of global IBS sx for at least 2 of the 1<sup>st</sup> 4 weeks after tx, the results were: 40.8% vs. 31.2%, P=0.01 in TARGET 1, 40.6% vs. 32.2%, P=0.03 in TARGET 2, and 40.7% vs 31.7%, P >0.001 in the two studies combined.

*Li J, Zhu W, Liu W, et al. Rifaximin for Irritable Bowel Syndrome A Meta-Analysis of Randomized Placebo-Controlled Trials. Medicine 95(4):e2534. January 2016.*

A meta-analysis of studies of Rifaximin treatment for IBS was performed. 108 original studies were identified, and utilizing pre-specified inclusion and exclusion criteria, 4 eligible studies were identified, which included 1803 participants ranging in age from 18 to 45.

The primary outcome was the overall relief of IBS sx. The fixed effects model showed that at the end of the treatment period, the remission of overall IBS sx was significantly greater in patients treated with Rifaximin. OR = 1.19, 95% CI: 1.08-1.32. There was no difference in adverse effects between Rifaximin and placebo.

**Recommendation:**

PA all indications of Xifaxan, and move to T4. Currently T3 with 59 utilizers in Q42015. All 59 were using 550mg. PA for IBS-D would include: 1) Dx of IBS-D 2) At least 18 years of age 3) Tried and failed 60 days (each) of: dietary modifications (FODMAP diet), loperamide, bile acid sequestrants, antispasmodics (hyoscyamine, dicyclomine), and tricyclic antidepressants. PA would be good for #126/365 days.

- a) “Modified grandfathering” – grandfather everyone using Xifaxan for 6 months
- b) “Indication-specific grandfathering” – grandfather those getting qty #42 for 90 days, and those getting qty #60 for 6 months – 1 year.

DUEC  
Jan 11-Jan25, 2016

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	Jill's NOTES	DUEC VOTE	DUEC DATE	IB VOTE	IB DATE
<b>NON-SPECIALTY DRUGS</b>									
Enstilar Aerosol	calcipotriene/betamethasone dipropionate foam 0.005%/0.064%	\$997.16/60g (foam)	Psoriasis	Tier 1 - betamethasone dipropionate cream 0.05% \$81/45gm. Calcipotriene cream 0.005% \$840/120gm	Exclude, use each product separately		2016 04 04		2016 04 19
Dyanavel XR	amphetamine extended release suspension 2.5 mg/mL	\$1094.998/454mL (\$2.35991/mL)	ADHD	Extended release amphetamine products tiered for children, Reference priced to 2.50/unit	Exclude, code 13		2016 04 04		2016 04 19
Quillichew ER	Methylphenidate HCl Chew Tab Extended Release 20mg, 30mg, 40mg	\$10.80/tablet	ADHD	Extended release amphetamine products tiered for children, Reference priced to 2.50/unit	Exclude, code 13		2016 04 04		2016 04 19
<b>SPECIALTY DRUGS</b>									
Viberzi tabs	eluxadoline	\$1,152/60-100mg tabs. Dose=200mg/day	Treatment of irritable bowel syndrome with diarrhea		Exclude, code 13		2016 04 04		2016 04 19
Upravi tabs	selexipag tabs	\$17,400/60 - 1600mcg tabs	Treatment of pulmonary hypertension to delay disease progression and reduce risk of hospitalization.		Jill. Cover, PA, QL		2016 04 04		2016 04 19
Zepatier tab 50-100mg	Elbasvir-grazoprevir tab 50-100mg	\$780/tab	Chronic Hepatitis C	All other Hep C treatments T4PA	Cover. PA		2016 04 04		2016 04 19

**Therapeutic Class: Insulins**  
 Rachael McCaleb, PharmD  
 April 2016

Insulin products are Food and Drug Administration (FDA) approved to improve glycemic control in patients with diabetes mellitus (DM) type 1 and 2. Available insulin products are summarized in Table 1.

Generic Name	Trade Name/ Manufacturer	Vial	Prefilled Disposable Pen
<b>Rapid-acting insulins</b>			
insulin lispro	HumaLOG <sup>®</sup> / Lilly	Yes	Yes
insulin aspart	NovoLOG <sup>®</sup> / Novo Nordisk Inc	Yes	Yes
insulin glulisine	Apidra <sup>®</sup> / Sanoi Avnetis US	Yes	Yes
<b>Short-acting insulin</b>			
insulin regular	NovoLIN <sup>®</sup> / Novo Nordisk Inc HumuLIN <sup>®</sup> / Lilly	Yes	No
<b>Intermediate-acting insulins</b>			
insulin NPH (isophane suspension)	NovoLIN N <sup>®</sup> / Novo Nordisk Inc HumuLIN N <sup>®</sup> / Lilly	Yes	Yes
<b>Long-acting insulins</b>			
insulin glargine	Lantus <sup>®</sup> / Sanoi Avnetis US	Yes	Yes
	Toujeo <sup>®</sup> / Sanoi Avnetis US	No	Yes
insulin detemir	Levemir <sup>®</sup> / Novo Nordisk Inc	Yes	Yes
insulin degludec	Tresiba <sup>®</sup> / Novo Nordisk Inc	No	Yes
<b>Combination Products</b>			
insulin degludec/insulin aspart	Ryzodeg <sup>®</sup> 70/30/ Novo Nordisk Inc	No	Yes
Insulin aspart protamine suspension/insulin aspart	NovoLOG <sup>®</sup> Mix 70/30/ Novo Nordisk Inc	Yes	Yes
Insulin lispro protamine/insulin lispro	HumaLOG <sup>®</sup> Mix 75/25/ Lilly	Yes	Yes
	HumaLOG <sup>®</sup> Mix 50/50/ Lilly		
Insulin NPH suspension/insulin regular solution	NovoLIN <sup>®</sup> 70/30/ Novo Nordisk Inc HumuLIN <sup>®</sup> 70/30/ Lilly	Yes	Yes (HumuLIN only)

Table 1

NPH=neutral protamine Hagedorn

## Summary of Evidence:

### TYPE 1 DIABETES: Rapid vs Short Acting

- For type 1 diabetes, clinical evidence indicates that insulin glulisine and aspart cause a minimally significantly greater reduction in from baseline compared to regular insulin. *The difference in HbA<sub>1c</sub> was never greater than 0.5% in any clinical trial, with most trials having a modest difference around 0.15%.* Whereas, insulin lispro was indicated to have a similar effect on the reduction in HbA<sub>1c</sub> from baseline compared to regular insulin. Additionally, insulin lispro and aspart resulted in minimally significantly lower post-prandial blood glucose levels compared to regular insulin. *The difference in post-prandial blood glucose levels was never greater than 35 mg/dL with both groups (rapid-acting insulin and regular insulin) meeting the ADA guideline recommended post-prandial blood glucose level of less than 180 mg/dL.*
  - One head-to-head study in pediatric patients of insulin glulisine compared to insulin lispro indicated that significantly more patients using insulin glulisine (38.4%) were able to achieve ADA age-specific recommendations for HbA<sub>1c</sub> compared to insulin lispro (32%).
  - One head-to-head study in pediatric patients of insulin aspart compared to insulin lispro indicated that significantly more patients using insulin aspart (59.7%) were able to achieve ADA age-specific recommendations for HbA<sub>1c</sub> compared to insulin lispro (43.8%).
  - Rates of symptomatic hypoglycemia events were comparable between the rapid-acting insulins and regular insulin. However, there is weak evidence that insulin glulisine resulted in significantly more hypoglycemia episodes compared to insulin aspart and lispro. *One study showed an increase rate of about 10 per patient-year with insulin glulisine compared to insulin aspart and lispro.*

### TYPE 2 DIABETES: Rapid vs Short Acting

- For type 2 diabetes, clinical evidence indicates that insulin glulisine, lispro, and aspart have been shown to be at least as effective as regular insulin in HbA<sub>1c</sub> reduction. However, insulin glulisine and lispro resulted in significantly lower post-prandial blood glucose levels compared to regular insulin. *The difference in post-prandial blood glucose levels was never greater than 20 mg/dL with both groups (rapid-acting insulin and regular insulin) meeting the ADA guideline recommended post-prandial blood glucose level of less than 180 mg/dL.* The rapid-acting insulins, insulin glulisine, aspart, and lispro, are associated with similar rates of hypoglycemia compared to regular insulin in patients with type 2 diabetes.

### **TYPE 1 & 2 DIABETES: Rapid vs Short Acting**

- The rapid-acting insulins have been shown to result in significantly higher patient satisfaction compared to regular insulin in patients with type 1 and type 2 diabetes. Results based on a diabetes quality of life (DQOL) questionnaire which consist of 55 items group in 4 subscales (satisfaction, impact, social/vocational worry, and diabetes related worry).

### **TYPE 1 DIABETES: Long vs Intermediate Acting**

- Long-acting analogs, insulin glargine and detemir, have been shown to be at least as effective as neutral protamine Hagedorn (NPH) insulin in HbA<sub>1c</sub> reduction in patients with type 1 diabetes, with some studies showing a significant improvement associated with insulin glargine and detemir compared to NPH insulin. *The difference in HbA<sub>1c</sub> was never greater than 0.5% in any clinical trial.* Clinical trials comparing insulin detemir and glargine support comparability in efficacy between the products. The newer long-acting analog, insulin degludec, has been shown to be at least as effective as the other long-acting analogues, insulin glargine and detemir, in patients with type 1 diabetes. However, insulin degludec results in significantly fewer episodes (27- 40%) of nocturnal hypoglycemia compared to insulin glargine and detemir.
  - Insulin glargine and detemir have been shown to result in significantly lower fasting blood glucose and less day-to-day variation in self monitored blood glucose compared to NPH. *However, the difference was never greater than 15 mg/dL and there was no difference between groups and ability to meet the ADA's guideline recommended fast blood glucose level of 80 -130 mg/dL.* Long-acting analogs, insulin glargine, detemir, and degludec, have been shown to have similar effects on fasting blood glucose levels.

### **TYPE 2 DIABETES: Long vs Intermediate Acting**

- Long-acting analogs, insulin glargine and detemir, have been shown to be at least as effective as neutral protamine Hagedorn (NPH) insulin in HbA<sub>1c</sub> reduction in patients with type 2 diabetes. Several studies showed that insulin glargine and detemir resulted in significantly lower post-prandial blood glucose levels compared to NPH insulin. *However, the difference was never greater than 35 mg/dL.* The long-acting insulin analogs, insulin glargine and detemir, resulted in significantly fewer episodes of nocturnal hypoglycemia compared to NPH insulin in clinical studies. *The difference in episodes of nocturnal hypoglycemia between the long acting and NPH insulins ranges from 9 -15%.* However, the long-acting insulin analogs resulted in similar rates of overall episodes of severe hypoglycemia compared to NPH insulin.
  - One head-to-head study did indicate superiority of insulin detemir compared to biphasic insulin aspart in

- reduction of HbA<sub>1C</sub> from baseline. Additionally, insulin detemir resulted in not statistically significant reduction post-prandial blood glucose levels compared to biphasic insulin aspart.
- In insulin naïve and experienced patients with type 2 diabetes, insulin glargine U-300 was shown to be non-inferior to insulin glargine U-100 in reduction of HbA<sub>1C</sub> from baseline. Both insulin glargine U-100 and insulin glargine U-300 result in similar fasting blood glucose and percentage of patients able to achieve an HbA<sub>1C</sub> <7% at 26 weeks.
    - Two head-to-head trials have shown that insulin glargine U-300 results in significantly fewer episodes of severe and nocturnal hypoglycemia (21-23%) compared to insulin glargine U-100 in insulin experienced type 2 diabetic patients.
    - One head-to-head trial showed that insulin glargine U-300 resulted in a significantly lower risk (24%) of hypoglycemia compared to insulin glargine U100 in insulin naïve type 2 diabetic patients. Insulin glargine U300 resulted in fewer episodes of severe and nocturnal hypoglycemia episodes compared to insulin glargine U100; however, the difference was not statistically significant.
  - Clinical trials comparing insulin detemir and glargine support comparability in efficacy and safety between the products.
  - The newer long-acting insulin analog, insulin degludec, has been shown to be at least as effective as insulin glargine in HbA<sub>1C</sub> reduction in insulin naïve and experienced patients with type 2 diabetes. Clinical data shows that insulin degludec results in significantly lower fasting blood glucose levels compared to insulin glargine. Additionally, insulin degludec resulted in significantly fewer episodes of symptomatic and nocturnal hypoglycemia compared to insulin glargine. There are no head-to-head comparator trials of insulin degludec and insulin detemir or NPH insulin.
  - Several observational studies have reported an increased risk of breast cancer with insulin glargine use compared to other insulin products. However, these studies have several methodological issues including time-lag bias, lack of lag period, inclusion of prevalent users, and short follow-up.

## FUTURE

- Basaglar (insulin glargine) injectable a long-acting recombinant human insulin analogue. Reference product (Lantus<sup>®</sup>) insulin glargine. Product will come available to the market in December 2016.
  - Indications:
    - Control of hyperglycemia due to type 1 and 2 diabetes in patients >17 years old
    - Control of hyperglycemia due to type 1 diabetes in patients >6 years old

**Recommendations:**

- Maintain Humulin or Novolin as preferred but move to T1 copay
  - Coverage for vials and pens
- Include one rapid-acting and one long-acting insulin analogue as preferred as a T2 copay
  - Coverage for vials and pens
  - Remaining rapid-acting and one long-acting insulin analogues will be excluded from plan
  - All current members on an excluded analogue will NOT be grandfathered and will be given a 90 day grace period following the implementation of the contract to switch to a preferred analogue
- Require price protection for the life of the contract