



AGENDA

**State and Public School Life and Health Insurance Board
Drug Utilization and Evaluation
Committee
EBD Board Room, 501 Woodlane, Suite 500**

August 5, 2013 – 1:00 PM

- 1. Call to Order** *Dr. Kat Neill, Chair*
- 2. Approval of Minutes** *Dr. Kat Neill, Chair*
- 3. Zytiga/Contraceptives/Medical Foods** *Jill Johnson, UAMS*
- 4. Amphetamine/Antidepressants/ARB** *David Keisner, Jill Johnson, UAMS*
- 5. Second Review Drugs (Lyrica)** *Jill Johnson, UAMS*
- 6. New Drugs** *Jill Johnson, UAMS*
- 7. Plan Performance Summary**..... *Dwight Davis, UAMS*
- 8. Director's Report** *Doug Shackelford, EBD*

**Next Meeting
November 4th**

**State and Public School Life and Health Insurance
Board Clinical and Fiscal Drug Utilization and
Evaluation Committee
Minutes
April 8, 2013**

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday, April 8, 2013 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Little Rock, AR.

Members present:

Matthew Hadley
Kat Neill
Dr. William Golden
Larry Dickerson
Scott Pace
Dr. Hank Simmons
Connie Bennett
John Kirtley

Members absent:

Mark McGrew
Dr. Joe Stallings

Jason Lee, Executive Director, Employee Benefits Division of DFA.

OTHERS PRESENT

Jill Johnson, Dwight Davis, David Keisner, Jordan Brazeal, Jenny Stephens, Willis Johnson, Tyler , Chris McDearmon; UAMS College of Pharmacy/EBRx; Connie Bennett, Informed Rx; John Kirtley, State Board of Pharmacy; Doug Shackelford; Michelle Hazelett, Sherri Saxby, Melida Vasquez, Peggy Robinson, Stella Green, Latryce Long, Tracy Butler-Oberste, Makesha Thompson, Leslie Smith, Lori Eden, Janna Keathley, EBD; Bridget Johnson, Pfizer, Allison Hollis, Amy Chiaro, UAMS; Warren Tyes, Merck; Rhonda Walthall, Wayne Whitley, AHTD; Mark DeClerk, Dawn Davis, Takisha Sanders, Health Advantage; Barry Fielder, Quail Choice; Treg Long, ACR; Charlene Kaiser, Amgen

CALL TO ORDER

Meeting was called to order by Dr. Matthew Hadley, Chairman.

APPROVAL OF MINUTES

The motion was made by Dr. Hadley to approve the February 4, 2013 minutes. Neill made the motion to approve. Dr. Simmons seconded. All were in favor. Minutes were approved.

TABLED, SECOND REVIEW, & NEW DRUGS by Jill Johnson, UAMS

Johnson reported and the Committee reviewed Tabled, Second Review, & New Drugs. The following are the recommendations:

TABLED ITEMS:

1. **Cometriq** – Treatment of patients with progressive, metastatic medullary thyroid carcinoma

Recommendation: Exclude due to experimental and investigational status

Dr. Golden motioned to exclude. Neill seconded. All were in favor.

2. **Oxtellar XR** – Extended release form of oxcarbazepine for treatment of partial seizures.

Recommendation: Exclude due to similar therapies on formulary

Dr. Golden motioned to exclude. Neill seconded. All were in favor.

3. **Stivarga** – Treatment of patients with metastatic colorectal cancer who have been previously treated with currently available therapies.

Recommendation: Table with review in 6 months.

Dr. Kumpuris requested further discussion due to the extended six weeks of survival. Dr. Hadley inquired have the Board approve extended life medicine in the past. If the drug is approved consider other drugs of this kind can we decline those in the future if this one is approved. Dr. Golden would like to continue further discussion when more supported evidence is available.

Dr. Golden motioned to table with review in 6 months. Dickerson seconded. All were in favor.

SECOND REVIEW ITEMS:

1. **Naprelan** – Treatment of patient with pain or osteoarthritis

Recommendation: Exclude for new patients and provide current users 90-day notice (July 8, 2013).

Dr. Golden motioned to exclude. Dr. Neill seconded. All were in favor.

2. **Intuniv** – Treatment of patients with ADHD

Recommendation: Exclude for new patients and provide current users 90-day notice.

Dr. Simmons motioned to exclude. Dr. Neill seconded. All were in favor.

3. **Gleevec** – Treatment of patients with chronic myeloid leukemia

Recommendation: Add PA to currently covered medication.

Dr. Golden motioned to approved with a PA. Dickerson seconded. All were in favor.

4. **Linzess** – Treatment of patients with irritable bowel syndrome

Recommendation: Coverage on Tier 3 with a PA; require PA in 90-days.

Dr. Golden motioned to approve. Dr. Neill seconded. All were in favor.

5. **Amitiza** – Treatment of patients with irritable bowel syndrome

Recommendation: Add PA to currently covered medication. Coverage on Tier 3.

Dr. Golden motioned to approve. Dr. Neill seconded. All were in favor.

FIRST REVIEW OF NEW MEDICATIONS:

1. **Gattex** – Treatment of patients with short bowel syndrome

Recommendation: Exclude

Dr. Simmons motioned to exclude. Dickerson seconded. All were in favor.

2. **Nesina** – Treatment of patients with type 2 diabetes

Recommendation: Coverage with Tier 3 with PA

Dr. Golden motioned to approve. Dickerson seconded. All were in favor.

3. **Kazano** – Treatment of patients with type 2 diabetes

Recommendation: Coverage with Tier 3 with PA

Dr. Golden motioned to approve. Dickerson seconded. All were in favor.

4. **Oseni** – Treatment of patients with type 2 diabetes

Recommendation: Coverage with Tier 3 with PA

Dr. Golden motioned to approve. Dickerson seconded. All were in favor.

5. **Uceris** – Treatment of patients with ulcerative colitis

Recommendation: Exclude

Dr. Neill motioned to exclude. Pace seconded. All were in favor.

6. **Delzicol** – Treatment of patients with ulcerative colitis

Recommendation: Exclude

Dr. Neill motioned to exclude. Pace seconded. All were in favor.

7. **Pomalyst** – Treatment of patients with multiple myeloma

Recommendation: Cover on Tier 3 with PA

Dr. Golden motioned to approve. Dickerson seconded. All were in favor.

Dr. Golden reports a Cancer Committee is becoming essential to making proper decisions on certain medications. Pace reports the cost of the medication is a concern.

8. **Ravicti Liquic** – Treatment of patients with urea cycle disorder

Recommendation: Medical Coverage Only – Case Manager Required

Dickerson motioned Case Management Medical Study Only. Dr. Neill seconded.

9. **Fulyzaq** – Treatment of patients with non-infectious diarrhea in patients with HIV/AIDS

Recommendation: Exclude

Dr. Simmons motioned to exclude. Pace seconded. All were in favor.

10. **Abilify Maintena** – Treatment of patients with schizophrenia

Recommendation: Exclude

Neill motioned to exclude. Dr. Simmons seconded. All were in favor.

11. **Kynamro** – Treatment of patients with homozygous familial Hypercholesterolemia

Recommendation: Exclude

Pace motioned to exclude. Dr. Simmons seconded.

12. **Juxtapid** - Treatment of patients with homozygous familial Hypercholesterolemia

Recommendation: Exclude

Pace motioned to exclude. Dr. Simmons seconded.

Johnson also reports the following Medications should not be reviewed because they are Medical and not under the realm of pharmacy:

- Jetrea
- Skyla
- Kadcylla
- Varizig

ANTIDEPRESSANT CLASS REVIEW by Jill Johnson, UAMS

A class review was conducted for both SSRI and SNRI type medications. Johnson reports Duloxetine was not more effective than some other new antidepressant agents in the acute phase treatment of major depression and it was less well tolerated than escitalopram and venlafaxine as more pts allocated to duloxetine withdrew from treatment before study end.

There are no substantial differences in efficacy among 2nd generation AD's for major depressive disorder.

Mirtazapine has a significantly faster onset of action than citalopram, fluoxetine, paroxetine, and sertraline in MDD.

For dysthymia, no HTH evidence exists; data insufficient; some evidence pts under 50 did not improve vs placebo.

Subsyndromal depression: no difference between citalopram and sertraline.

Seasonal affective disorder; No HTH evidence exists.

MDD in kids: no HTH trial.

GAD: No major differences in fluoxetine & sertraline; or between paroxetine & escitalopram or venlafaxine except one study favoring escitalopram over paroxetine.

OCD: No major differences in efficacy between paroxetine & escitalopram, sertraline and venlafaxine; or between venlafaxine or escitalopram.

Panic DO: No major differences in efficacy between citalopram and escitalopram; inconclusive about paroxetine vs. venlafaxine ER.

PTSD: No major differences in efficacy between sertraline vs. citalopram, nefazodone, or venlafaxine.

Social anxiety disorder: No major differences in efficacy between paroxetine vs. escitalopram or venlafaxine ER.

Recommendation: To proceed with Reference Pricing of SSRI and SNRI medications with 120 days of notice to current users. Cymbalta Tier 2 with a PA if the data supports it.

Pace motioned to approve. Dr. Simmons seconded. All were in favor.

PPI/H2 ANTAGONIST CLASS REVIEW by Jill Johnson, UAMS

A review was conducted for PPI medications.

Recommendation: To incorporate the Over-The-Counter medications into the Reference Pricing/Co-Pay structure of the full formulary (\$10 tier 1 co-pay or Reference Price)

Lee reports the effective date will be at the discretion of the Benefits Committee.

Pace motioned to approve. Dr. Simmons seconded. All were in favor.

DIRECTOR'S REPORT by Jason Lee, Executive Director

The election of new Officers was held. Dr. Hadley nominated Kat Neill for Chair. Dickerson seconded. All were in favor. Neill is approved as the new Chair.

Dickerson nominated Dr. Simmons for Vice-Chair. Neill seconded. All were in favor. Dr. Simmons is approved as the new Vice-Chair.

Lee thanked Dr. Hadley for his two years of service as Chair. Lee also announced the next meeting will be held August 5, 2013.

Meeting adjourned.

**Zytiga (abiraterone) for metastatic prostate cancer
Reconsideration for DUEC, August 5, 2013
Jill Johnson, Pharm.D., BCPS**

Current Coverage: Excluded

Recent discussion below:

DUEC-EBD Drug	Generic Name	Jill's notes/recommendations	DUEC Date	DUEC's final vote	Insurance Date	Insurance Board final vote	PA criteria/Notes
Zytiga	Abiraterone	10/4/2011: I recommended T3PA. Drug has limited medical benefit. QL of 120/30d. No 90 day fills. Criteria are: 1. Dx of metastatic prostate cancer, 2. has the pt received prior chemotherapy containing docetaxel. N Engl J Med 2011; 364:1995-2005. 1000mg (250mg tablets) daily. Extended overall survival by 3.9m (14.8 vs 10.9m). No difference in withdrawal due to AE's. Noteworthy: all authors were heavily invested and conflicted, many being employees of the manufacturer. Trial was (abir + pred) vs (plac + pred). The plac group took their meds a median of only 4 months while the abir group took abir a median of 8 months. <u>The DUEC alternatively chose to exclude the drug.</u> <u>To date 10/29/12: no new trials are out on Zytiga.</u>	11/5/12	continue to exclude	11/14/12	continue to exclude	
Zytiga 250mg tab	abiraterone	T3PA. Drug has limited medical benefit. QL of 120/30d. No 90 day fills. Criteria are 1. Dx of metastatic prostate cancer, 2. has the pt received prior chemotherapy containing docetaxel. N Engl J Med 2011; 364:1995-2005. 1000mg (250mg tablets) daily. Extended overall survival by 3.9m (14.8 vs 10.9m). No difference in withdrawal due to AE's. Noteworthy: all authors were heavily invested and conflicted, many being employees of the manufacturer. Trial was (abir + pred) vs (plac + pred). The plac group took their meds a median of only 4 months while the abir group took abir a median of 8 months.	10/4/11	Exclude	10/11/11	Exclude	A trial in prost CA pts w/o previous CTX showed improved PFS, a trend toward improved OS, delayed clinical decline and initiation of CTX in pts w/ met castration-resistant prost CA. NEJM Dec 10, 2012.

Review of the evidence:

- de Bono JS, et al. Abiraterone and increased survival in metastatic prostate cancer. NEJM. 1011;364:1995-2005.
Randomized trial 2:1 ratio. N=1195 prostate CA patients who already received docetaxel and had disease progression; also maintained androgen deprivation (serum testosterone level <50ng/dL); all were ECOG 0 or 1 (90%), or 2 (10%). All pts received prednisone 5mg BID and were randomized to either abiraterone 1000mg (4-250mg tablets) daily or placebos daily.
Primary endpt: overall survival; secondary endpts: % pts with at least a 50% decrease in PSA from baseline after 4 weeks, time to PSA progression (25% increase over baseline).
Negatives: Authors were heavily conflicted. Statistician employed by the independent clinical research organization provided the analysis to the independent data and safety monitoring committee whose members were invited by the sponsor. The independent DSMC recommended unblinding, then analyses of the data were performed by a statistician employed by the sponsor. Results were reviewed by the authors. Publication did not say whether any results were changed due to this re-analysis.

Results: Median duration of treatment was 8m for the abiraterone group, 4m for placebo. A pre-planned interim analysis was planned after 534 deaths occurred. **After 552 deaths, 42% occurred in the abiraterone group, 55% placebo. OS hazard ratio was 0.66; 95%CI, 0.55 to 0.78; p<0.001). Median overall survival was 14.8m Abir. vs 10.9m plac. All secondary endpts supported superiority of abiraterone except in ECOG 2 pts where it was not. Safety was similar between abir and placebo.**

2. Ryan CJ, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. N Engl J Med 2013;368:138-48.
Randomized trial. N=1088 metastatic prostate CA pts w/ or w/o PSA progression, ongoing androgen deprivation (serum testosterone <50ng/dL), ECOG 0 or 1, who had received antiandrogen therapy previously. Randomized 1:1 to abiraterone 1000mg (4-250mg tabs daily) + prednisone 5mg BID OR placebo + prednisone 5mg BID.
Co-Primary endpts: Radiographic PFS and OS
Secondary endpts: time to opiate use for cancer-related pain, times to initiation of cytotoxic CTX, time to ECOG performance decline, time to PSA progression.
Results: The radiographic PFS and OS were reported together and were statistically significant. **Authors reported OS separately and stated that at the planned interim analysis of OS, after 333 deaths, 27% in the abiraterone group had died and 34% of the placebo pts had died. Median survival was 27.2 months in the placebo group; median survival was not reached in the abiraterone group.**
time to opiate use for cancer-related pain: not reached in abir vs 23.7m placebo (HR 0.69; 95%CI, 0.57 to 0.83, p< 0.001)
times to initiation of cytotoxic CTX: 25.2m abir, 16.8m plac(HR0.58; 95% CI, 0.49 to 0.69; p<0.001)
time to ECOG performance decline: 10.9m abir ,12.3m plac (HR for decline 0.82; 95%CI, 0.71 to 0.94; p-0.005)
time to PSA progression: 11.1m abir vs 5.6m plac (HR .49; 95%CI, 0.42 to 0.57; p<0.001)
Safety:
Abiraterone had 4% more fluid retention, 6% more hypokalemia, 9% more hypertension, 7% more ALT increase, and 6% more AST increase vs placebo.
Negatives: Authors were heavily conflicted. No statement on who owned, analyzed, and controlled the data.

3. Logothetis CJ, et al. Effect of abiraterone acetate and prednisone compared with placebo and prednisone on pain control and skeletal-related events in pts with metastatic castration-resistant prostate cancer; exploratory analysis of data from the COU-AA-301 randomised trial. Lancet Oncol. 2012;13:1210-17.
This was an exploratory analysis of reference #1 above. The analysis was performed immediately prior to the timepoint of unmasking and crossover from the placebo group to the abiraterone group. Pain intensity was defined a priori in the analysis plan.
Negative: Employees of Janssen participated in trial design, data collection, and data analysis, and had a supporting role in data interpretation and writing of this report.
Results:
 - Pain intensity palliation: two consecutive follow-up visits (at least 4 weeks apart) at which the pain intensity score was at least 30% lower than that at baseline (previously reported as a clinically meaningful decrease"), without an increase in analgesic use (defined as a ≥ 1 point increase on the WHO analgesic scale). Duration of pain intensity palliation was also assessed in all patients meeting these criteria.
RESULTS: 45% of aber pts vs 28.5% for placebo pts, p=0.0005. Median duration of pain intensity palliation was 4.2m aber vs 2.1m placebo, p=0.0056.
 - Pain intensity progression: two consecutive follow-up visits at which the pain intensity score increased by 30% or more without a decreased analgesic usage score, or an increase in analgesic usage score of 30% or greater.
RESULTS: not reached, NS
 - Pain interference palliation: mean pain interference score (ie, the mean of the scores for the pain interference items) decreased by 1.25 points or more compared with baseline at two consecutive follow-up visits; we derived this threshold from the baseline standard deviation according to a generally accepted estimation process."
RESULTS: 60% aber pts vs 38% of placebo, p=-0.0002.
 - Pain interference progression: increase of 1.25 points or more in the mean pain interference score at two consecutive follow-up visits.
RESULTS: not reported.
 - Skeletal events were similar in both groups. NS.

RECOMMENDATION:

T3PA. Current evidence supports coverage. The criteria: 1. Dx of metastatic castration resistant prostate cancer, 2. Concomitant use of prednisone 5mg twice daily. QL of 4-250mg tablets per day. 124/31d.

Antidepressants (AD)

DUEC April 2, 2013

Jill Johnson, Pharm.D., BCPS

EBD March 2013	Tier	PA	Q L	MDD in kids/adolescents
SNRI's				
cymbalta	3	N	N	
Effexor XR	3	Y	N	
venlafaxine ER	1	Y	N	
Effexor	3	N	N	
venlafaxine	1	N	N	
Pristiq	**EXCLUDED*			
Savella	3	N	Y	
Savella titration pack	3	N	Y	
SSRI's				
Celexa	3	N	Y	
citalopram	1	N	Y	
Lexapro	3	N	N	
escitalpram	1	N	N	
Zoloft	3	N	N	
sertraline	1	N	N	
Prozac	3	N	N	
fluoxetine	1	N	N	preferred ¹
Paxil CR	3	N	N	
paroxetine HCL ER	1	N	N	
Paxil	3	N	N	
paroxetine HCL	1	N	N	
Pexeva (paroxetine mesylate)	2	N	N	
Luvox CR	3	N	N	
fluvoxamine	1	N	N	
Viibryd	**Excluded**			
mirtazapine-tetracyclic, central a2 blocker that increases release of NE and serotonin; does not inhibit reuptake of NE or S.				

Summary:

1. Duloxetine was NOT more effective than some other new antidepressant agents in the acute phase treatment of major depression and it was less well tolerated than escitalopram and venlafaxine as more pts allocated to duloxetine withdrew from treatment before study end.²

2. The newest Oregon EPC report on 2nd Generation antidepressants (March 2011).⁵

- There are no substantial differences in efficacy among 2nd generation ADs for major depressive disorder.
- Mirtazapine has a significantly faster onset of action than citalopram, fluoxetine, paroxetine, and sertraline in MDD.
- For dysthymia, no HTH evidence exists; data insufficient; some evidence pts under 50 did not improve vs placebo.
- Subsyndromal depression: no difference between citalopram and sertraline.
- Seasonal affective disorder: No HTH evidence exists.
- MDD in kids: no HTH trials
- GAD: No major differences between fluoxetine & sertraline; or between paroxetine & escitalopram or venlafaxine except one study favoring escitalopram over paroxetine.
- OCD: No major differences in efficacy between paroxetine & escitalopram, sertraline and venlafaxine; or between venlafaxine & duloxetine or escitalopram.
- Panic DO: No major differences in efficacy b/w citalopram and escitalopram; inconclusive about paroxetine vs venlafaxine ER.
- PTSD: No major differences in efficacy between sertraline vs citalopram, nefazodone, or venlafaxine.
- Social anxiety disorder: No major differences in efficacy between paroxetine vs escitalopram or venlafaxine ER.

Adverse Effects:

- Diarrhea worse with sertraline than with bupropion, citalopram, fluoxetine, mirtazapine, paroxetine, venlafaxine.
- Discontinuation rates: meta-analyses of efficacy show overall discontinuation rates are similar. Venlafaxine has a higher DC rate due to adverse events and a lower rate of DC because of lack of efficacy than SSRI as a class.
- N/V: meta-analyses of 15 studies indicate venlafaxine has more NV than SSRIs as a class.
- Weight change: mirtazapine leads to higher weight gains than citalopram, fluoxetine, paroxetine, and sertraline.
- Sexual SEs: Bupropion causes significantly less sexual dysfunction than escitalopram, fluoxetine, paroxetine, and sertraline. Among SSRIs, paroxetine is the worst.

Fibromyalgia

- Duloxetine worked better than placebo for fibromyalgia in one study at 3 months but not 6 months.⁶
- SNRIs duloxetine and milnacipran (Savella) provided a small incremental benefit over placebo in reducing pain. The superiority of duloxetine and milnacipran over placebo in reducing fatigue and limitations of QOL was not substantial. They were not superior to placebo in reducing sleep problems. The dropout rates due to adverse events were higher for both drugs than for placebo. The most frequently reported symptoms leading to stopping meds were N, dry mouth, constipation, HA, somnolence/dizziness, and insomnia. Rare complications of both drugs include suicidality, liver damage, abnormal bleeding, elevated BP, and urinary hesitation.³

References:

1. Hetrick SE, McKenzie JE, Cox GR, Simmons MB, Merry SN. Newer generation antidepressants for depressive disorders in children and adolescents. Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD004851. DOI: 10.1002/14651858.CD004851.pub3. Copyright © 2012 The Cochrane Collaboration.
2. Cipriani A, Koesters M, Furukawa TA, Nossè M, Purgato M, Omori IM, Trespidi C, Barbui C. Duloxetine versus other anti-depressive agents for depression. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD006533. DOI: 10.1002/14651858.CD006533.pub2.
3. Häuser W, Urrútia G, Tort S, Üçeyler N, Walitt B. Serotonin and noradrenaline reuptake inhibitors (SNRIs) for fibromyalgia syndrome. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD010292. DOI: 10.1002/14651858.CD010292.
4. Cipriani A, Purgato M, Furukawa TA, Trespidi C, Imperadore G, Signoretti A, Churchill R, Watanabe N, Barbui C. Citalopram versus other anti-depressive agents for depression. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD006534. DOI: 10.1002/14651858.CD006534.pub2.
5. Second Generation Antidepressants. Drug Effectiveness Review Project. March 2011 Update. OHSU.
6. Russell IJ, et al. Efficacy and safety of duloxetine for treatment of fibromyalgia in patients with or without major depressive disorder: results from a 6-month, randomized, double-blind, placebo-controlled, fixed-dose trial. Pain. 2008;136:432-44.

Proposal:

Implement reference pricing for second generation antidepressants.

Lyrica (pregabalin) for DUEC/EBD Consideration
 Jill Johnson, Pharm.D., BCPS
 August 5, 2013

Currently T3 without PA. Projected annual spend-\$1,220,000

Lyrica (pregabalin) is brand only. Per WSJ, Pfizer said in a written statement: "With this decision, Pfizer will exclusively provide pregabalin as Lyrica to patients through December 30, 2018, in the U.S., pending generic company appeal and further litigation."¹

Pregabalin, like gabapentin, is an amino acid derivative of gamma-amino butyric acid (GABA analogue). Pregabalin is the pharmacologically active S-enantiomer of 3-aminomethyl-5-methyl-hexanoic acid, and has a similar pharmacological profile to gabapentin. Both agents have been shown to be effective for neuropathic pain disorders, however, only pregabalin has been FDA approved for both the management of diabetic peripheral neuropathy and post herpetic neuralgia.

Pregabalin provides similar efficacy to gabapentin, however, at lower doses. Pregabalin has higher bioavailability (90% versus 33-66%) and is rapidly absorbed (peak: 1 hr). Gabapentin is more slowly absorbed (peak: 3 to 4 hours post-dose). Repeated dosing and adherence mitigates the difference.

Drugs for neuropathic pain (DERP 2011):²

Drug	Brand name	FDA indications for neuropathic pain	Recommended dosing for neuropathic pain
Gabapentin	Neurontin	Postherpetic neuralgia	Start 300mg, titrate to 900mg, increase up to 1800mg (divided TID)
Pregabalin (no generic)	Lyrica	Diabetic neuropathy, postherpetic neuralgia	Start 150mg, inc. to 300mg (divided TID); Start 150mg, inc to 75-150mg BID—adj for renal dysfunction
Carbamazepine	Carbatrol	Trigeminal neuralgia	Start 200mg daily, increase to max of 1200mg daily (divided BID. Most maintained on 400-800mg daily. Attempt to reduce dose to minimum effective level, or discontinue, at least q3m. Start 100mg bid, increase to max of 1200mg daily (divided BID). Most are maintained on 400-800mg daily. Attempt to reduce dose or DC q3m.
	Tegretol, XR, CR Eptol		
Topiramate	Topamax, Sprinkle	None	NA
Oxcarbazepine	Trileptal	None	NA
Lacosamide	Vimpat	None	NA
Lamotrigine	Lamictal, CD, ODT, XR	None	NA
Phenytoin	Dilantin	None	NA
Levetiracetam	Keppra, XR	None	NA
Valproic acid/divalproex	Depakote, ER, Depakene, Epival ECT Depacon, Stavzor	None	NA
SNRIs			
Duloxetine	Cymbalta	Diabetic neuropathy	60mg daily; lower starting dose and gradual increase in pts with renal impairment
Venlafaxine	Effexor, XR	None	NA
Desvenlafaxine	Pristiq	None	NA
Milnaciparn	Savella	None	NA
Topical analgesic			
Lidocaine	Lidoderm	Postherpetic neuralgia	Up to 3 patches for up to 12 h within a 24 hour period
Tricyclic antidepressants			
Amitriptyline	Elavil	None	NA
Desipramine	Norpramin	None	NA
Nortriptyline	Aventyl, Pamelor	None	NA
Protriptyline	Aventyl	None	NA
Imipramine	Tofranil	None	NA
Doxepin	Sinequan, Silenor	None	NA

For diabetic neuropathy and postherpetic neuralgia, based on very small studies, moderate-strength direct evidence did not support a statistically significant difference between gabapentin, pregabalin, and lamotrigine compared with tricyclic antidepressants in the rate of response, defined as a 50% or more reduction in baseline pain analyzed individually or when pooled (relative risk, 1.0; 95% CI, 0.84 to 1.18).²

Differences were also not found in other comparisons of pregabalin, duloxetine, gabapentin, and oxcarbazepine or comparisons of 5% lidocaine patch and amitriptyline or gabapentin.²

As of 7/9/13, there are no available direct comparisons or other evidence to support pregabalin's superiority over gabapentin in neuropathic pain, diabetic neuropathy, or any other pain syndrome. Adding an additional drug such as immediate release morphine to a neuropathic pain drug is a common and useful approach. One trial looked at duloxetine, pregabalin, or duloxetine + gabapentin in pts with inadequate response to gabapentin, however, fewer than 10% at baseline were taking a gabapentin dose adequate for neuropathic pain (>1800mg/day). Ninety percent of patients enrolled in the trial should not have been classified as having an inadequate gabapentin response since an adequate dose was never achieved.³

Indirect comparisons are all we have at this time to compare the efficacy of pregabalin and gabapentin. From these, no difference exists between the drugs. Consistent nonsignificant differences support gabapentin (over pregabalin) having a ≥50% pain reduction (Table 5), pain reduction on 2 different pain scales (Table 6), and a higher withdrawal rate due to adverse events with pregabalin vs gabapentin (Table 15).

From DERP:²

Table 5. Indirect comparison of pain measured as ≥50% pain reduction

Drug	Total N	Relative risk (95% confidence interval)
Compared with placebo		
Duloxetine	681	1.86 (1.52 to 2.28)
Pregabalin	3636	1.92 (1.53 to 2.40)
Gabapentin	852	2.23 (1.75 to 2.85)
Lamotrigine	875	1.11 (0.84 to 1.47)
Oxcarbazepine	493	1.51 (0.91 to 2.50)
Lacosamide	808	1.22 (0.89 to 1.67)
Indirect comparison		
Duloxetine vs. pregabalin		0.97 (0.72 to 1.31)
Duloxetine vs. gabapentin		0.83 (0.61 to 1.15)
Duloxetine vs. lamotrigine		1.68 (1.19 to 2.36)
Duloxetine vs. lacosamide		1.52 (1.05 to 2.21)
Duloxetine vs. oxcarbazepine		1.23 (0.71 to 2.13)
Pregabalin vs. lamotrigine		1.73 (1.21 to 2.0)
Pregabalin vs. lacosamide		1.57 (1.06 to 2.31)
Pregabalin vs oxcarbazepine		1.27 (0.73 to 2.22)
Gabapentin vs. pregabalin		1.09 (0.78 to 1.55)
Gabapentin vs. lamotrigine		2.01 (1.39 to 2.91)
Gabapentin vs. lacosamide		1.82 (1.22 to 2.72)
Gabapentin vs. oxcarbazepine		1.48 (0.84 to 2.60)
Lamotrigine vs. lacosamide		0.91 (0.60 to 1.38)
Oxcarbazepine vs. lacosamide		1.23 (0.68 to 1.23)

Table 6. Significant indirect comparisons of pain reduction on 3 different scales

Drug	Mean difference (95% confidence interval)	Indirect comparison	Difference of difference (95% confidence interval)
11-point Likert Scale			
Duloxetine	-1.11 (-1.42 to -0.82)	Duloxetine vs. lacosamide	-0.62 (-0.97 to -0.27)
Pregabalin	-1.00 (-1.22 to -0.69)	Duloxetine vs. lamotrigine	-0.63 (-1.21 to -0.05)
Gabapentin	-1.31 (-1.80 to -0.81)	Pregabalin vs. lacosamide	-0.50 (-0.83 to -0.18)
Lacosamide	-0.49 (-0.69 to -0.30)	Gabapentin vs. lacosamide	-0.81 (-1.35 to -0.28)
Lamotrigine	-0.48 (-0.98 to 0.02)	Gabapentin vs. lamotrigine	-0.83 (-1.53 to -0.12)
0-100 Visual Analogue Scale			
Pregabalin	-10.82 (-13.90 to -7.73)	Pregabalin vs. lacosamide	-4.65 (-9.25 to -0.04)
Gabapentin	-11.72 (-20.26 to -3.18)	Pregabalin vs topiramate	-7.19 (-12.03 to -2.35)
Lacosamide	-6.17 (-9.58 to -2.75)		
Oxcarbazepine	-10.02 (-16.02 to -4.01)		
Topiramate	-3.63 (-7.35 to 0.10)		
0-45 Short Form of McGill Pain Questionnaire			
Pregabalin	-3.94 (-5.36 to -2.52)	Pregabalin vs. lamotrigine	-3.68 (-5.53 to -1.84)
Gabapentin	-4.73 (-6.64 to -2.83)	Gabapentin vs. lamotrigine	-4.48 (-6.72 to -2.24)
Lamotrigine	-0.26 (-1.43 to 0.92)		

Table 15. Indirect comparisons of withdrawals due to adverse events

Drug	Placebo rate	Relative risk (95% confidence interval)
Compared with placebo		
Duloxetine	0.04	3.03 (1.82 to 5.03)
Pregabalin	0.06	2.42 (1.89 to 3.08)
Gabapentin	0.08	1.70 (1.10 to 2.62)
Lacosamide	0.08	2.07 (1.24 to 3.47)
Lamotrigine	0.11	1.75 (1.21 to 2.53)
Oxcarbazepine	0.08	3.90 (2.18 to 6.97)
Topiramate	0.08	2.91 (2.13 to 3.97)
Indirect comparison		
Duloxetine vs. pregabalin		1.25 (0.71 to 2.20)
Duloxetine vs. gabapentin		1.78 (0.91 to 3.48)
Duloxetine vs. lacosamide		1.46 (0.71 to 3.02)
Duloxetine vs. lamotrigine		1.73 (0.92 to 3.24)
Pregabalin vs. gabapentin		1.42 (0.87 to 2.34)

Fibromyalgia

NO HTH trials. Indirect evidence only. See references 4,5,& 6.

Both gabapentin and pregabalin are superior to placebo in fibromyalgia. By indirect evidence only (gabapentin or pregabalin vs placebo), there appears to be no difference between gabapentin and pregabalin regarding “30% improvement in pain response” or discontinuation due to adverse events.

Table 3. Indirect Comparisons: Results for the 30% Pain Response End Point

Treatment	Relative Risk (95% Credible Interval)*								
	Fluoxetine	Gabapentin	Milnacipran 100 mg/day	Milnacipran 200 mg/day	Pregabalin 300 mg/day	Pregabalin 450 mg/day	TCA's	Tramadol plus Paracetamol	Placebo
Duloxetine	0.89 (0.49, 1.49)	1.00 (0.64, 1.56)	1.25 (0.95, 1.64)	1.18 (0.90, 1.54)	1.20 (0.92, 1.57)	1.06 (0.81, 1.38)	1.39 (0.52, 4.14)	1.01 (0.65, 1.52)	1.64 (1.32, 2.04)
Fluoxetine		1.12 (0.64, 2.19)	1.41 (0.85, 2.48)	1.32 (0.81, 2.35)	1.35 (0.82, 2.41)	1.19 (0.73, 2.13)	1.56 (0.67, 4.45)	1.14 (0.66, 2.03)	1.84 (1.15, 3.15)
Gabapentin			1.26 (0.83, 1.87)	1.18 (0.79, 1.75)	1.21 (0.79, 1.81)	1.06 (0.69, 1.61)	1.40 (0.49, 4.28)	1.01 (0.58, 1.66)	1.65 (1.11, 2.39)
Milnacipran 100 mg/day				0.94 (0.79, 1.14)	0.96 (0.74, 1.23)	0.85 (0.66, 1.09)	1.11 (0.43, 3.27)	0.80 (0.53, 1.19)	1.31 (1.09, 1.59)
Milnacipran 200 mg/day					1.02 (0.79, 1.30)	0.90 (0.71, 1.14)	1.18 (0.45, 3.43)	0.86 (0.57, 1.25)	1.39 (1.18, 1.66)
Pregabalin 300 mg/day						0.88 (0.74, 1.05)	1.15 (0.45, 3.32)	0.84 (0.56, 1.23)	1.36 (1.14, 1.64)
Pregabalin 450 mg/day							1.31 (0.52, 3.80)	0.95 (0.64, 1.38)	1.55 (1.30, 1.86)
TCA's								0.73 (0.24, 1.80)	1.18 (0.41, 2.98)
Tramadol plus paracetamol									1.62 (1.16, 2.36)

*Estimated from mixed treatment comparison models adjusting for months of follow-up and percentage of females in the study. A relative risk greater than 1 favors the treatments listed in the treatment column. Credible intervals are the nonparametric approximation to traditional, parametrically estimated confidence intervals.
TCA's, tricyclic antidepressants.

Table 5. Indirect Comparisons: Results for Discontinuations Because of Adverse Events

Treatment	Relative Risk (95% Credible Interval)*								
	Fluoxetine	Gabapentin	Milnacipran 100 mg/day	Milnacipran 200 mg/day	Pregabalin 300 mg/day	Pregabalin 450 mg/day	TCA's	Tramadol plus Paracetamol	Placebo
Duloxetine	3.77 (1.12, 24.37)	1.05 (0.54, 2.14)	1.07 (0.68, 1.62)	0.86 (0.56, 1.27)	1.07 (0.70, 1.65)	0.82 (0.53, 1.23)	2.53 (1.47, 4.27)	0.88 (0.50, 1.52)	1.88 (1.30, 2.67)
Fluoxetine		0.28 (0.04, 1.07)	0.28 (0.04, 0.94)	0.23 (0.04, 0.75)	0.28 (0.04, 0.95)	0.22 (0.03, 0.72)	0.67 (0.10, 2.34)	0.23 (0.03, 0.82)	0.50 (0.08, 1.62)
Gabapentin			1.02 (0.50, 1.91)	0.83 (0.41, 1.53)	1.03 (0.51, 1.91)	0.79 (0.40, 1.43)	2.41 (1.13, 4.77)	0.84 (0.38, 1.72)	1.81 (0.93, 3.21)
Milnacipran 100 mg/day				0.81 (0.62, 1.05)	1.01 (0.68, 1.50)	0.77 (0.53, 1.13)	2.38 (1.49, 3.79)	0.83 (0.48, 1.42)	1.76 (1.32, 2.37)
Milnacipran 200 mg/day					1.25 (0.87, 1.81)	0.95 (0.67, 1.37)	2.93 (1.91, 4.61)	1.02 (0.60, 1.74)	2.18 (1.69, 2.84)
Pregabalin 300 mg/day						0.76 (0.55, 1.04)	2.35 (1.45, 3.82)	0.81 (0.48, 1.38)	1.75 (1.29, 2.37)
Pregabalin 450 mg/day							3.08 (1.92, 4.96)	1.07 (0.65, 1.78)	2.29 (1.73, 3.04)
TCA's								0.35 (0.19, 0.64)	0.74 (0.48, 1.13)
Tramadol plus paracetamol									2.13 (1.32, 3.45)

*Estimated from mixed treatment comparison models adjusting for months of follow-up and percentage of females in the study. A relative risk greater than 1 favors the treatments listed in the first column. Credible intervals are the nonparametric approximation to the traditional, parametrically estimated confidence intervals (see text). TCA's, tricyclic antidepressants.

Recommendation:

Option 1: ^{lyrica} Exclude pregabalin. No available evidence supports the clinical efficacy superiority over gabapentin for neuropathic pain or for fibromyalgia. Both drugs lower neuropathic pain compared to placebo.

Option 2: Apply reference pricing to pregabalin based on generic gabapentin. The plan would provide the same cost amount towards pregabalin as it does for gabapentin so it would be a covered drug. Covered drugs are subject to out of pocket maximums.

References:

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- Tanenbarg RJ, Irving GA, Risser RC, et al. Duloxetine, pregabalin, and duloxetine plus gabapentin for diabetic peripheral neuropathic pain management in patients with inadequate pain response to gabapentin: an open-label, randomized, noninferiority comparison. *May Clin Proc.* 2011;86(7):615-624.
- Tzellos TG, Toulis KA, Goulis DG, Papazisis G, et al. Gabapentin and pregabalin in the treatment of fibromyalgia: a systematic review and a meta-analysis. *J Clin Pharm and Therapeutics.* 2010;35:639-56.
- Hauser W, Bernardy K, Uceyler N, Sommer C. Treatment of fibromyalgia syndrome with gabapentin and pregabalin- a meta-analysis of RCTs. *Pain.* 2009;145:69-81. Roskell NS, Beard SM, Zhao Y, Le TK. A metaanalysis of pain response in the treatment of fibromyalgia. *Pain Practice.* 2011;11(6):516-27.

DRUG NAME	Generic Name	SIMILAR THERAPIES ON FORMULARY/ AWP	PRICING (AWP)	INDICATION	Connie Notes	Consultant's Notes	DUEC Vote	IB Vote
Signifor injection (specialty drug)	Pasireotide		\$17,000/month	Tx of Cushing's disease for whom pituitary surgery is no an option or has not been curative. Dose = 0.6 - 0.9mg subQ bid	Only available through an exclusive single specialty pharmacy. Not available through BriovaRx	Exclude. EBRx P8Twiced exclude due to DM, cost with lack of data; also no comparison to adrenalectomy, a definitive therapy. This drug is longterm maintenance with high cost.		
Suclear Kit	sodium sulfate, potassium sulfate, magnesium sulfate, and polyethylene glycol-electrolyte solution	Colyte(\$45), Golyte (\$24), PEG 3350(\$28), Nulytely (\$32)	\$77/kit	Bowel prep kit		Exclude based on cost. Many other PEG available. Suclear available at least 2 ways: Solution; oral: sodium sulfate 17.5 g, potassium sulfate 3.13 g, magnesium sulfate 1.6 g, Sodium benzoate, sucralose. In 180 mL with mixing container. Powder for solution; oral: PEG 3350 210 g, sodium chloride 5.6 g, sodium bicarbonate 2.86 g, potassium chloride 0.74 g. With cherry, lemon-lime, orange, and pineapple flavor packs. In 2 L bottles. No information on whether "Kit" contains something more.		
Invokana tabs	canagliflozin		30/300mg tabs = \$315.60	Tx of adults w/ Type 2 diabetes. Dose = 100-300mg/day	First in a new class called "glucuretic". Acts on kidneys to increase the loss of glucose in the urine. NOTE: Since the AWP of the 100mg tab and 300mg is the same, I would consider a QL of 60 for the 100mg tabs. If a member needs a 300mg dose, more cost effective to take 1-300mg tab instead of 3-100mg tabs.	Exclude. FDA is requiring five postmarketing studies for canagliflozin: a cardiovascular outcomes trial; a bone safety study; two pediatric studies under the Pediatric Research Equity Act, including a pharmacokinetic and pharmacodynamic study and a safety and efficacy study; and an enhanced pharmacovigilance program to monitor for malignancies, serious cases of pancreatitis, severe hypersensitivity reactions, liver abnormalities, photosensitivity reactions, and adverse pregnancy outcomes. High incidence of vaginal candidiasis and/or UTI. NO outcomes data. Lowered A1C by 1% (300mg) or 0.75% (100mg). Exclude until outcomes data. In addition to canagliflozin, a handful of other SGLT2 inhibitors are in the pipeline. In January 2012, the SGLT2 inhibitor dapagliflozin (Forxiga—AstraZeneca, Bristol-Myers Squibb), was not approved by FDA because of breast and bladder cancer concerns; however, it was approved in Europe a few months later. In March 2013, another SGLT2 inhibitor, empagliflozin (Boehringer Ingelheim—Eli Lilly), was submitted to FDA for approval.		
Tecfidera caps (specialty drug)	BG-12, dimethyl fumarate	Other oral agents to treat MS are Gilenya (\$5,562/28 days) and Aubagio (\$4,565/28 days)	\$5,400/30 days	Tx of patients with relapsing forms of multiple sclerosis. Dose = 480mg/day	Available in specialty pharmacies including BriovaRx	T3 PA. What if they are on other MS drug therapy? Tested against plac in 2y, R, DB, PC trial in pts with RRMS. Primary endpt was # of relapsed patients after 2y. Tecl 27% relapsed vs 46% w/ placebo (p<0.0001). Not intended to be compared with glatiramer although the 2 were both compared to placebo.		
TOBI Podhair caps (specialty drug)	tobramycin	Tobi Nebu Soln (\$8,583/28 days)	\$8,583/28 days	Management of cystic fibrosis patients with Pseudomonas aeruginosa. Dose= 112mg (4-28mg caps) bid for 28 days	Portable and requires no nebulizer, refrigeration, or power source to deliver medicine. Inhaled orally with Podhaler device.	Exclude. Journal of Cystic Fibrosis 10 (2011) 54–61. RCT compared TIP vs TIS. Cough was higher in TIP than TIS (TIP: 25.3% vs TIS 4.3%). Overall discontinuation rate was higher for TIP 26.9% vs TIS18.2%. SAEs were similar. The proportion of patients requiring any new antipseudomonal antibiotic was significantly higher with TIP than TIS (64.9% versus 54.5%, p = 0.0148). Increases in FEV1 % predicted from baseline to D28 were noninferior. The lower limit (-0.67%) of the one-sided 85% [CI] (equivalent to 70% two-sided) was within the predefined 6% margin for predefined non-inferiority indicating that TIP was non-inferior to TIS. Mean duration of administration was 5.6min TIP vs 19.7min TIS, p<0.0001. Global satisfaction & convenience was greater for TIP.		

Cystaran Opth Soln (specialty drug)	cysteamine 0.44% (ophthalmic solution)		\$1,050/15ml bottle	Tx of corneal cystine crystal accumulation in patients with cystinosis. Dose = 1 drop in each eye every waking hour	Available from Accredo Specialty Pharmacy only	Specialty tier. Cysteamine acts as a cystine-depleting agent by converting cystine to cysteine and cysteine-cysteamine mixed disulfides and reducing corneal cystine crystal accumulation. From the PI: Clinical efficacy was evaluated in controlled clinical trials in approximately 300 patients. The primary efficacy end point was the response rate of eyes that had a reduction of at least 1 unit in the photo-rated Corneal Cystine Crystal Score (CCCS) at some time point during the study when baseline CCCS ≥1, or a lack of an increase of more than 1 unit in CCCS throughout the study when baseline CCCS <1. Study 1 combined the data from three smaller studies. For eyes with a lower baseline of CCCS <1, the response rate was 13% (4/30) [95% CI: (4, 32)]. For eyes with a higher baseline of CCCS ≥1, the response rate was 32% (94/291) [95% CI: (27, 38)]. Study 2 evaluated ocular cystinosis patients who had a baseline of CCCS ≥1. The response rate was 67% (10/15) [95% CI: (38, 88)]. Study 3 also evaluated ocular cystinosis patients; for eyes with a baseline of CCCS ≥1, the response rate was 33% (3/9) [95% CI: (8, 70)]. Corneal crystals accumulate if CYSTARAN is discontinued.	
Cerefolin tabs	foliate and B12 combo			Multiple vitamin		This is a medical food. Pricing: \$411.64 for #90. No info on plain Cerefolin. Cerefolin NAC contains L-methylfolate 6mg, methylcobalamin 2mg, NAC 600mg, B2 5mg.	
Ospemifene 60mg tabs	Ospemifene	Symptomatic vaginal atrophy that does not respond to nonhormonal vaginal lubricants may require Rx therapy. Rx therapies available to this point have been oral and local estrogen therapies. (Premarin tabs of Premarin Vaginal Cream	\$189.60/30 days	Tx of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy (VVA). Dose = 60mg/day First treatment approved for VVA that is not a systemic or local estrogen.		Menopause. 2003;10(5):433-439. Showed improved estrogenic effects on vaginal epithelium by increased intermediate and superficial cells in repeat Pap smears without endometrial hyperplasia. J Bone Miner Metab (2006) 24:314-318 showed similar advantageous effects on bone turnover surrogate markers as raloxifene. May be an alternative to women seeking to avoid estrogen exposure. Not yet compared to topical Premarin for dyspareunia.	
Simbrinza Opth Susp	brinzolamide-brimonidine	Azopt (brinzolamide 1%) \$145/10ml. Brimonidine 0.2%-\$65/10ml bottle	\$105/8ml bottle	Beta-blocker free, fixed combination therapy for glaucoma/ocular hypertension. Dose = 3 drops/day		T3. Brinzolamide (carbonic anhydrase inhibitor) + brimonidine (α2 agonist). Consensus states prostaglandins are 1st line. Some metaanalyses found PGs to be more effective than beta blockers, CAinhibitors, and alpha agonists. Nonresponders should seek sgy. Also available are: dorzolamide 2% (generic) 10mL-\$66.75 Trusopt (brand) dorzolamide 2%, 5&10mL-\$92.04 Azopt (brand brinzolamide) 1%, 2.5, 10--\$145.26, 15mL Combigan (brimonidine + timolol). 5mL\$112.51	
Sirturo 100mg tabs	bedaquiline		\$35,908/24 weeks therapy	First new antibacterial indicated for the tx of tuberculosis in over 40 years and is indicated as part of a combination therapy for adults with pulmonary multi-drug resistant tuberculosis (MDR-TB)Dose=400mg/day for 2 weeks, then 200mg three times a week. Total duration is 24 weeks	Data from a clinical trial has associated Sirturo with an increased risk of death. Therapy should be directly observed to ensure compliance. In 2011, 98 cases of MDR-TB were reported in the US by the CDC	Consider specialty tier without restriction since the AR Health Dept determines all therapy for TB. Dr. Naveen Patil. For MDRTB as part of combo tx. Dose is 400mg qd for 2 weeks, then 200mg T1W for 24 w under DOT. If T3PA, criteria would be. 1. Dx of MDRTB. 2. At least 3 other TB antibiotics with shown susceptibility in vitro. Mortality was higher with bedaquiline (11.4%) vs placebo (2.5%). QT prolongation is a problem. Allow initial fill without PA (3 days) if this can be arranged.	

Diclois tabs 10/10mg	doxylamine 10mg and pyridoxine 10mg delayed release tabs			Treatment of pregnancy induced nausea/vomiting			Exclude or T3. The "new" Bendectin. Taken 2-3/day--\$530/month. 10mg of doxylamine, 10mg pyridoxine. Doxylamine 25mg is OTC. Aldex-AN is Rx but is 5mg chewable and expensive (\$249.20/100, \$2.49ea X 2/dose is \$5/dose X TID is \$15/day or \$465/31d; then add pyridoxine. Considerations: It's finite. Promethazine or ondansetron are alternatives and are generic.	
Liptruzet tabs	ezetimibe/atorva statin	Zetia 10mg = \$198/30 days. Atrovastatin 20mg = generic Lipitor.	\$198/30 days	Tx of hypercholesterolemia/hyperlipoproteinemia		Liptruzet is same price as Zetia - member paying 1 copay.	Exclude. ENHANCE showed combined therapy with ezetimibe and simvastatin did not result in a significant difference in changes in intima-media thickness, as compared with simvastatin alone, despite decreases in levels of LDL cholesterol and C-reactive protein. Consider excluding ezetimibe.	
Procybi delayed-release	cysteamine caps (specialty drug)	Cystagon (immediate release cysteamine) 500-50mg/\$190. 500-150mg/\$555	bottle of 60-25mg = \$4,482. bottle 250-75mg = \$18,675	For treatment of cystinosis			Exclude. Can use IR. For nephropathic cystinosis in age 6&up. Maintenance dose is 2g/d in 4 divided doses. Noninferior to Cystagon IR capsules at maintaining WBC cystine levels in patients with cystinosis but at a lower total daily dose. Article N/A full text: http://www.ncbi.nlm.nih.gov/pubmed/22554716# . IR is must less costly.	
Minastrin 24 chewable tab			\$99/28 days	Oral contraceptive			Exclude. No info as of 7/18/13.	
Quartette tabs			\$329/91 days	Oral contraceptive - 91 day regimen			Exclude. 4-phase OC; different from Natazia. Quartette is also extended cycle-91 days.	
Mekimist tabs (specialty drug)	Trametinib (a MEK inhibitor, aka MAPK kinase)		\$8,700/30 day supply	Indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test. Dose = 2mg once daily	Available in specialty pharmacies including Briovax	Specialty Tier, PA. Criteria: 1. Dx of metastatic melanoma, 2. ECOG 0-1 at initial request, 3. Braf V600e or V600k mutation confirmed by FDA approved test. Notes: may allow even if brain mets; Limit to 15 days supply like Zelboraf. NEJM. 2012;367:107-14. Before 2010, no systemic therapy had been shown to improve OS in metastatic melanoma, (only modest improvements with interferon). Ipilimumab (Yervoy), a monoclonal Ab targeting cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), and vemurafenib (Zelboraf), a selective BRAF inhibitor, have both been shown to improve OS. We cover Yervoy on the medical side. We cover Zelboraf (oral) w/ a PA (requiring Dx of unresectable or metastatic, previously untreated stage IIIC or stage IV melanoma that tested positive for the BRAF V600E mutation on real-time polymerase-chain-reaction assay. (Not the wildtype BRAF), allow a 15 days supply. @6m the OS was 84% vs 64% in the dacarbazine group in that study. Activating mutations in serine-threonine protein kinase B-RAF (BRAF), a constituent of the MAP kinase signal-transduction pathway, were first described in 2002 and have been identified in approximately 50% of patients with advanced melanoma. The most commonly observed BRAF mutation, V600E, and the next most common, V600K, account for 95% of the BRAF mutations found in all patients with cancer. Activated BRAF phosphorylates and activates MEK proteins (MEK1 and MEK2), which then		
Tafimar caps (specialty drug)	Dabrafenib (a selective BRAF inhibitor)		\$7,600/30 day supply	Indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation, as detected by an FDA-approved test. Dose = 150mg twice daily	Available in specialty pharmacies including Briovax	Exclude. NO OS data yet. Revisit in 1/2014. NEJM. 2012;367:1694-703. Difficult publication reporting 4 parts		
Belviq tabs	Lorcaserin	N/A -	\$239/30 day supply	Anti-obesity	GPI 6125** already set to reject on plan	Exclude. Not medically necessary to date. 3 Phase 3 trials. Measured >5% weight loss from baseline. RCT, 2 y trial, N=3182. 48% Belviq vs 20% plac (year 1), p<0.0001. Belviq 67.9% vs plac 50.3% (year 2). Without valvulopathy. Trial completion rate 55		
dysport				cervical dystonia, glabellar lines		Already covered for cervical dystonia. Specialty tier with PA.		

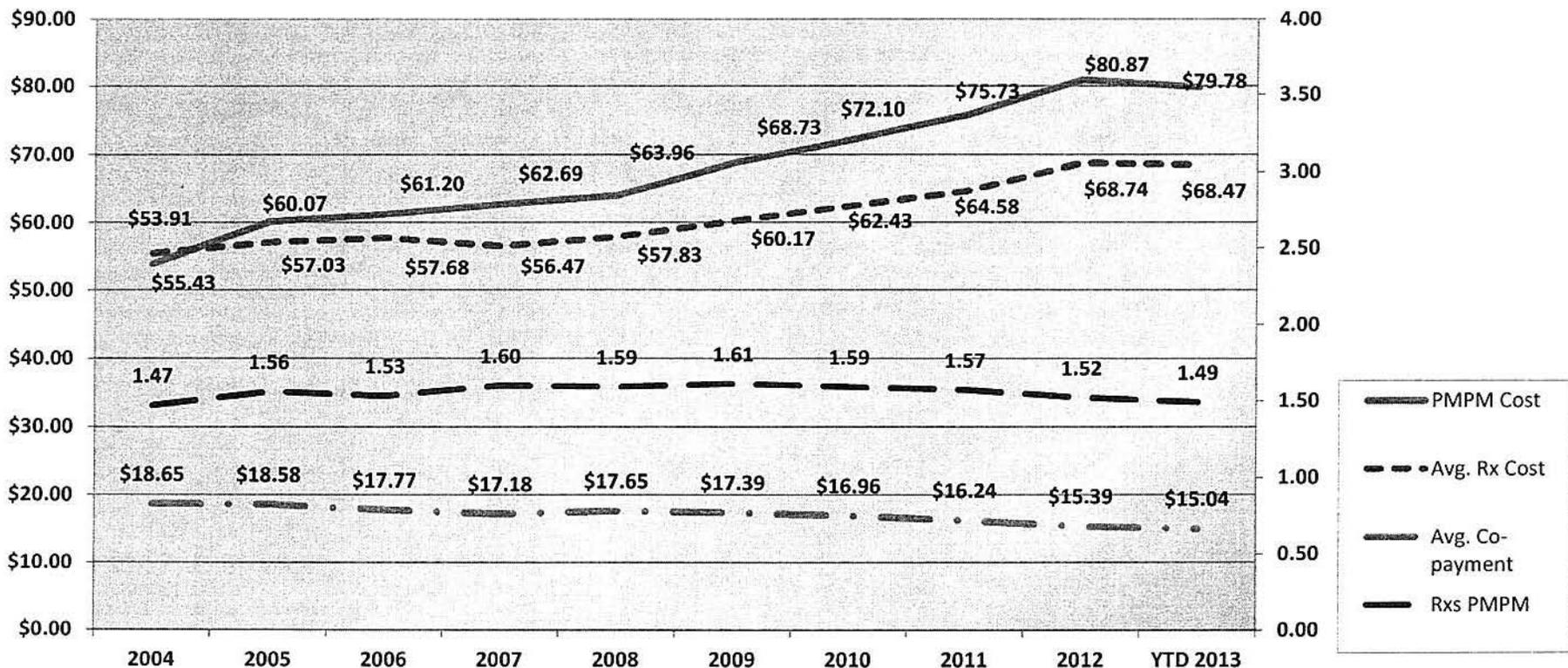
Breo Ellipta Inh (fluticasone furoate/vilanterol)		Advair Disk (\$258), Advair HFA (\$240), Duera (\$268), Symbicort (\$247)	\$320/mo	Tx of bronchitis, COPD, emphysema	Advantage - once daily dosing. BREO = brand name for the medication combination. Ellipta = name for the inhalation device	Exclude. Indicated for COPD. Trial was vs placebo, not other ICS/LABA combos. (Boschia JA, et al. Effect of once daily fluticasone furoate/vilanterol on 24 hour pulmonary function in patients with COPD: a R, 3-way, incomplete block, crossover study. Clin Therapeutics. 2012;34(8):1655-1666. The drug was better than placebo. Not yet indicated for asthma. One trial evaluating safety and tolerability. More expensive than any of the others.
LidoRx 3% gel	Lidocaine 2% jelly - \$19/30ml		\$147/30ml bottle	Topical anesthesia	New dosage strength	Exclude. There is already OTC : 0.5%, 2%, 4%, 5% gels available. There is also Rx 2% jelly.
Prolensa Solution 0.07%	bromfenac ophthalmic soln	Bromday 0.09% (\$205/1.7ml), Bromfenac 0.09% \$145/2.5ml	\$205/1.6ml	Tx of ocular pain/inflammation		Exclude. Ophthalmic NSAID. This is the only 0.07%. There is brand and generic bromfenac 0.09% soln. Pay more for less. There were several trials in PubMed but they seemed to all use 0.09%. The 2 studies in the PI were vs placebo. It works better than placebo for post cataract removal on the endpoints inflammation and pain.
Prezista Susp 100mg/ml (specialty drug)	darunavir	Prezista tabs pricing: 75mg/\$2.72;150mg/\$5.45;400mg/\$21.8 1.82;600mg/\$21.8 7;800mg/\$43.63	\$725/200ml bottle (\$3.46/100mg)	Tx of HIV infection	New dosage form. Prezista currently covered by plan	Line extension. Consider upper age limit for the suspension or consider exclusion if other tablets or capsules are on profile.
Namenda XR caps (7,14,21,28 mg and titration pack)	mementine	Namenda immediate release. Dose = 20mg/day. \$318/30 days	\$302/30 days	Treatment of Alzheimer's disease. Dose = 28mg/day	Namenda immediate release expected to be available in generic version early 2015.	Propose to PA all existing mementine, allowing access for MMSE 14 or less. Once approved, the pt would be approved for life. Consider move to T3 for both IR and XR. Price is similar. If cover XR, place QL of 1tab/day (31/31d). IR is currently T2. IR is BID with doses >5mg. Target is 20mg daily given 10mg BID. ArchNeuro Meta-analysis: Mementine lacks evidence of benefit in AD if MMSE score is 14 or less. Schneider LS, et al. Lack of Evidence for the efficacy of mementine in mild AD. Arch Neurol. 2011;68(8):991-998. CochSystRev, Mementine in dementia: Main results: 1. Moderate to severe AD. Two out of three six month studies show a small beneficial effect of mementine. Pooled data indicate a beneficial effect at six months on cognition (2.97 points on the 100 point SIB, 95% CI 1.68 to 4.26, P < 0.00001), activities of daily living (1.27 points on the 54 point ADCS-ADLsev, 95% CI 0.44 to 2.09, P = 0.003) and behaviour (2.76 points on the 144 point NPJ, 95% CI 0.88 to 4.63, P=0.004), supported by clinical impression of change (0.28 points on the 7 point CIBIC+, 95% CI 0.15 to 0.41, P < 0.0001). 2. Mild to moderate AD. Pooled data from three unpublished studies indicate a marginal beneficial effect at six months on IIT cognition (0.99 points on the 70 point Consider upper age limit to select out children or others who cannot swallow and are not currently using other tablets or capsules.
Afinitor tabs for oral suspension (2,3 and 5mg) (specialty drug)		Afinitor 5mg = \$315/tab.	AWP = \$315/tab	New dosage formulation (Disperz) tabs for suspension - for children with rare brain tumor	Disperz tabs = same price as regular tabs	
Suprax 400mg capsules		Suprax 400mg tabs. \$20.17/tab	\$20.17/cap		new dosage formulation	Cover 400mg tab or capsule with a QL of 1 per rx. Exclude all other brand Suprax. Alternative 3GCSs are available (cefepodoxime, and cefdinir (Omnicef).
Suprax Suspension 500mg/5ml		Suprax 200mg/5ml = \$511/75ml	10ml bottle = \$171, 20ml bottle = \$342	Antibiotic - third generation cephalosporin	New dosage strength	Exclude
Zenzedi 2.5mg tabs	dextroamphetamine sulfate	Dextroamphetamine 5mg \$2.90/tab	\$5.17/tab	Tx of ADHD and narcolepsy	Zenzedi is available in 2.5,5,7.5, and 10mg tabs. All strengths are available generically except 2.5 and 7.5mg	Exclude or RP to other generics. This is a branded generic. Only 2.5mg tablet. Generic is scored 5mg tab. Use:ADHD, narcolepsy. Very few start at 2.5mg tab (very young).
Zenzedi 7.5mg tabs	dextroamphetamine sulfate		\$5.17/tab	Tx of ADHD and narcolepsy		Exclude or RP to other generics. This is a branded generic. Only 2.5mg tablet. Generic is scored 5mg tab. Use:ADHD, narcolepsy. Very few start at 2.5mg tab (very young).
Flumist				Influenza virus vaccine live quadrivalent intranasal suspension		Cover for free. Added another B strain (previously had 2 A strains and 1 B strain).

Fluzone inj				Influenza virus vaccine live quadrivalent injection		Cover for free. Added another B strain (previously had 2 A strains and 1 B strain).		
EX Flu Shot Kit				influenza virus vaccine split quadrivalent inj kit		Exclude kits		
EZ Flu Shot Kit PF			\$328/unit			Exclude kits		
Topicort Spray 0.25%(desoximetasone)		desoximetasone topical cream \$10.61/15gm tube	\$502/100ml bottle	Topical, medium to high-potency synthetic fluorinated corticosteroid		This is the only spray. There are both brand and generic 0.25% creams and ointments.		
Nymalize Solution (nimodipine) 60mg/20ml		Nimodipine 30mg caps \$5,352/21 days	\$9,000/21 days of therapy	Treatment of subarachnoid hemorrhage. 60mg by mouth every 4 hours x 21 days	New oral formulation may help reduce potentially fatal medication errors.	Exclude. Use nimodipine capsules or nicardipine. No evidence of fatal medication error reduction vs oral capsule. Nimodipine 30mg oral capsules available. CochSysRev says oral nimodipine reduces post SAH disability.		
Simponi	Golimumab					For UC. 2 trials in UC. Induction/remission. Other for maintenance. Added to PA criteria.		
Revlimid	lenalidomide 20mg					New strength for patients needing to step down 5mg due to neutropenia. Dx is for mantle cell lymphoma (a NHL) after 2 prior therapies (including 1 w/bortezomib). The dose is 25mg qd. Trials supporting revlimid in this cancer are phase 1&2 measuring overall and complete response rates. A large % (45%) drop out. We need a more comprehensive approach. Will not add mantle cell lymphoma due to lack of data in this type of cancer. NO OS data.		

**Employee Benefits Division
Prescription Drug Program
Plan Performance Summary**

CY 2004 – July 2013

Employee Benefits Division (EBD) Prescription Drug Program Trend Analysis - 2004 – July 2013



The chart above tracks the following parameters related to plan performance between 2004 and 2011; (**PMPM Cost** – Blue Line) and three primary drivers of PMPM Cost; (**Average Claim Cost** – Red Line), (**Average Co-payment** – Green Line), and (**Utilization Rate** – Black Line). Note that the Utilization Rate (Rxs/Member/Month) is tracked by the right-hand vertical axis and all other parameters are tracked by the left-hand vertical axis.

Brand / Generic Usage Summary 2004 – July 2013

Year	Generic %	Avg. Plan Paid/Rx		
		Generics	Brands	Overall
2004	46.07%	\$13.11	\$57.01	\$36.78
2005	52.52%	\$14.20	\$65.26	\$38.44
2006	57.86%	\$14.93	\$74.20	\$39.91
2007	64.98%	\$13.88	\$86.44	\$39.29
2008	69.92%	\$14.20	\$100.56	\$40.18
2009	71.57%	\$15.19	\$112.24	\$42.78
2010	75.30%	\$16.86	\$132.66	\$45.47
2011	77.88%	\$18.11	\$154.70	\$48.33
2012	81.20%	\$21.78	\$189.67	\$53.35
YTD 2013	84.15%	\$22.54	\$217.37	\$53.43

The table above summarizes the following parameters pertaining to the plan's generic drug usage between 2004 and July 2013; (1) Generic Dispensing Rate, (2) Avg. Plan Paid/Rx for Generics, (3) Avg. Plan Paid/Rx for Brands, and (4) Blended Avg. Plan Paid/Rx

Specialty Drug Usage Summary

2004 – July 2013

Calendar Year	Total Plan Paid	Total Plan Paid for Specialty Drugs	Avg. Plan Paid/Specialty Rx	Specialty % of Total Rx's	Specialty Spend as % of Total Plan Paid
2004	\$81,605,224	\$7,046,248	\$988.69	0.3%	8.6%
2005	\$91,539,227	\$10,023,899	\$1,128.92	0.3%	11.0%
2006	\$92,699,095	\$10,751,182	\$1,213.15	0.3%	11.6%
2007	\$96,681,390	\$13,108,089	\$1,336.80	0.3%	13.6%
2008	\$98,828,258	\$15,648,548	\$1,496.09	0.3%	15.8%
2009	\$105,880,896	\$17,448,151	\$1,602.78	0.3%	16.5%
2010	\$114,729,112	\$19,387,783	\$1,792.66	0.3%	16.9%
2011	\$125,182,115	\$20,054,719	\$1,951.24	0.3%	16.0%
2012	\$140,171,349	\$22,849,667	\$2,155.11	0.3%	16.3%
YTD 2013	\$83,812,393	\$14,565,186	\$2,324.90	0.3%	17.4%

The table above summarizes the following parameters related to the plan's Specialty Drug usage between 2004 and July 2013. (1) Total Plan Paid for all Prescription Drugs, (2) Total Plan Paid for Specialty Drugs, (3) Avg. Plan Paid/Specialty Rx, (4) Rx's for Specialty Drugs as % of Total Rx's, and (5) Plan Paid for Specialty Drugs as % of Total Plan Paid.

Specialty Drug Pricing History¹ Since 1/1/2010

Drug	Therapeutic Use	Total Plan Paid 2Q2013	Since 1/1/2010	
			Number of Price Increases	% Change since 1/1/2010
Humira	Rheumatoid Diseases	\$1,008,433	6	46.0%
Enbrel	Rheumatoid Diseases	\$866,952	6	45.0%
Copaxone	Multiple Sclerosis	\$717,670	5	67.0%
Gleevec	Oncology	\$476,797	7	67.0%
Rebif	Multiple Sclerosis	\$224,026	7	74.0%
Avonex ²	Multiple Sclerosis	\$147,612	3	19.0%
Betaseron	Multiple Sclerosis	\$130,768	7	62.0%
Revlimid	Oncology	\$210,010	4	20.0%
Norditropin	Growth Hormone	\$172,108	4	23.0%
Tarceva	Oncology	\$55,438	6	43.0%
Subtotal		\$4,009,814		
All Specialty		\$6,091,763		

¹ – Pricing Source: Medispan Master Drug Database – Wolters Kluwer Health 2013

² - Avonex package evaluated appears to have entered the market in April 2012

Recent Cost Containment Initiatives Implementation Date: June 2013

Drug / Drug Category	EBD Action	1Q2013			June-July 2013			Monthly Savings	Annualized Savings
		# of Rxs	Total Plan Cost	Plan Paid/Month	# of Rxs	Total Plan Cost	Plan Paid/Month		
Lovaza	Exclusion	936	\$160,260	\$53,420	0	\$0	\$0	\$53,420	\$641,040
Glumetza	Exclusion	82	\$35,656	\$11,885	0	\$0	\$0	\$11,885	\$142,624
Nasal Steroids	Reference Pricing	8,341	\$275,618	\$91,873	4,318	\$105,101	\$52,551	\$39,322	\$471,866
Overactive Bladder Agents	Reference Pricing	2,645	\$313,353	\$104,451	1,567	\$92,330	\$46,165	\$58,286	\$699,432
Testosterone	Topical Exclusion / limit coverage to injectable	937	\$315,603	\$105,201	292	\$24,650	\$12,325	\$92,876	\$1,114,512
Totals		12,941	\$1,100,490	\$366,830	6,177	\$222,081	\$111,041	\$255,790	\$3,069,474

Upcoming Initiatives for August 2013

Drug / Drug Category	EBD Action	Projected Annual Savings
Intuniv	Exclusion	\$73,000
Naprelan	Exclusion	\$141,000
Proton Pump Inhibitors	Adj. of Reference Price	\$1,000,000
Totals		\$1,214,000