AGENDA

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

August 3, 2015

1:00 p.m.

EBD Board Room – 501 Building, Suite 500

I. Call to Order.....Dr. Hank Simmons, Chairman

II. Approval of April 6, 2015 Minutes .....Dr. Hank Simmons, Chairman

III. Delivery Coordination Workgroup.....Dr. Geri Bemberg, UAMS

IV. Benlysta Review .....Dr. Jill Johnson, UAMS

V. New Drugs.....Dr. Jill Johnson, UAMS

VI. EBD Report .....Dr. Geri Bemberg, UAMS

Upcoming Meetings

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
August 03, 2015

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday August 3, 2015 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Little Rock, AR.

Voting Members present:
Dr. William Golden
Dr. Scott Pace
Dr. John Kirtley
Larry Dickerson
Dr. Hank Simmons – Chairman

Non-Voting Members present:
Dr. Jill Johnson
Connie Bennett
Dr. Geri Bemberg

Members absent:
Melodee Harris
Dr. Kat Neill – Vice Chairman
Dr. Appathurai Balamurugan

Lori Eden, Deputy Director, Employee Benefits Division

OTHERS PRESENT
Dwight Davis, Geri Bemberg, UAMS College of Pharmacy; Sherry Bryant, Ethel Whittaker, Janna Keathley, Gretchen Baggett, Tracy Tidwell, EBD; Gini Ingram, ACHI; Marc Watts, ASEA; Steve Johnston, N. Nordisk; Charlene Kaiser, Amgen; Takisha Sanders, Health Advantage; Wayne Whitley, Ronda Walthall, AHTD; Sharon Jackson, GSK; Bridgett Johnson, Pfizer; Andy Davis, Arkansas Democrat Gazette; Martha Hill, Jim Chapman, Brian Strickland, Gilead; Sam Smothers, Astra Zeneca

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 April 3, 2015 minutes. Dr. Kirtley made the motion to approve. Pace seconded. All were in favor.

Minutes Approved.

DELIVERY OF COORDINATION WORK GROUP REPORT: *by Dr. David Keisner, UAMS*

The following report resulted from a meeting of the DUEC on August 3, 2015 with Dr. Hank Simmons presiding.

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

Cancer and non-cancer drugs were reviewed by the DCWG and a report was made to the DUEC on August 3rd. Recommendations from this report are outlined below.

	Current Coverage	Proposed Coverage for 2015
Targretin (bexarotene) capsules	T4, No PA Required	T4PA (grandfather existing members)
Targretin (bexarotene) Gel	T4 No PA Required	Exclude (no current utilizers)
Acute lymphoblastic leukemia (All)		
Blincyto (blinatumomab)	New Drug	Exclude
Hematopoietic Stem Cell Mobilization		
Mozobil (plerixafor)	Medical, no PA Required	Medical PA

Dr. Kirtley motioned to approve the delivery coordination group recommendations. Dickerson seconded. All were in favor.

Motion Approved

B. Belimumab (Benlysta) – Follow Up: *by, Dr. Jill Johnson, UAMS*

The Board voted to exclude this drug in November 2014 with 90 day notice and no grandfathering. At this time, the DUEC recommends that we change our grandfathering policy for this drug for patients who were previously on the medication under the plan. DUEC will revisit the coverage policy in six (6) months. Dickerson motioned to revisit in six (6) months. Dr. Kirtley seconded. All were in favor.

Motion Approved

2. NEW DRUGS

Johnson reported on new drugs. The review covered products released March 2 – June 6, 2015.

Recommended Additions:

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	DUEC VOTE
Proair Respi Aer	Albuterol sulfate aer po BA 108 mcg/act	$60/1 box (90mcg base)	New Dosage formulation of Proair-treatment of asthma	Proair HFA inhaler (tier2) -$53/inhaler 90mcg base	Tier 2
Corlanor Tabs	Ivabradine tabs	$450/60 – 7.5 mg tabs	Treatment of heart failure		Tier 3 PA
Fosrenol Powder	Lanthanum carnonbate Oral Powder pack	1000mg powder pack $11.21	New Dosage form. Also available in chewable tabs. For treatment of hyperphosphatemia	Fosrenol tabs 1000mg chewable tab $11.21	Tier 3
Ritalin LA Caps 60 mg	Methylphenida te caps SR 24hr 60mg (LA)	$10.94/cap	Treatment of ADHD/norcolepsy	Methylphenidate ER ($5 each) T1 w/Qls. Ritalin LA T3 w/QL. LA amphetamines are RP'd for members age >26y.	Tier3, QL 1/1. RP for age >26y.
Stiolto AER Respimat	Tiotropium br [Spiriva] and olodaterol [Striverdi]	$378/4GM	Combination inhaled anticholinergic and a LABa used for COPD, emphysema	Spiriva (T2) Striverda-coded as reject at seq 1 and coded as PA at seq 10??	Tier 3

1. **Proair Respi Aer – Pace motioned to approve. Dickerson seconded. All were in favor. Motion Approved.**
2. **Corlanor Tabs – Pace motioned to approve. Dickerson seconded. All were in favor. Motion Approved.**
3. **Fosrenol Powder – Kirtley motioned to approve. Dickerson seconded. All were in favor. Motion Approved.**
4. **Ritalin LA Caps 60 mg – Kirtley motioned to approve. Dickerson seconded. All were in favor. Motion Approved.**
5. **Stiolto AER Respimat – Kirtley motioned to approve. Dickerson seconded. All were in favor. Motion Approved.**

Recommended Exclusions

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES	DUEC

				ON FORMULARY/AWP	VOTE
Fentanyl TD Patch	Fentanyl Tansdermal patch	$65.00//$94.00/$129-New strengths available from one source – Mylan	New dosage formulations. Treatment of mild-moderate pain.	Generic strengths ranging from 12mcg – 100 mcg from multiple mfg. Currently covered T1 with quantity limits. Pricing examples:50 mcg/$26,75mcg/$40, 100mcg$53	Excld, code 13
Nuvessa Gel 1.3%	Metronidazole vaginal gel 1.3%	$186/application-dosage= one single application	Treatment of bacterial vaginosis	Metronidazole Vag gel 0.75% 70 gm tube=$33. (dosage = 1-2 times a day for 5 days.	Excld, code 13.
Toujeo Sol Inj 300IU/ML	Insulin glargine sol pen-injector 300 units/ml	$402/3pens (1,350 units)($0.30/unit)	Type 1 and type 2 diabetes	Lantus 100u/ml – tier 2 ($.30/unit)	Excld, code 13.
Natesto Gel 5.5Mg	Testosterone nasal gel	$238/bottle	Treatment of hypogonadism	Topical testosterone products excluded. Injectable testosterone covered tier 1 with PA	Excld, code 13
Zohydro ER Caps-10/15/20/30/40/50MG	Hydrocodone birartrate cap SR 12 hour abuse-deterrent	$7.37 - $9.00/tab depending on strength	Moderate-severe pain	Zohydro (non-abuse deterrent excluded by plan	Excld, code 13
Avycaz IV Solution	Ceftazidine-avibactam sod IV soln	N/A	Treatment of intraabdominal infections. Pyelonephritis, UTI – not in scope of pharmacy benefits.		N/A hospital
Cresemba Caps	Isavuconazonium sulfate caps	$1,176/14 caps	Azole antifungal indicated for treatment of adults with invasive aspergillosis or invasive mucormycosis Dose= 2 caps every 8 hours x 6 doses then 2 caps daily	Itraconazole (tier1) - $900/90caps. Vfend $2,653/30caps	Excld.
Cresemba Inj 372 MG	Isavuconazonium sulfate IV solution	N/A	Azole antifungal indicated for treatment of adults with invasive aspergillosis or invasive mucormycosis-not in scope of pharmacy benefits		N/A Hospital
Liletta IUD	Levonorgestrel releasing IUD 18.6 mcg/day (52mg total)	$750 each	Intrauterine contraceptive	IUD's excluded under pharmacy benefits	N/A Medical

Omidria Inj 1-0.3%	Phenylephrine-ketorolac intraocular soln 1-0.3%	$558/4ml	For use during cataract surgery or intraocular lens replacement to maintain pupil size by preventing intraoperative miosis and to reduce post operative ocular pain – out of scope of pharmacy benefits		N/A Medical
Pristiq 25 MG Tab	Desvenlafaxone succinate tab SR 24hr 25mg tab	$9.26/capsule	New dosage formulation	Other dosage strengths of Pristiq excluded under pharmacy benefits	Excld
Provida DHA Caps	Prenatal vitamin	$2/capsule	Prenatal vitamin	Other dosage strength	Excld
Saxemda Inj 6MG/ML	Liraglutide (weight mgmt.) soln pen inj 6mg/ml	$1,281/box of 3 pens	Treatment of obesity as an adjunct to a reduced-calorie diet and increased physical activity.	Anti-obesity agents excluded under pharmacy benefits	Excld code 9
Namzaric Caps	Memantine[Namenda]-donepezil[Aricept] cap SR 24hr	$386/30 caps (28mg mematine, donepezil 10mg)	Treatment of Alzheimer's disease	Tier 3 options: Namenda 10mg $296/60);Namenda XR 28 mg ($356/30); Aricept 10mg ($1,070/30);donepezil 10mg ($963/30)	Excld code 13
Argatroban Inj	Argatroban inj IV soln 250mg/250ml	N/A	Synthetic IV thrombin inhibitor not in scope of pharm benefit.		N/A
Levoleucovor inj 50mg	Levoleucovorin calcium inf 175mg/17.5ml	N/A	For treatment of methotrexate toxicity not of Pharm benefit		N/A
Aptensio XR Caps	Methylphenidate ER 24 hr caps	$7.80/cap	Treatment of ADHD/narcolepsy	Methylphenidate ER ($5 each) covered tier 1 w/Qls. Ritalin LA tier 3 w/QL. La amphetamines are RP'd for mbs. 26 age	Excld 13
Saphris Sublingual Tabs	Asenapine maleate sublingual tabs	$16.65/2.5mg	New 2.5 mg sblingual dose. Other dosages: 5 and 10mg. Used for bipolar disorder and schizophrenia	Saphris excluded under pharmacy benefit	Excld 13
Tivorbex Caps	Indomethacin 20 and 40mg caps	$4.20/cap	Lower dosage form of indomethacin	Indomethacin generic cv T1 25mg=$0.35	Excld 13
Enbrace HR Caps	Prenatal vitamin	$4.31/Cap	Prenatal vitamin	Various generics	Excld 7
Caya Diaphragm	Diaphragm arc-spg	$90/each	Contraceptive	Diaphragms excld under pharm benefit	Cover at 100%
Doryx 50mg Tabs	Doxycycline hyclate tab delayed release 50mg	$11.98/tab	Anti-infective agent. New dosage strength	Other dosage strengths of doxycycline hyclate delayed release coded	Excld 13

				to reject	
Varizig 125 units	Varicella-zoster immune glob(human)Im inj 125u/1.2ml	$1,422/1.2ml vial	For varicella (chicken pox) infection prophylaxis		N/A
IRENKA CAPS40MG	Duloxetine HCL 40mg	$8.72/40mg cap	Antidepressant	Duloxetine reference priced on plan	Excld 13
Ionsys Pad 40mcg/AC	Fentanyl HCL iontophoretic TD system 40mcg/act	$240 patch	A patient crtl iontophoretic transdermal system providing ondemand systemic delivery of fentanyl for up to 24hrs or a max of 80 doses, whichever comes first	Should only be used for hospitalized patients and should be discontinued before patients are discharged	N/A Hospital

Other Exclusions:

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	DUEC VOTE
Hysingla ER	Hydrocodone bitartrate ER 24 Hr Abuse-Deterrent	$7.88-$40/cap depending on strength	Pain management	Other long-acting pain meds available	Exclude, code 13 effective 1/1/16
Namenda XR & Titration Pack	Memantine hydrochloride ER 24 hour capsule	$12.88/cap	Mild-to-moderate dementia of the Alzheimer type	Currently covering Namenda IR	Exclude, code 13

6. **Fentanyl TD Patch – Dickerson motioned to exclude. Kirtley seconded. All were in favor. Motion approved.**
7. **Nuvessa – Kirtley motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
8. **Toujeo Sol Inj 300Iu/ML - Dickerson motioned to exclude. Kirtley seconded. All were in favor. Motion approved.**
9. **Natesto Gel 5.5Mg – Kirtley motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
10. **Zohydro ER Caps,10/15/20/30/40/50mg. – Dickerson motioned to exclude. Kirtley seconded. All were in favor. Motion approved.**
11. **Cresemba Caps – Kirtley motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
12. **Cresemba Inj 372 MG – Kirtley motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
13. **Pristiq – Pace motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
14. **Provida DHA Caps – Pace motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
15. **Saxemda Inj 6MG/ML – Pace motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
16. **Namzaric Caps – Pace motioned to exclude with a 90 day notice. Dickerson seconded. All were in favor. Motion approved.**
17. **Aptensio XR Caps – Dickerson motioned to exclude. Pace seconded. All were in favor. Motion approved.**

18. **Saphris Sublingual Tabs – Kirtley motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
19. **Tivorbex Caps – Kirtley motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
20. **Enbrace HR Caps – Kirtley motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
21. **Caya Diaphragm – Kirtley motioned to exclude. Dickerson seconded. All were in favor. Motion approved.**
22. **Doryx 50mg Tabs – Kirtley motioned to exclude. Pace seconded. All were in favor. Motion approved.**
23. **IRENKA CAPS40MG – Kirtley motioned to exclude. Pace seconded. All were in favor. Motion approved.**
24. **Hysingla ER – Kirtley motioned to exclude. Pace seconded. All were in favor. Motion approved.**
25. **Namenda XR & Titration Pack – Kirtley motioned to exclude. Pace seconded. All were in favor. Motion Approved.**

Specialty Drugs:

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	DUEC VOTE
Lenvima	Lenvatinib	$2,790/pak (15-24mg caps)	Treatment of pts w/locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC). Dose= up to 24mg daily in 28 day cycle.	DCWG to address in October 2015 meeting	Excld
Docetaxel 200mg/20ml for IV infusion	Docetaxel		Not pharmacy		N/A
Farydak(limited disb)	Panobinostat lactate capsules	6-20mg caps=$8,232. Dose=20mg on day 1,3,5,8,10,12	A histone deacetylase inhibitor, in combination with bortezomib & dexamethasone, is indicated for the treatment of patients with multiple myeloma who have receive at least 2 prior regimens.		Excld 1
Novoeight Inj	Antihemophilic factor (recombinant)for inj-1500 units, 2000units,3000 units	$1.91 /unit	Treatment of hemophilia A	Other hemophilia A treatments	T4 PA
Aranesp Inj 100mcg	Darbepoetin alfapolysorbate 80 soln inj 10mcg/0.4ml	$85.14/syringe	Treatment of Anemia	Other dosage strengths	T4 PA

Kalydeco Pak -50 & 75 mg	Ivacaftor packet	Each dose=$512 each	Treatment of cystic Fibrosis	Kalydeco tab 150mg tab ($512/tab)	T4 PA
Mircera Inj 200 mcg	Methoxy polyethylene glycol-epoetin beta inj 200 mcg/0.3ml	$432/syringe	Treatment of Anemia	Other dosage strengths of Mircera	T4 PA
Jadenu Tabs (limited)	Deferasirox tabs	90 mg=$34;180mg=$68;360 mg=$136	A new formulation of Exjade	Exjade for oral suspension covered under specialty tier.	T4 PA
Natpara Inj (limited)	Parathyroid hormone for injection cartridge	$9,500/2-50mcg cartridges for subcutaneous injection	Treatment of hypocalcemia and hypoparathyroidism		Exc1 13
Cholbam Caps	Cholic acid caps	#30-50mg caps $9,930 #30-250mg caps$29,880	For treatment of bile acid synthesis disorders,, peroxisomal disorders, Zellweger spectrum disorders	N/A	Excld 1

26. **Lenvima – Kirtley motioned to exclude. Pace seconded. All were in favor. Motion approved.**
27. **Farydak (limited disb) - Kirtley motioned to exclude. Pace seconded. All were in favor. Motion approved.**
28. **Novoeight Inj – Kirtley motioned to approve. Pace seconded. All were in favor. Motion approved.**
29. **Aranesp Inj 100MCG – Kirtley motioned to approve. Pace seconded. All were in favor. Motion approved.**
30. **Kalydeco Pak 50 and 75mg – Kirtley motioned to approve. Pace seconded. All were in favor. Motion approved.**
31. **Mircera Inj 200mcg – Kirtley motioned to approve. Pace seconded. All were in favor. Motion approved.**
32. **Jadenu Tabs (limited) – Kirtley motioned to approve. Pace seconded. All were in favor. Motion approved.**
33. **Natpara Inj (limited) – Dickerson motioned to approve. Kirtley seconded. All were in favor. Motion approved.**
34. **Cholbam Caps – Dickerson motioned to exclude. Kirtley seconded. All were in favor. Motion approved.**
35. **Juztapid 30,40,60mg caps – Dickerson motioned to exclude. Kirtley seconded. All were in favor. Motion approved.**

<u>Compound Kits/Bulk Chemicals/No Indication</u>

BRAND NAME	GENERIC NAME	PRICING (AWP)	INDICATION	SIMILAR THERAPIES ON FORMULARY/AWP	DUEC VOTE
Menthocin pad Lidocain	Lidocaine-capsaicin-men-methyl sal patch				Excld
Procarbazine powder					Not Address
Permavan Pad	Lidocaine-dm-trolamine salicylate patch				Not Address
Remaxazon	Lidocaine-capsaicin-chondroitin-glucos patch				Excld
Comfort EZ Pad	Methyl salicylate-lidocaine-menthol patch				Excld
Pharm Ch Tsx Pad	Methyl salicylate-lidocaine-menthol				Excld
Sorbitol Cry Candy	Sorbital candy base				Excld
Methylmethacrylate crosspolymer powder					Not Address
Pullulan powder					Not Address
Sodium bitartrate					Not Address
Canoginex Spray	Camphor-histamine-menthol				Not Address
Lidovin Cream 3.95%	Lidocaine cream 3.95%				Excld
Lidozol Cream 3.75%	Lidocaine crm 3.75%				Excld
Tetramex Spray	Tetracaine-men-spry				Excld
Anodynerx Pad	Capsaicin-lidociane				Excld
Dermacinrx Kit Combo	Chlorhexidine soln				Excld
Nazirex Cream	Levocetirizine crm				Excld
Dermacinrx Kit Silapak	Dimethicone cream				Excld
Atendia Pad	Lidocaine-menthol				Excld
Betamethasone sod7mg/ml	Mfg: US Compound				Not Address
Betamethasone sod (6-6)mg/2ml	Mfg: US Compound				Not Address
Dermacinrx Kit	Diclofenac sod tab 75mg				Excld
Dermacinrix Kit SilaPak	Triamcinolone acet cream 0.1%				Excld
Methylprednisolone acetate 100mg.	Mfg: US Compound				Not Address
Testone Cik kit	Testosterone cypionate IM inj in oil 200mg/ml				Not Address
Betamethasone sodium 25mg/ml					Not Address
Kudzu root powder					Excld
Methyprednisolone 40mg/ml	Mfg: US Compound				Not Address
Testosterone implant pellets	Mfg: US Compound				Not Address
Triamcinolone/lidocaine	Mfg: US Compound				Not Address

Testosterone inj 250mg	Mfg: US Compound				Not Address
Vit K2 bulk powder					N. Add
Capsaicin powder					N. Add
Dermacinrx Solution	External vehicles				Excld
Renovo lido5 cream	Lidocaine-capsaicin				Excld
Urevaz Cream	Urea cream 44%				Excld
I-Lids cleans Soln	Hypochlorous acid cleanser 0/01%				Excld
Mic Combo Inj	Mfg: US Compound				N. Add
Test EO-Pro-Inj Cyp 220	Mfg: US Compound				Excld
Brompheniram Inj 10mg/ml	Mfg: US Compound				N. Add
Estradiol Implant Pellet	Mfg: US Compound				N. Add
Sod Hyaluronate-Lidocaine PF Soln	Mfg: US Compound				N. Add
Hyaluronidase Bovine	Mfg: US Compound				N. Add
Lincomycin HCl-lidocain	Mfg: US Compound				N. Ad
Medroxprogesterone	Mfg: US Compound				N. Add
Testosterone Impland	Mfg: US Compound				N. Add
Triamcinolone Acetonide	Mfg: US Compound				N. Add
Pine Bark Extract	Mfg: US Compound				N. Add
Renuu Nl Pad 2-30%	Mfg: US Compound				Excld
Anasept SPR	Mfg: US Compound				Excld
Citrus Pow Bergamot	Citrus bergamot oral powder250mg				Excld
Ademetionnine powder					N. Add
Calcium amino acid chelate granules					N. Add
Magnesium amino acid chelate powder					N. Add
Tocopherols powder					Excld
Dermacinrx Inflam					Excld
Misc:					
Toxicol Salv Kit	Toxicology saliva collection kit		Not in pharm bene		N/A
Thallous Inj TL 201	Thallous chloride TL 201 inj		Diagnostic aid not in pharmacy benefit		N/A
Glucagon Inj 1MG	Glucagon HCl diagnostic for inj		Not in pharmacy benefit		N/A

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

Dr. Bemberg reported the health insurance rates for 2016 will remain the same as 2015 rates. Moving forward rebates will be processed internally.

Bennett reported the mid year trend of the plan performance is 7.8% about 2 1/2% lower than the benchmark. The generic dispensing rate increased by 1.4%, almost a 90% dispensing rate. One of the top twenty (20) trending classes in non-specialty meds are the anticoulagants. The largest increase is in the specialty drugs.

Kirtley motioned to adjourn. Pace seconded. All were in favor.

Meeting Adjourned

BEXAROTENE (TARGRETIN)

GEL:

FDA approved indication: Topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

-in studies, patients required to have failed or been intolerant to at least two prior therapies (including systemic, irradiation, and other skin-directed therapies)

Topical therapies (aka skin-directed therapies)		
	Response rate	**AWP (LexiComp)**
Steroid	90%	
Tazarotene (off label)	58%	0.05% (30 g): $329.32 0.1% (30 g): $349.84
Imiquimod (off label)	~50% (very small studies)	5% (12 applications): $796.93
Mechlorethamine	~50%	0.016% (60g): $3,480
Bexarotene 1% gel	Stage IA and IB: 28% Stage II: 0%	1% (60g): $15,551.50
Local radiation	Up to 100%	
Phototherapy (UVB, NB-UVB, PUVA)	62-81%	
Total skin electron beam therapy (reserved for severe symptoms, refractory disease due to "toxicities and lack of superior long term outcomes")	>90%	

CAPSULES:

FDA approved indication: Treatment of cutaneous manifestations of cutaneous T cell lymphoma (CTCL) who are refractory to at least one prior therapy

Systemic Therapies		
	Response rate	**AWP for 30d supply (LexiComp)**
Tretinoin	12% (little data)	~$8,000 (45 mg/m^2 divided BID)
Isotretinoin	43-100% (some studies very small)	~$1,500 (1 mg/kg/day)
Acitretin	59% (though some pt on combo tx)	$1152.5 (25 mg daily)
Interferon alpha	Up to 70%	~$10,000 (20 mu thrice weekly)*
Bexarotene	Early stage: 54% Advanced stage: 45-55%	~$70,000 (300 mg/m^2 daily)
Romidepsin	34%	~$30,000 (14 mg/m^2 weekly x 3 q4w)
Vorinostat	30%	~$14,000 (400 mg daily)
Extracorporeal photopheresis	50-70%	
Methotrexate	33-58%	~$100 (25 mg weekly)

BLINATUMOMAB (BLINCYTO)

MOA (LexiComp):

Blinatumomab is a bispecific CD19-directed CD3 T-cell engager which binds to CD19 expressed on B-cells and CD3 expressed on T-cells. It activates endogenous T cells by connecting CD3 in the T-cell receptor complex with CD19 on B-cells (malignant and benign), thus forming a cytolytic synapse between a cytotoxic T-cell and the cancer target B-cell. Blinatumomab mediates the production of cytolytic proteins, release of inflammatory cytokines, and proliferation of T cells, which result in lysis of CD19-positive cells.

FDA approved indication:

Treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)

	Clofarabine + chemo	**Chemotherapy**	**Liposomal vincristine (Marqibo)**	**Blinatumomab (Blincyto)**
CR rate	44%	47-73%	20%	43%
Median overall survival	6.5 mo	6-7.7 mo (all pt) 8-10.2 (pt with CR)	5 mo (all pt) 7.7 mo (pt with CR)	6.1 mo (all pt) Among pt with CR: MRD response: 11.5 mo MRD non-response: 6.7 mo
Toxicities	Infection, hepatotoxicity		Neuropathy, febrile neutropenia, constipation	Cytokine release syndrome (11%)
Cost	Clofarabine: 20 mg vial: $3204.46 Induction dose: 25 mg/m^2/d x 5d; may repeat after 21d Consolidation dose: 20 mg/m^2/d x 5d; may repeat once)		5 mg vial: $12630.40 Dose: 2.25 mg/m^2 weekly Median of 4 doses (range 1-18) given in trial: ~$50,000	35 mcg vial: $3814.28 Dose: Cycle 1: 9 **mcg**/d d1-7 followed by 28 **mcg**/d d8-28 Cycle 2-5: 28 **mcg**/d d1-28 Cycles repeat every 6 weeks Give 2 cycles as induction; if CR achieved, may give up to 3 consolidation cycles Cycle 1: ~$95,000 Cycles 2-5: ~$107,000

References:
-Acute Lymphocytic Leukemia NCCN guideline. Version 2.2014.
-Topp et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. Lancet Oncol 2015; 16: 57–66.

Bemberg
May 2015

Plerixafor (Mozobil)
Hematopoietic Stem cell Mobilizer

Indication: Mobilization of hematopoietic stem cells (HSC) for collection and subsequent autologous transplantation (in combination with filgrastim) in patients with non-Hodgkin lymphoma (NHL) and multiple myeloma (MM)

Plerixafor should be initiated after the patient has received filgrastim once daily for a minimum of 4 days, and may be repeated until sufficient cell collection for autologous transplant, up to a maximum of 4 days.

Dosed based on actual body weight at 0.24mg/kg. In renal impairment with a CrCl of ≤50mL/min, decrease to 0.16mg/kg. Maximum dose is 40mg, and dosing has not been studied in patients >175% of ideal body weight.

Adverse effects include fatigue, headache, dizziness, diarrhea, nausea, injection site reactions, and arthralgia.

Evidence

Plerixafor and G-CSF for autologous stem cell mobilization in patients with NHL, Hodgkin's lymphoma, and multiple myeloma: results from the expanded access program.

Before US approval, an expanded access program provided plerixafor to patients with NHL, Hodgkin's lymphoma, or MM who had not previously failed mobilization and were otherwise candidates for auto-SCT. (multi-center, open-label, single arm) Patients were given G-CSF, then plerixafor 0.24mg/kg starting day 4 with apheresis on day 5, repeating until collection was complete. 104 patients received ≥1 day of plerixafor.
Of the 43 NHL patients treated, 74% met the target number of cells; of the 7 HD patients, 57% met the target; and of the 54 MM patients, 89% met the target.

Plerixafor and G-CSF versus placebo and G-CSF to mobilize hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma

Phase 3, multicenter, randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of plerixafor with G-CSF. Patients received G-CSF subcu daily for up to 8 days. Beginning on day 4, patients received either plerixafor or placebo. Starting day 5, patients began daily apheresis for up to 4 days or until ≥$6x10^6$ CD34+ cells/kg were collected. Primary endpoint - % of patients collecting $6x10^6$ CD34+ cells/kg in less than or equal to 2 aphereses. 106 of the 148 (71.6%) of the patients receiving plerixafor and 53 of the 154 (34.4%) receiving placebo met the primary endpoint. 54% of plerixafor group reached target after 1 apheresis, whereas 56% of the placebo group required 4 aphereses to reach target.
Post-transplant results: After 12 months of follow-up, 141 of 148 (95.3%) of the plerixafor patients were alive versus 148 of 154 (96.1%) of the placebo patients.

Phase III Prospective Randomized Double-Blind Placebo-controlled Trial of Plerixafor plus Granulocyte colony-Stimulating Factor Compared with Placebo Plus Granulocyte Colony-Stimulating Factor for Autologous Stem-Cell Mobilization and Transplantation for Patients with non-Hodgkin's Lymphoma

Patients w/ NHL requiring autologous hematopoietic stem-cell transplant in 1st or 2nd complete or partial remission were eligible. Patients received GCSF subcu daily for up to 8 days. Beginning day 4, patients received either plerixafor or placebo subcu for up to 4 days. Starting on day 5, patients began daily apheresis for up to 4 days or until ≥$5x10^6$ CD34+ cells/kg were collected. Primary endpoint was the % of patients who collected ≥$5x10^6$ CD34+ cells/kg in 4 or fewer apheresis days.
89/150 (59%) of patients in the plerixafor group and 29/148 (20%) in the placebo group met the primary endpoint. For patients who had undergone transplant after the initial mobilization, patient survival at 12 months was 119/135 (88.1%) in the plerixafor group and 71/82 (86.6%) in the placebo group.

Recommendation: Restrict coverage of plerixafor (Mozobil) to patients with MM or NHL who have failed to achieve an adequate response to filgrastim for a minimum of 4 days.

Resources:

1. Shaughnessy P, Uberti J, Devine S, et al. Plerixafor and G-CSF for autologous stem cell mobilization in patients with NHL, Hodgkin's lymphoma, and multiple myeloma: results from the expanded access program. Bone Marrow Transplant (2013) 48;777-781.
2. DiPersio JF, Stadtmauer EA, Nademanee A, et al. Plerixafor and G-CSF versus placebo and G-CSF to mobilize Hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma. Blood (4 June 2009)113:23; 5720-5726.
3. DiPersio JF, Micallef IN, Stiff PJ, et al. Phase III Prospective Randomized Double-Blind Placebo-Controlled Trial of Plerixafor Plus Granulocyte Colony-Stimulating Factor Compared with Placebo plus Granulocyte Colony-Stimulating Factor for Autologous Stem-Cell Mobilization and Transplantation for Patients with non-Hodgkin's Lymphoma. J Clin Oncol 27:4767-4773.

DUEC Meeting
8/3/15

EBRx
Jill Johnson, Pharm.D., BCPS

Proprietary: DO NOT DISTRIBUTE other than EBRx/EBD Board/DUEC members

Belimumab (Benlysta) - follow-up
Holly Rowton
July 22, 2015

FDA Approved Uses: Treatment of SLE

Evidence:

Disease Control and Safety of Belimumab Plus Standard Therapy Over 7 Years in Patients with Systemic Lupus Erythematosus.

- **Design**: open-label, uncontrolled 7 year study. **Inclusion Criteria**: Patients who had completed the phase II, placebo controlled, randomized, double blinded 52 weeks study AND the open-label, uncontrolled 24 week study with an improvement in PGA score and no severe SLE flare in the last 30 days of the study. Patients had to have a SELENA-SLEDAI (SS) score of 6 or above for the original study. All patients were treated with Belimumab 10mg/kg in the long-term continuation study.
    - **Results**: Efficacy Endpoints – Determined by SRI response. SRI is a composite responder index that includes one measure of disease activity improvement (≥4-point decrease in SELENA–SLEDAI score) and two measures to ensure that the improvement in disease activity is not offset by a worsening of disease in organ systems (i.e., no new British Isles Lupus Assessment Group A and no more than one new B score) or by a decline in overall health status (i.e., <0.3-point increase from baseline in Physician's Global Assessment score)
    - 46% of antibody positive patients receiving treatment achieved an SRI response versus 29% with placebo in the original 52 week study. With the continuation study 57% of patients achieved an SRI response by year 2, and 65% by year 7.
    - Seronegative patients also showed an increase in response but by a lower percentage for years 1 and 2 but similar in years 3-7.
    - Similarly, SFI and BILAG flares showed a similar response (reducing over time from 70.9% to 44.7% for all flares by year 7) for all patients on Belimumab regardless of antibody status.
    - Corticosteroid use also decreased over time with a 55% reduction for those who remained on belimumab at year 7 (n=177).
- **Conclusion**: This study simply reflects that those who respond to belimumab within the first year and avoid serious AE during that time, tend to have a stabilization of their SLE even through year 7. This study has selection bias and so is not helpful as to a determination as to initial coverage.
- *Ginzler EM, Wallace DJ, Merrill JT, et al. Disease Control and Safety of Belimumab Plus Standard Therapy Over 7 Years in Patients with Systemic Lupus Erythematosus. J Rheumatol 2014; 41:300-7*

Belimumab in the treatment of systemic lupus erythematosus: high disease activity predictors of response

- **Design:** Pooled univariate and multivariate analyses (N=1684) identified baseline factors associated with an increased benefit of belimumab versus placebo as seen in the BLISS -52, and BLISS-76 trials.. These factors included the Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA–SLEDAI) ≥10, low complement (low C3 <90 mg/dl and Low C4 <16 mg/dl), anti-dsDNA positivity (≥30 IU/ml), and corticosteroid use of >7.5mg per day.
- Results: Statistically significant outcomes indicating that patients with greater baseline disease activity—as reflected by a SELENA–SLEDAI score of 10 or greater, corticosteroid use and low complement levels—benefited most from belimumab treatment. In these subgroups of patients, a range of clinical benefits with belimumab treatment was demonstrated, including improved disease activity, reduced risk of flares and an effect on steroid reduction.
- Low-Complement levels and high autoantibody levels have been associated with and increased risk of renal disease and severe SLE flares. Corticosteroid –related damage found to accumulate with long term (15 years) therapy
- *van Vollenhoven RF, Petri MA, Cervera R. Belimumab in the treatment of systemic lupus erythematosus: high disease activity predictors of response. Ann Rheum Dis* 2012; **71**:1343–1349

Real life experience on the effect of Belimumab in patients with active systemic lupus

- **Case Study:** Twenty patients with musculoskeletal symptoms were evaluated, three were discontinued for different reasons and seventeen completed eight injections of Belimumab during a six month period. Disease activity was evaluated by the SELENA-SLEDAI (SS) score, and only patients with score above 8 had the indication to receive belimumab. The functional assessment of chronic therapy fatigue (FACIT fatigue 13 items) was employed before and after the six month period. All patients were Caucasian and female with average age of 36.

- Results: 15 patients completed the study. The mean SS score (10.2 + −1.1) reduced to (1.1 + − 1.2) anti ds DNA antibody from 180 to 60U, 11 patients had anti DNA antibodies above the normal range (40U), C3 levels increased from 62 mg/dL to 98 mg/dL and corticosteroid dosage reduced from 20 mg to 7.5 mg/day. The mean FACIT score was 37.6 + −3.8 and improved to 48.8 + −3.3 after six months of belimumab treatment (a score of 52 on the FACIT represents zero fatigue). One patient with active joint issues and severe vasculitis went into remission on belimumab and 5 mg of prednisone.
- *Scheinberg and Golmia: Real life experience on the effect of Belimumab in patients with active systemic lupus. SpringerPlus 2014 3:758.*

Other: NICE Guidance: currently not recommended, but a review of the guidance was scheduled for the 6th Appraisal Committee meeting on June 23, 2015. The results are not yet published.

Conclusion: Belimumab may be particularly effective in patients characterised by higher SLE disease activity at baseline, who are identified by anti-dsDNA positivity, hypocomplementaemia, or requiring treatment with corticosteroids.

Recommendation: approve with PA. Patients must still be symptomatic after being on dMARDs, have corticosteroids use of >7.5mg per day, have hypocomplementaemia (C3 <90 mg/dl and/or C4 <16 mg/dl), and/or be anti-dsDNA positive (≥30 IU/ml, or who have shown marked improvement while on previously. Marked improvement may be shown by serious decline since having been removed from the medication. Patients who do not show marked improvement after 6 months should be discontinued.

Outcome: Reversed decision and decided to grandfather the person(s) who appealed, however, will not cover any new requests for the medication.

DUEC New Drugs--March 2, 2015 -June 6, 2015									
BRAND NAME	**GENERIC NAME**	**PRICING (AWP)**	**INDICATION**	**SIMILAR THERAPIES ON FORMULARY/AWP**	**EBRx recommendation**	**DUEC DATE**	**DUEC VOTE**	**IB Date**	**IB Vote**
NON-SPECIALTY DRUGS									
FENTANYL TD PATCH 37.5MCG/62.5MCG/87.5MCG	fentanyl transdermal patch	$65/$94/$129 - new strengths only available from one source - Mylan	New dosage formulations. Treatment of mild-moderate pain	Generic strengths ranging from 12mcg - 100mcg from multiple mfg. Currently covered T1 with quantity limits. Pricing examples: 50mcg/$26, 75mcg/$40, 100mcg/$53	Exclude new strengths, code 13. (handout)	2015 08 03			
NUVESSA GEL 1.3%	metronidazole vaginal gel 1.3%	$186/application - dosage= one single application	Treatment of bacterial vaginosis	Metronidazole Vag gel 0.75% 70gm tube = $33. (dosage = 1-2 times a day for 5 days.	Exclude, code 13. (handout)	2015 08 03			
TOUJEO SOL INJ 300IU/ML	insulin glargine sol pen-injector 300 units/ml	$402/3 pens (1,350 units)($0.30/unit)	Type 1 and type 2 diabetes	Lantus 100u/ml - tier 2 ($0.30/unit)	Exclude, code 13 (handout)	2015 08 03			
NATESTO GEL 5.5MG	testosterone nasal gel	$238/bottle	Treatment of hypogonadism	Topical testosterone products excluded. Injectable testosterone covered tier 1 with PA	Exclude, code 12 (handout)	2015 08 03			
ZOHYDRO ER CAPS-10/15/20/30/40/50 MG	hydrocodone bitartrate cap SR 12 hour abuse-deterrent	$7.37-$9.00/tab depending on strength	Moderate-severe pain	Zohydro (non-abuse deterrent) excluded by plan	Exclude, code 13. (handout)	2015 08 03			
AVYCAZ IV SOLUTION	ceftazidime-avibactam sod IV soln	N/A	Treatment of intraabdominal infections, pyelonephritis, UTI - not in scope of pharmacy benefits		NA hospital	2015 08 03			
CRESEMBA CAPS	isavuconazonium sulfate caps	$1,176/14 caps	Azole antifungal indicated for treatment of adults with invasive aspergillosis or invasive mucormycosis Dose= 2caps every 8 hours x 6 doses then 2 caps daily	Itraconazole (tier 1) - $900/90caps. Vfend $2,653/30 caps	EXCLUDE. Per PI: Trial 1, Noninferiority trial vs voriconazole in invasive aspergillosis. Noninferiority established. Trial 2, one armed non-controlled trial in invasive mucormycosis patients. No conclusions could be drawn.(Handout)	2015 08 03			
CRESEMBA INJ 372MG	isavuconazonium sulfate IV solution	N/A	Azole antifungal indicated for treatment of adults with invasive aspergillosis or invasive mucormycosis - not in scope of pharmacy benefits		NA Hospital	2015 08 03			
LILETTA IUD	levonorgestrel releasing IUD 18.6 mcg/day (52mg total)	$750 each	intrauterine contraceptive	IUD's excluded under pharmacy benefits	Exclude, code 13.Liletta releases levonorgestrel 15.6mcg/d over 3 years ($750.00/3y; $20.83/m over 36m). Mirena initially releases levonorgestrel 20mcg/y, then rate subsequently decreases. Mean release rate over 5y is levonorgestrel 14mcg/d ($972.61/5y; $16.21/m over 60m).	2015 08 03			

OMIDRIA INJ 1-0.3%	phenylephrine-ketorolac intraocular soln 1-0.3%	$558/4ml	For use during cataract surgery or intraocular lens replacement to maintain pupil size by preventing intraoperative miosis and to reduce post operative ocular pain - out of scope of pharmacy benefits		NA Medical. Used during ophthalmic surgery.	2015 08 03			
PRISTIQ 25MG TAB	desvenlafaxine succinate tab SR 24hr 25mg tab	$9.26/capsule	New dosage formulation	Other dosage strengths of Pristiq excluded under pharmacy benefits	RP with other antidepressants	2015 08 03			
PROVIDA DHA CAPS	prenatal vitamin	$2/capsule	Prenatal vitamin	multiple generics	Exclude, code 7-vitamin policy.	2015 08 03			
SAXEMDA INJ 6MG/ML	liraglutide (weight management) soln pen-injector 6mg/ml	$1,281/box of 3 pens	Treatment of obesity as an adjunct to a reduced- calorie diet and increased physical activity.	Anti-obesity agents excluded under pharmacy benefits	Exclude, code 9-not medically necessary.	2015 08 03			
NAMZARIC CAPS	memantine[NAMEDA] - donepezil[ARICEPT] cap SR 24hr	$386/30 caps (28mg mematine,donepezil 10mg)	Treatment of Alzheimer's disease	Tier 3 options: Namenda 10mg ($296/60);Namenda XR 28mg ($356/30); Aricept 10mg ($1,070/30); donepezil 10mg ($963/30)	Exclude, code 13.	2015 08 03			
PROAIR RESPI AER	albuterol sulfate aer po BA 108mcg/act	$60/1 box (90mcg base)	New dosage formulation of Proair - treatment of asthma	Proair HFA inhaler (tier 2) - $53/inhaler 90mcg base	T2	2015 08 03			
CORLANOR TABS	ivabradine tabs	$450/60 - 7.5mg tabs	Treatment of heart failure		T3PA	2015 08 03			
ARGATROBAN INJ	argatroban inj IV soln 250mg/250ml	N/A	Synthetic IV thrombin inhibitor - not in scope of pharmacy benefits		NA Hospital	2015 08 03			
LEVOLEUCOVOR INJ 50MG	levoleucovorin calcium inf 175mg/17.5ml	NA	For treatment of methotrexate toxicity - not in scope of pharmacy benefits		NA Hospital	2015 08 03			
APTENSIO XR CAPS	methylphenidate ER 24hr caps	$7.80/cap	Treatment of ADHD/narcolepsy	Methylphenidate ER ($5 each) covered teir 1 w/ QLs. Ritalin LA tier 3 w/ QL. LA amphetamines are RP'd for members age >26 y.	Exclude, code 13	2015 08 03			
FOSRENOL POWDER	lanthanum carbonate oral powder pack	1000mg powder pack = $11.21	New dosage form. Also available in chewable tabs. For treatment of hyperphosphatemia	Fosrenol tabs 1000mg chewable tab = $11.21 each	T3	2015 08 03			
SAPHRIS SUBLINGUAL TABS	asenapine maleate sublingual tabs	$16.65/2.5mg	New 2.5mg sblingual dose. Other dosages: 5 and 10mg. Used for bipolar disorder and schizophrenia	Saphris excluded under pharmacy benefit	Exclude, code 13	2015 08 03			
TIVORBEX CAPS	indomethacin 20 and 40mg caps	$4.20/cap	Lower dosage form of indomethacin	Indomethacin generic covered tier 1 (25mg=$0.35)	Exclude, code 13	2015 08 03			
ENBRACE HR CAPS	prenatal vitamin	$4.32/cap	Prenatal vitamin	various generics	Exclude, code 7.	2015 08 03			
CAYA DIAPHRAGM	diaphragm arc-spring	$90/each	contraceptive	Diaphragms excluded under pharmacy benefit	ACA?	2015 08 03			
RITALIN LA CAPS 60MG	methylphenidate caps SR 24hr 60mg (LA)	$10.94/cap	Treatment of ADHD/narcolepsy	Methylphenidate ER ($5 each) T1 w/ QLs. Ritalin LA T3 w/ QL. LA amphetamines are RP'd for members age >26 y.	T3, QL 1/1. RP for age>26.	2015 08 03			
STIOLTO AER RESPIMAT	tiotropium br[SPIRIVA] and olodaterol[STRIVERDI]	$378/4GM	combination inhaled anticholinergic and a LABA used for COPD,emphysema	SPIRIVA (T2) STRIVERDI - coded as reject at seq 1 and coded as PA at seq 10??	T3. (handout)	2015 08 03			

DORYX 50MG TABS	doxycycline hyclate tab delayed release 50mg	$11.98/tab	Anti-infective agent. New dosage strength	other dosage strengths of doxycycline hyclate delayed release coded to reject	Exclude, code 13	2015 08 03			
VARIZIG 125 UNITS	varicella-zoster immune glob(human) IM inj 125u/1.2ml	$1,422/1.2ml vial	For varicella (chickenpox) infection prophylaxis		NA hospital	2015 08 03			
IRENKA CAPS 40MG	duloxetine HCL 40mg	$8.72/40mg cap	Antidepressant	Duloxetine reference priced on plan	Exclude, code 13. (handout)	2015 08 03			
IONSYS PAD 40MCG/AC	fentanyl HCL iontophoretic TD system 40mcg/act	$240/patch	A patient-controlled iontophoretic transdermal system providing on-demand systemic delivery of fentanyl for up to 24 hours or a maxium of 80 doses, whichever comes first.	SHOULD ONLY BE USED FOR HOSPITALIZED PATIENTS AND SHOULD BE DISCONTINUED BEFORE PATIENTS ARE DISCHARGED	NA hospital	2015 08 03			
SPECIALTY DRUGS						2015 08 03			
LENVIMA	lenvatinib	$2,790/pak (15 - 24mg caps)	Treatment of pts w/ locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).Dose= up to 24mg daily in 28 day cycles		Exclude. DCWG to address October 2015.	2015 08 03			
DOCETAXEL 200MG/20ML FOR IV INFUSION	docetaxel		not in scope of pharmacy benefits		NA	2015 08 03			
FARYDAK (Limited Distribution Specialty)	panobinostat lactate capsules	6-20mg caps = $8,232. Dose=20mg on day 1,3,5,8,10,12	A histone deacetylase inhibitor, in combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received at least two prior regimens, including bortezomib and an immunomodulatory agent.		Exclude, code 1. (handout)	2015 08 03			
NOVOEIGHT INJ	antihemophilic factor(recombinant) for inj - 1500 units, 2000units, 3000 units	$1.91/unit	Treatment of hemophilia A	Other hemophilia A treatments - specialty tier	T4 PA	2015 08 03			
ARANESP INJ 100MCG	darbepoetin alfa-polysorbate 80 soln inj 10mcg/0.4ml	$85.14/syringe	Treatment of anemia	Other dosage strengths covered under specialty tier	T4 PA	2015 08 03			
KALYDECO PAK - 50 AND 75MG (Limited Distribution Specialty)	ivacaftor packet	Each dose = $512 each	Treatment of cystic fibrosis	Kalydeco tab 150mg tab ($512/tab) covered under specialty tier	T4 PA	2015 08 03			
MIRCERA INJ 200MCG	methoxy polyethylene glycol-epoetin beta inj 200mcg/0.3ml	$432/syringe	Treatment of anemia	Other dosage stengths of Mircera excluded under plan	T3 PA	2015 08 03			
JADENU TABS (Limited Distribution Specialty)	deferasirox tabs	90mg=$34;180mg=$68;360mg=$136	A new formulation of EXJADE - once daily oral tablet for iron chelation	Exjade for oral suspension covered under specialty tier. 125mg=$34;250mg=$68;500mg=$136	T4PA	2015 08 03			
NATPARA INJ (Limited Distribution Specialty)	parathyroid hormone for injection cartridge	$9,500/2-50mcg cartridges for subcutaneous injection	Treatment of hypocalcemia and hypoparathyroidism		Exclude, code 1 & 13	2015 08 03			

CHOLBAM CAPS - (Limited Distribution Specialty)	cholic acid caps	#30-50mg caps=$9,930 #30 - 250mg caps=$29,880	For treatment of bile acid synthesis disorders, peroxisomal disorders, Zellweger spectrum disorders - General dosing guidelines: treatment with cholic acid should be initiated and monitored by an experienced hepatologist or pediatric gastorenterologist	NA	Exclude, code 1"Recommendation: Exclusion. Dosing in bile acid synthesis d.o.: 10-15mg/kg daily. 80kg manX15mg/kg=1200mg or 5 capsules daily or $4980/day Concomitant familial hypertriglyceridemia: 11-17mg/kg. There are no trials in PubMed. DailyMed has 2 trials with incomplete data and 1 case series. Until there are clinical endpoints, the drug should be excluded."	2015 08 03			
JUXTAPID 30,40,60mg caps (Limited Distribution Specialty)	lomitapide mesylate caps	$1237/cap	New dosage formulations	Juxtapid excluded by plan	Exclude, code 1	2015 08 03			
IXINITY	coagulation factor IX (recombinant) for inj 1500 units	$1.75/unit	Treatment of hemophilia		NA hospital	2015 08 03			
COMPOUND KITS/BULK CHEMICALS/NO INDICATION						2015 08 03			
MENTHOCIN PAD LIDOCAIN	lidocaine-capsaicin-men-methyl sal patch				Exclude	2015 08 03			
Procarbazine powder(bulk)					not addressed	2015 08 03			
PERMAVAN PAD	lidocaine-dm-trolamine salicylate patch				not addressed	2015 08 03			
REMAXAZON	lidocaine-capsaicin-chondroitin-glucos patch				Exclude	2015 08 03			
COMFORT EZ PAD	methyl salicylate-lidocaine-menthol patch				Exclude	2015 08 03			
PHARM CH TSX PAD	methyl salicylate-lidocaine-menthol patch				Exclude	2015 08 03			
SORBITOL CRY CANDY	sorbitol candy base crystals				Exclude	2015 08 03			
Methylmethacrylate crosspolymer bulk powder					not addressed	2015 08 03			
Pullulan (bulk) powder					not addressed	2015 08 03			
Sodium bitartrate monohydrate (bulk) powder					not addressed	2015 08 03			
CANOGINEX SPRAY	camphor-histamine-menthol liqd spray				Exclude	2015 08 03			
LIDOVIN CREAM 3.95%	lidocaine cream 3.95%				Exclude	2015 08 03			

LIDOZOL CREAM 3.75%	lidocaine cream 3.75%				Exclude	2015 08 03			
TETRAMEX SPRAY	tetracaine-menthol-camphor liqd spray				Exclude	2015 08 03			
ANODYNERX PAD	capsaicin-lidocaine-menthol patch				Exclude	2015 08 03			
DERMACINRX KIT COMBOPAK	chlorhexidine soln-dimeth CR-silicone tape - homepathic kit				Exclude	2015 08 03			
NAZIREX CREAM	levocetirizine-loratadine cream compounding kit				Exclude	2015 08 03			
DERMACINRX KIT SILAPAK	dimethicone crea and silicone tape kit				Exclude	2015 08 03			
ATENDIA PAD	lidocaine-menthol patch				Exclude	2015 08 03			
Betamethasone sod phosphate & acet PF inj susp 7mg/ml	mfg: US Compounding				not addressed	2015 08 03			
Betamethasone sod phosphate & acet PD inj 12 (6-6)mg/2ml	mfg: US Compounding				not addressed	2015 08 03			
DERMACINRX KIT	diclofenac sod tab DR 75mg and lido-men-methyl sal patch kit				Exclude	2015 08 03			
DERMACINRX KIT SILAPAK	triamcinolone acet cream 0.1% and dimeth CR 5% and silicone tape				Exclude	2015 08 03			
Methylprednisolone acetate 100mg/ml inj susp	mfg: US Compounding				not addressed	2015 08 03			
TESTONE CIK KIT	testosterone cypionate IM inj in oil 200mg/ml				not addressed	2015 08 03			
Betamethasone sodium phosphate PF inj 25mg/ml	mfg: US Compounding				not addressed	2015 08 03			
Kudzu root powder					Exclude	2015 08 03			
Methylprednisolone w/lidocaine inj 40mg/ml	mfg: US Compounding				not addressed	2015 08 03			
Testosterone implant pellets	mfg: US Compounding				not addressed	2015 08 03			
Triamcinolone/lidocaine inj	mfg: US Compounding				not addressed	2015 08 03			
Testosterone inj 250mg/ml	mfg: US Compounding				not addressed	2015 08 03			
Vit K2 bulk powder					not addressed	2015 08 03			
Capsaicin powder (bulk) powder					not addressed	2015 08 03			
Dermacinrx solution	external vehicles - solution				Exclude	2015 08 03			
Renovo Lido5 cream	lidocaine-capsaicin cream				Exclude	2015 08 03			
Urevaz cream	urea cream 44%				Exclude	2015 08 03			

I-LIDS CLEANS SOLN	hypochlorous acid cleanser soln 0/01%				Exclude	2015 08 03			
MIC COMBO INJ	mfg: US Compounding				not addressed	2015 08 03			
TEST EO-PRO- INJ CYP 220	mfg: US Compounding				Exclude	2015 08 03			
BROMPHENIRAM INJ 10MG/ML	mfg: US Compounding				not addressed	2015 08 03			
ESTRADIOL IMPLANT PELLET	mfg: US Compounding				not addressed	2015 08 03			
SOD HYALURONATE-LIDOCAINE PF SOLN PREF SYR	mfg: US Compounding				not addressed	2015 08 03			
HYALURONIDASE BOVINE PF INJ	mfg: US Compounding				not addressed	2015 08 03			
LINCOMYCIN HCL-LIDOCAINE HCL INJ	mfg: US Compounding				not addressed	2015 08 03			
MEDROXYPROGESTERONE ACE-LIDOCAINE IM SUSP	mfg: US Compounding				not addressed	2015 08 03			
TESTOSTERONE IMPLANT PELLETS	mfg: US Compounding				not addressed	2015 08 03			
TRIAMCINOLONE ACETONIDE INJ SUSP	mfg: US Compounding				not addressed	2015 08 03			
Pine Bark Extract bulk powder					not addressed	2015 08 03			
RENUU NL PAD 2-30%	allantoin-petrolatum patch				Exclude	2015 08 03			
ANASEPT SPR	sodium hypochlorite liq 0.057%				Exclude	2015 08 03			
CITRUS POW BERGAMOT	citrus bergamot oral powder 250mg/0.25gm				Exclude	2015 08 03			
Ademetionnine (bluk) powder					not addressed	2015 08 03			
Calcium amino acid chelate (bulk) granules					not addressed	2015 08 03			
Magnesium amino acid chelate (bulk) powder 20%					not addressed	2015 08 03			
Tocopherols (bulk) powder 30%					Exclude	2015 08 03			
Dermacinrx Pak inflammatory	diclofen DR tab 75mg-ranitidine tab 150mg-capsaicin cr THPK				Exclude	2015 08 03			
MISC						2015 08 03			
TOXICOL SALV KIT	toxicology saliva collection kit		not in scope of pharmacy benefits		NA	2015 08 03			
THALLOUS INJ TL 201	thallous chloride TL 201 inj		diagnostic aid - not in scope of pharmacy benefits		NA	2015 08 03			
GLUCAGON INJ 1MG	glucagon HCl diagnostic for inj		not in scope of pharmacy benefits		NA	2015 08 03			

Fentanyl Patches

Currently, EBD covers fentanyl patches 12, 25, 50, 75, and 100mcg/hour. Costs, utilization, and proposed tier placement are below:

Fentanyl Patches		Utilizers	Rxs	Quantity	DS	AWP cost	AWP cost/patch	Current Tier	Proposed Tier
FENTANYL	100MCG/H	41	94	1,165	2,710	$62,438	$53.59	1	1
FENTANYL	87.5mcg/h	0	0	0	0	0	$129.22		Exclude
FENTANYL	75MCG/HR	48	99	1,235	2,943	$51,097	$41.37	1	1
FENTANYL	62.5mcg/h	0	0	0	0	0	$94.91		Exclude
FENTANYL	50MCG/HR	69	117	1,225	3,415	$32,864	$26.83	1	1
FENTANYL	37.5mcg/h	0	0	0	0	0	$65.31		Exclude
FENTANYL	25MCG/HR	102	173	1,910	5,037	$28,135	$14.73	1	1
FENTANYL	12MCG/HR	47	65	669	1,846	$13,582	$20.30	1	1

TABLE C[1]
DOSE CONVERSION GUIDELINES

Current Analgesic	Daily Dosage (mg/d)			
Oral morphine	60-134	135-224	225-314	315-404
IM/IV morphine	10-22	23-37	38-52	53-67
Oral oxycodone	30-67	67.5-112	112.5-157	157.5-202
IM/IV oxycodone	15-33	33.1-56	56.1-78	78.1-101
Oral codeine	150-447	448-747	748-1047	1048-1347
Oral hydromorphone	8-17	17.1-28	28.1-39	39.1-51
IV hydromorphone	1.5-3.4	3.5-5.6	5.7-7.9	8-10
IM meperidine	75-165	166-278	279-390	391-503
Oral methadone	20-44	45-74	75-104	105-134
IM methadone	10-22	23-37	38-52	53-67
	⇓	⇓	⇓	⇓
Recommended DURAGESIC® Dose	25 mcg/h	50 mcg/h	75 mcg/h	100 mcg/h

Alternatively, for adult and pediatric patients taking opioids or doses not listed in Table C, use the conversion methodology outlined above with Table D.

[1]**Table C should not be used to convert from DURAGESIC® to other therapies because this conversion to DURAGESIC® is conservative. Use of table C for conversion to other analgesic therapies can overestimate the dose of the new agent. Overdosage of the new analgesic agent is possible (see DOSAGE AND ADMINISTRATION - Discontinuation of DURAGESIC®).**

Recommendation: Exclude the new strengths. The old strengths provide adequate flexibility in dosing.

Metronidazole (Nuvessa) 1.3% vaginal gel
Topical Antibiotic

Indication: the treatment of bacterial vaginosis in non-pregnant women

From up to date: "BV resolves spontaneously in up to 1/3 of non-pregnant and ½ of pregnant women. Treatment is indicated for relief of symptoms in women with symptomatic infection and to prevent postoperative infection in those with asymptomatic infection prior to abortion or hysterectomy."

Drug	Strength	Dosing	Price/course	EBD Coverage to date (4/28/15)
Nuvessa	1.3%	1 applicatorful intravaginally **as a single dose**	$186.00 (5g)	excluded
MetroGel-Vaginal	0.75%	1 applicatorful intravaginally **once or BID** x 5 days	$226.24 (70g)	Brand Penalty
Vandazole	0.75%	1 applicatorful intravaginally **once daily** x 5 days	$33.71 (70g)	T1
*Metronidazole gel	0.75%	1 applicatorful intravaginally **once or BID** x 5 days	$33.71 (70g)	T1
Metronidazole IR tabs (off-label use)	500mg	500mg BID x 7 days	$10.19	T1
Flagyl ER tabs	750 mg	750mg once daily x 7 days	$143.58	T2

*This is priced much cheaper than the external metronidazole gel, which EBD's MAC price is for.

Oral metronidazole 500mg BID x 7 days and intravginal 0.75% metronidazole BID x 5 days have been shown in several trials to be equally effective (85.1% cure rate in the oral group vs 83.7% in the intravaginal group[1]) with a significant amount of oral metronidazole patients reporting more GI symptoms (51.8% in the oral grp vs. 32.7% in the intravaginal group[1])[1,2] In a small cost-effectiveness study (60 patients) looking at oral metronidazole vs Metrogel Vaginal for treating bacterial vaginosis, oral generic metronidazole was found to be the more cost-effective option.[3] Authors stated that "While the use of the more expensive Metrogel may be reasonable for patients experiencing side effects of oral…most patients should be treated with the less expensive generic."[3]

<u>From the Nuvessa package insert</u>
A single, randomized, double-blind, vehicle-controlled clinical trial was done. 292 patients were enrolled in the Nuvessa group, 285 in the vehicle group. Patients were instructed to administer the study drug once at bedtime. The results of the trial may be found below.

Table 1. The Efficacy of NUVESSA for the Treatment of Bacterial Vaginosis in a Randomized, Double-Blind, Vehicle-Controlled, Parallel Group Study

Outcome	NUVESSA N = 292 n (%)	Vehicle Gel N = 285 n (%)	Treatment Difference (%) [95% Confidence Interval]
Test of Cure (Day 21 to 30)			
Clinical Cure	108 (37.0)	76 (26.7)	10.3 (2.8, 17.9)
Bacteriological Cure	57 (19.5)	22 (7.7)	11.8 (6.3, 17.3)
Therapeutic Cure	49 (16.8)	18 (6.3)	10.5 (5.3, 15.6)

There are no studies comparing the new 1.3% one-time dose versus the standard 0.75% BID.

Recommendation: Exclude Nuvessa.
<u>Outcome:</u> Excluded due to having less costly alternatives.

Insulin Glargine Injection 300U (Toujeo SoloStar)

Erica Barr
4/27/15

Labeled Use: Toujeo is a long-acting human insulin analog indicated to improve glycemic control in adults with diabetes mellitus.

How Supplied/Dosed: Toujeo is a more concentrated preparation of insulin glargine compared to Lantus. It is thought that the smaller insulin depot with Toujeo leads to slower absorption. Current guidelines for those switching to Toujeo from Lantus suggest a direct unit to unit conversion; however, Pharmacist's Letter suggests "most patients will likely need a 10% or slightly higher dose of *Toujeo* to get glycemic control similar to *Lantus*." Toujeo comes in a 1.5mL pen, compared to the 3mL pen Lantus is supplied in.

Toujeo should NOT be used as an alternative to Humulin R U-500 for patients who need very high insulin doses. Toujeo's SoloStar pen can only deliver 80 units per dose.

Comparators:

Brand	How Supplied	AWP	Price/100U
Lantus* Subcutaneous	100 units/mL (10 mL)	$298.21	$29.82
Lantus* SoloStar Subcutaneous	100 units/mL (3 mL)	$89.46	$29.82
Toujeo SoloStar Subcutaneous	300 units/mL (1.5 mL)	**$134.19**	**$29.82**
Levemir (insulin detemir) Subcutaneous	100 units/mL (10mL)	$298.21	$29.82
Levemir FlexTouch Subcutaneous	100 units/mL (3mL)	$89.46	$29.82
Insulin glargine generic	(Expected as early as next year*)	-	-

*Lantus loses its patent February 2016

Adverse Drug Events: primarily signs of hypoglycemia: fatigue, mental confusion, redness, muscle weakness

Drug Interactions:

-*drugs that affect glucose metabolism:* adjustment of insulin dosage may be needed; closely monitor blood glucose

-*anti adrenergic drugs*: signs and symptoms of hypoglycemia may be reduced or absent

Contraindications: during episodes of hypoglycemia, hypersensitivity to Toujeo or one of its excipients

Evidence:

EDITION I- To evaluate maintenance of efficacy and safety of insulin glargine 300 U/mL (Gla-300) versus glargine 100 U/mL (Gla-100) in people with type 2 diabetes mellitus using basal plus meal-time insulin for 12 months:

Design: This was a multicenter, randomized, open-label, two-arm, phase 3a study. Participants completing the initial 6-month treatment period continued to receive Gla-300 or Gla-100, as previously randomized, once daily for a further 6-month open-label extension phase. Change in HbA_{1c}, fasting plasma glucose, insulin dose, hypoglycemic events* and body weight were assessed.

Results: Glycemic control was sustained in both groups (mean HbA_{1c} Gla-300, 7.24 %; Gla-100, 7.42 %). Mean daily basal insulin dose at 12 months was 1.03 U/kg for Gla-300 and 0.90 U/kg with Gla-100. Lower percentages of participants had ≥1 confirmed or severe hypoglycemic event* with Gla-300 than Gla-100 at any time of day (86% versus 92%; relative risk [RR] 0.94 [95% CI: 0.89 to 0.99]) and during the night (54% versus 65%; RR 0.84 [0.75 to 0.94]), while the annualized rates of such hypoglycemic events were comparable. There were no apparent between-treatment differences in adverse events.

Riddle MC, Bolli GB, Zieman M, Meuhlen-Bartmer I, Bizet F, Home PD. New insulin glargine 300 units/mL versus glargine 100 units/mL in people with type 2 diabetes using basal and mealtime insulin: glucose control and hypoglycemia in a 6-month randomized controlled trial (EDITION 1). *Diabetes Care* 2014; **37**: 2755–2762

***Important to Note**: The definition for a "hypoglycemic event" in all three trials was any blood sugar reading ≤70mg/dL, regardless of presence/absence of symptoms (also note "there were no apparent between-treatment differences in adverse events"). This was what was used in statistical analysis.

'Severe hypoglycemia' was defined by the researchers as events requiring assistance by another person to administer carbohydrate, glucagon or other therapy. From EDITION 1: "Severe hypoglycemia was infrequent, and events were too few for meaningful analysis. Only 4 participants (1%) in each treatment group reported severe hypoglycemia at any time of day.

EDITION II- To compare the efficacy and safety of new insulin glargine 300 units/mL (Gla-300) with glargine 100 units/mL (Gla-100) in people with type 2 diabetes using basal insulin (≥42 units/day) plus oral anti-hyperglycemic drugs

Design: This was a multicenter, open-label, two-arm study. Adults receiving basal insulin plus oral anti-hyperglycemic drugs were randomized to Gla-300 or Gla-100 once daily for six months. The primary end point was change in HbA_{1c}. The main secondary end point was percentage of participants with one or more nocturnal confirmed (≤70 mg/dL) or severe hypoglycemic events* from nine weeks to six months.
Results:

- Glycemic control improved similarly with both basal insulins; least squares mean (SD) reduction from baseline was −0.57% (0.09) for Gla-300 and −0.56% (0.09) for Gla-100 (mean difference −0.01% [95% CI −0.14 to 0.12]), with 10% higher dose of Gla-300.
- Less nocturnal confirmed (≤70 mg/dL) or severe hypoglycemia* was observed with Gla-300 from week 9 to month 6 (relative risk 0.77 [95% CI 0.61–0.99]; $P = 0.038$) and during the first 8 weeks.
- Fewer nocturnal and any time hypoglycemic events were reported during the entire 6-month period.
- No between-treatment differences in safety parameters were identified.

Yki-Järvinen H, Bergenstal RM, Ziemen M et al. New insulin glargine 300 U/mL versus glargine 100 U/mL in people with type 2 diabetes usingoral agents and basal insulin: glucose control and hypoglycemia in a 6-monthrandomized controlled trial (EDITION 2). *Diabetes Care* 2014; **37**: 3235–3243.

EDITION III- To compare the efficacy and safety of new insulin glargine 300 U/ml (Gla-300) with that of glargine 100 U/ml (Gla-100) in insulin-naïve people with type 2 diabetes using oral glucose-lowering drugs:
Design: This was a multicenter, open-label, parallel-group study. Participants were randomized to Gla-300 or Gla-100 once daily for 6 months, discontinuing sulfonylureas and meglitinides, with a dose titration aimed at achieving pre-breakfast plasma glucose concentrations of 80-100 mg/dL. The primary endpoint was change in HbA1c from baseline to 6 months. The main secondary endpoint was percentage of participants with ≥1 nighttime confirmed* (≤70 mg/dl) or severe hypoglycemia from 9 weeks to 6 months. Other measures of glycemic control and hypoglycemia, weight change and insulin dose were assessed.
Results:

- Glycemic control was sustained in both groups (mean HbA_{1c} Gla-300, 7.24%; Gla-100, 7.42%).
- Mean daily basal insulin dose at 12 m was 1.03 U/kg for Gla-300 and 0.90 U/kg with Gla-100.
- Lower percentages of participants had ≥1 confirmed (70 mg/dL) or severe hypoglycemic event* with Gla-300 than Gla-100 at any time of day (86% versus 92%; relative risk [RR] 0.94 [95% CI: 0.89 to 0.99]) and during the night (54% versus 65%; RR 0.84 [0.75 to 0.94]), while the annualized rates of such hypoglycemic events were comparable.
- There were no apparent between-treatment differences in adverse events.

Riddle MC, Bolli GB, Zieman M, Meuhlen-Bartmer I, Bizet F, Home PD. New insulin glargine 300 units/mL versus glargine 100 units/mL in insulin-naïve people with type 2 diabetes on oral glucose-lowering drugs: a randomized controlled trial (EDITION 3). *Diabetes Care* 2015; 4: 386-94.

Conclusions for all three: "Gla-300 was as effective as Gla-100 and associated with a lower risk of hypoglycemia during the night and at any time of the day."
From **Pharmacist's Letter**:
"Toujeo will cost about the same per unit as Lantus or Levemir. But most patients will likely need a 10% or slightly higher dose of Toujeo to get glycemic control similar to Lantus."
The *PL Voices* produced by **Pharmacist's Letter** suggest that there may be a role for Toujeo in patients that have had recurrent hypoglycemia, specifically overnight hypoglycemia problems. This video suggests that, otherwise, patients that are stable and doing well on Lantus should not be switched to Toujeo.

Summary: Toujeo appears to be a poor attempt to continue to control the insulin glargine market with Lantus's patent coming to an end. The studies do not take presence of hypoglycemia symptoms into consideration and can therefore be argued to study an endpoint that is not clinically significant. Referencing *Pharmacist's Letter*, the ≥10% increase in U/day that is often seen between Lantus and Toujeo makes it less cost-effective as well.

Recommendation: Exclude from coverage.

Outcome: Excluded from coverage. The trials are flawed in that they focus on hypoglycemic episodes in patients taking other hypoglycemic drugs than glargine. They also defined hypoglycemia too generously and censored endpoints even if they were asymptomatic.

Natesto® (testosterone) nasal gel CIII, 5.5 mg/ACT (11 g)
Nghia Tran, P4, April 17, 2015

Label Uses: Natesto® is an androgen indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) **OR** Hypogonadotropic hypogonadism (congenital or acquired)

Limitations of use: Safety and efficacy of Natesto® in males less than 18 years old have not been established

Comparator Drugs

AWP Cost Comparison for a month supply			
Drug	Dosing Regimen for hypogonadism **OR** hypogonadotropic hypogonadism (males):	AWP	AWP for Month Supply
Natesto® Nasal Gel	11 mg (2 pump actuations); 1 actuation per nostril administered intranasally 3x/d (6 to 8 hours apart)	5.5 MG/ACT (11 g): $238.80 60 Actuations/6 Act/d = 10 Day Supply	$716.40
AndroGel® (1%) Pump Transdermal Gel	50 mg applied QD in the am to the shoulder and upper arms, or abdomen. Each actuation delivers 12.5 mg of testosterone (4 actuations = 50 mg)	12.5 MG/ACT (1%) (75 g): $267.02 60 Actuations/4 Actuations Per Day = 15 Day Supply	$534.04
AndroGel® (1.62%) Pump Transdermal Gel	40.5 mg applied once daily in the morning to the shoulder and upper arms. Each actuation delivers 20.25 mg of testosterone (2 actuations = 40.5 mg)	20.25 MG/ACT (1.62%) (75 g): $517.93 60 Actuations/2 Actuations Per Day = 30 Day Supply	$517.93
Fortesta® (2%) Pump Transdermal Gel	Fortesta: 40 mg once daily in the morning. Apply to the thighs. Each actuation delivers 10 mg of testosterone (4 actuations = 40 mg)	10 MG/ACT (2%) (60 g): $460.19 120 Actuations/4 Actuations Per Day = 30 Day Supply	$460.19
Vogelxo® (1%) Pump Transdermal Gel	Vogelxo: 50 mg applied once daily to the shoulder and/or upper arms. Each actuation delivers testosterone 12.5 mg (4 actuations = 50 mg)	12.5 MG/ACT (1%) (75 g): $267.03 60 Actuations/4 Actuations Per Day = 15 Day Supply	$534.06

MOA: Principal endogenous androgen responsible for promoting the growth and development of the male sex organs and maintaining secondary sex characteristics in androgen-deficient males

Contraindications: Men with carcinoma of the breast or known or suspected prostate cancer; pregnant or breast-feeding women (testosterone may cause fetal harm)

Adverse Effects: PSA increased, headache, rhinorrhea, epistaxis, nasal discomfort, nasopharyngitis, bronchitis, upper respiratory tract infection, sinusitis, and nasal scab

Drug Interactions: Androgens may decrease blood glucose and therefore may decrease insulin requirements in diabetic patients. Changes in anticoagulant activity may be seen with androgens and more frequent monitoring of International Normalized Ratio (INR) and prothrombin time is recommended in patients taking warfarin. Use of testosterone with corticosteroids may result in increased fluid retention and use with caution, particularly in patients with cardiac, renal, or hepatic disease

A 90-Day, Randomized, Dose-Ranging Study, Including Potential Dose Titration, Evaluating the Efficacy and Safety of Intranasal TBS-1 in the Treatment of Male Hypogonadism

- Natesto® was evaluated in a phase III multicenter, open-label, 90-day clinical study
- N=306 hypogonadal men with morning testosterone concentrations ≤ 300 ng/dL received Natesto® were randomized
- Patients were instructed to self-administer Natesto® (11 mg of testosterone) intranasally either two or three times daily
  - N=228 pts (5.5 mg per nostril of TBS-1 BID for a total daily dose of 22 mg/day)
  - N=78 (5.5 mg per nostril of TBS-1 TID for a total daily dose of 33 mg/day)
- 17 subjects who had no post-baseline data; 12 subjects in the BID group and 5 subjects in the TID Group
  - For the 12 discontinuations in the BID group, 9 were due to withdrawal of consent, 2 were due to lost to follow-up, and 1 was due to other reasons
- Primary Endpoint: the percentage of patients with an average serum total testosterone concentration within the normal range of 300 to 1050 ng/dL on Day 90 in at least 75% of treated subjects
  - N=73 hypogonadal men were included in the statistical evaluation of efficacy (total testosterone pharmacokinetics) on Day 90 based on the ITT population
  - 66 of the 73 patients in the TID group (90.4%) within the normal range 300 to 1050 ng/dL on Day 90
- Funded by Trimel Pharmaceutical Corporation
- No publication in journal

Berg, J.,Block, B., et al. A 90-Day, Randomized, Dose-Ranging Study, Including Potential Dose Titration, Evaluating the Efficacy and Safety of Intranasal TBS-1 in the Treatment of Male Hypogonadism ClinicalTrials.gov Identifier: NCT01446042

Recommendation: Exclude b/c did not study outcomes, only lab values; not peer-reviewed or published; expensive/dose frequently

Outcome: Exclude.

Hydrocodone Single Entity ER Products

Hydrocodone Extended Release--Sole ingredient										
Zohydro ER oral capsule	BID dosing	pkg size	cost/60	AWP/unit (7/24/15)	AWP cost/d	Current utilization	Current Tier	(AWP-13%)/unit	Cost/day @ BID	Proposed
Dosed w/ TD hydrocodone divided by 2; given bid	10 mg	60	442.08	$7.37	$14.74	0	Excluded	$6.41	$12.82	
	15 mg	60	472.32	$7.87	$15.74	0	Excluded	$6.85	$13.70	
	20 mg	60	487.44	$8.12	$16.25	0	Excluded	$7.06	$14.12	
	30 mg	60	502.56	$8.38	$16.75	0	Excluded	$7.29	$14.58	
	40 mg	60	517.68	$8.63	$17.26	0	Excluded	$7.51	$15.02	
	50 mg	60	540	$9.00	$18.00	0	Excluded	$7.83	$15.66	
Hysingla ER oral tablet	QD dosing							Avg cost/unit paid	Paid cost/day	
Dosed with TD hydrocodone QD	20 mg	60	473.04	$7.88	$7.88	4	Covered	$5.85	$5.85	
	30 mg	60	690.48	$11.51	$11.51	3	Covered	$9.14	$9.14	
	40 mg	60	930.24	$15.50	$15.50	2	Covered	$13.04	$17.39	
	60 mg	60	1288.08	$21.47	$21.47	3	Covered	$17.87	$17.87	
	80 mg	60	1736.64	$28.94	$28.94	2	Covered	$23.56	$23.56	
	100 mg	60	2209.68	$36.83	$36.83	1	Covered	$31.93	$31.93	
							Covered	(AWP-13%)/unit	Cost/day @ BID	
	120 mg	60	2448.72	$40.81	$40.81	0	Covered	$35.50	$35.50	

COMPARISONS										
Oxycontin Tab		DaCon		AWP/unit	AWPcost/day	utilizers	Copay/rx	Avg cost/unit	Paid cost/d	
	10MG CR	2.19		$3.23	$7.07	46	T2	$2.14	$4.68	
	15MG CR	2.08		$4.76	$9.89	17	T2	$3.53	$7.35	
	20MG CR	2.39		$6.02	$14.40	46	T2	$4.76	$11.38	
	30MG CR	2.09		$8.38	$17.51	27	T2	$6.94	$14.53	
	40MG CR	2.36		$10.32	$24.35	42	T2	$8.57	$20.20	
	60MG CR	2.38		$14.61	$34.76	22	T2	$12.56	$29.95	
	80MG CR	2.63		$18.00	$47.35	11	T2	$15.74	$41.32	
OXYCODONE	TAB 10MG ER	3.43		$3.06	$10.48	13	$31.47	$2.38	$8.15	
	TAB 20MG ER	2.15		$5.82	$12.52	10	T1	$5.05	$10.87	
	TAB 40MG ER	2.38		$8.78	$20.90	6	T1	$7.76	$18.48	
	TAB 80MG ER	2.57		$17.15	$44.09	3	T1	$15.30	$39.34	
MORPHINE SUL CAP	10MG ER	1.48		$4.73	$7.00	2	T1	$4.01	$5.95	
	20MG ER	2		$5.22	$10.45	2	T1	$3.58	$7.17	
	30MG ER	2		$5.68	$11.36	1	T1	$3.75	$7.50	
	45MG ER	1		$8.50	$8.50	1	T1	$6.99	$6.99	
	50MG ER	2		$9.50	$19.01	1	T1	$6.63	$13.27	
	60MG ER	1.25		$11.13	$13.91	3	$123.72	$6.60	$8.25	
	90MG ER	1		$16.73	$16.73	4	T1	$14.70	$14.70	
	100MG ER	2		$19.01	$38.01	1	T1	$13.50	$27.00	
MORPHINE SUL TAB	15MG ER	2.1		$1.68	$3.52	66	T1	$0.36	$0.75	
	30MG ER	2.44		$3.17	$7.74	63	T1	$0.66	$1.61	
	60MG ER	3		$6.21	$18.64	17	T1	$1.49	$4.48	
	100MG ER	2.62		$9.20	$24.10	11	T1	$2.26	$5.93	
	200MG ER	3		$18.38	$55.15	1	T1	$13.13	$13.13	
OPANA ER	TAB 5MG	2		$2.79	$5.58	2	T2	$1.90	$3.81	
	TAB 10MG	2		$5.36	$10.72	1	$58.58	$3.91	$7.81	
	TAB 15MG	2.38		$7.43	$17.69	4	T2	$6.18	$14.67	
	TAB 20MG	2		$9.50	$19.01	4	T2	$7.95	$15.89	
	TAB 30MG	2		$13.68	$27.36	3	T2	$11.70	$23.41	
OXYMORPHONE TAB HCL	5MG	3		$3.30	$9.89	3	T1	$2.38	$7.14	

	10MG	2.75		$6.03	$16.60	3	$122.00	$2.97	$8.17	
OXYMORPHONE TAB	7.5MG ER	2		$2.71	$5.42	1	T1	$2.01	$4.02	
	10MG ER	2		$3.48	$6.96	2	T1	$2.96	$5.92	
	15MG ER	2		$5.17	$10.34	1	T1	$3.81	$7.61	
	20MG ER	3.5		$6.17	$21.61	2	$86.33	$4.78	$16.72	
	30MG ER	2.4		$8.89	$21.32	2	T1	$7.85	$18.84	
	40MG ER	2		$11.60	$23.20	1	T1	$10.16	$20.33	
METHADONE TAB	5mg	3.1		$0.29	$0.90	22	T1	$0.04	$0.13	
	10mg	5.29		$0.33	$1.72	51	T1	$0.08	$0.44	

Recommendations:

1. Exclude Hysingla; send letters to 15 utilizers to get a prescription for a different LA opiate effective 1/1/16.
2. Continue excluding Zohydro; adequate LA opiate alternatives at lower cost are available.

Hydrocodone long-acting formulations (Zohydro and Hysingla)

Andrew Mullings-Lewis

7/24/15

Currently, the most common utilizers are using Oxycontin 10mg CR (n=46), 20mg (n=46), and 40mg (n=42), at two times daily. Hydrocodone, the active component of Zohydro and Hysingla, is believed to be two thirds the potency oxycodone in terms of analgesia. Table 1 illustrates the scenarios and cost increases of switching Oxycontin users to Zohydro and Hysingla in a patient.

Table 1

Current Product	Daily Cost*	Equianalgesic amount	Proposed Product	New Daily Cost	Daily Cost Increase
Oxycontin 10mg BID(20mg oxycodone daily)	$7.07	30mg hydrocodone daily	Zohydro ER 15mg BID Hysingla ER 30mg Daily	$15.74 $11.51	$ 8.67 $ 4.44
Oxycontin 20mg BID (40mg oxycodone daily)	$14.40	60mg hydrocodone daily	Zohydro ER 30mg BID Hysingla ER 60mg Daily	$16.75 $21.47	$ 2.35 $ 7.07
Oxycontin 40mg BID (80mg oxycodone daily)	$24.35	120mg hydrocodone daily	Zohydro ER 60mg BID Hysingla ER 120mg Daily	N/A $40.81	N/A $16.46

*Calculated average from actual patient usage and often greater than BID dosing (2.08 – 2.63 tabs/day average)

Morphine and hydrocodone are generally believed to be equipotent at equivalent doses. Morphine's generic availability provide cost savings across all levels compared to Zohydro and Hysingla. Additionally, a MAC is used for oral morphine products.

Equianalgesic Opioid Dosing

	Equianalgesic Doses (mg)	
Drug	**Parenteral**	**Oral**
Morphine	**10**	**30**
Buprenorphine	**0.3**	**0.4 (sl)**
Codeine	**100**	**200**
Fentanyl	**0.1**	**NA**
Hydrocodone	**NA**	**30**
Hydromorphone	**1.5**	**7.5**
Meperidine	**100**	**300**
Oxycodone	**10***	**20**
Oxymorphone	**1**	**10**
Tramadol	**100***	**120**

*Not available in the US

McPherson ML. *Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing.* Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010. Copyright ASHP, 2010. Used with permission. NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

Isavuconazole (Cresemba)

372mg vial for IV infusion

186mg capsules

Indication: Treatment of invasive aspergillosis and mucormycosis in adults

Strengths: IV: 372mg isavuconazonium sulfate (200mg isavuconazole); Capsule: 186mg isavuconazonium sulfate (100mg isavuconazole)
Switching between the IV and PO formulations is acceptable. For maintenance dosing, it is not necessary to restart loading dose when switching between formulations.

Drug	Strengths	Dosing for Aspergillosis	Price	Price/treatment
Isavuconazole (Cresemba)	IV: 372 mg PO Cap: 186mg	**Initial:** 372mg q8h x 6 doses. **Maintenance**: 372mg once daily, starting 12-24h after the last loading dose	**IV (372mg)**: $286.20 (1) **PO Capsule (186mg)**: $1176 (14) $84/cap	**$9902.40** (See below for treatment assumptions)
Voriconazole	IV: 200mg PO tab: 50mg, 200mg	**IV**: Initial: 6mg/kg q12h x 2 doses Maintenance: 4mg/kg q12h **Oral**: Maintenance: <40kg: 100mg q12h ≥40kg: 200mg q12h Duration of tx should be a minimum of 6-12wks or throughout period of immunosuppression	**IV (200mg)**: $152.58 (1) **PO Tablet** **50mg**: $351.79 (30) $11.73/tab **200mg**: $1407.17 (30) $46.91/tab	**$6,405.42** (See below for treatment assumptions)

Price/treatment calculated using the mean treatment data from the trials found in the package insert. Treatment duration: 47 days with 8 days IV administration.
Cresemba: 12 total IV doses, 39 PO doses of 2 capsules each. 78 capsules (7 blister caps/sheet; need 11 sheets)
Voriconazole: Assuming a 70kg patient = 400mg IV q12h x 2 doses day 1. 200mg q12h x 7 days, 39 PO days at 200mg BID.

Amphotericin B is the drug of choice for treating mucormycosis, with posaconazole serving as rescue therapy for those who are unable to tolerate Ampho B. Isavuconazole is recommended for those who cannot tolerate posaconazole.

Interactions: Isavuconazole is thought to have fewer interactions than Voriconazole, CYP3A4 inhibitors and inducers.

Adverse effects: N/V/diarrhea (26%/25%/25%), headache (17%), elevated LFTs (16-17%), hypokalemia (14-19%), constipation (13-14%), dyspnea (12-17%), cough, peripheral edema (11-15%), back pain

Evidence:
Treatment of Invasive Aspergillosis (Package insert)
R, DB, NI active controlled trial evaluating the safety and efficacy of Cresemba vs Voriconazole for 1` treatment of invasive aspergillosis or other fungal infections. Stratified by history of allogeneic bone marrow transplant, uncontrolled

malignancy at baseline and geographic region. Infection caused by *Aspergillus* species was identified in 30% of the subjects.

Pts received a LD of IV 372mg Cresemba q8h for 48 h. Starting day 3, pts got 372mg IV or PO Cresemba QD. Voriconazole pts received Voriconazole IV LD of 6mg/kg q12h for 24 h followed by 4mg/kg IV q12h for the next 24 h.. Therapy was then allowed to be switched to oral at 200mg q12h. Max treatment duration was 84 d. Mean duration was 47 d for both groups, of which 8-9 d was IV.

Table 7. All-Cause Mortality Through Day 42

	CRESEMBA		Voriconazole		
	N	All-cause Mortality n (%)	N	All-cause Mortality n (%)	Difference[a] (95% CI)%
ITT	258	48 (18.6)	258	52 (20.2)	-1.0 (-8.0, 5.9)
Proven or Probable Invasive Aspergillosis	123	23 (18.7)	108	24 (22.2)	-2.7 (-13.6, 8.2)

[a] Adjusted treatment difference (CRESEMBA-voriconazole) by Cochran-Mantel-Haenszel method stratified by the randomization factors.

Table 8. Overall Response Success at End-of-Treatment

	CRESEMBA		Voriconazole		
	N	Success n (%)	N	Success n (%)	Difference[a] (95% CI)%
Proven or Probable Invasive Aspergillosis	123	43 (35.0)	108	42 (38.9)	-4.0 (-16.3, 8.4)

[a] Adjusted treatment difference (CRESEMBA-voriconazole) by Cochran-Mantel-Haenszel method stratified by the randomization factors.

Aspergillosis:

Astellas Pharma Inc. A Phase III, Double Blind, Randomized Study to Evaluate Safety and Efficacy of BAL 8557 Versus Voriconazole for Primary Treatment of Invasive Fungal Disease Caused by Aspergillus Species or Other Filamentous Fungi. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 June 20]. Available from: https://clinicaltrials.gov/show/NCT00412893 NLM Identifier: NCT00412893.

- Design: randomized, double-blind, non-inferiority active controlled trial which evaluated the safety and efficacy of CRESEMBA versus voriconazole for primary treatment of invasive fungal disease caused by Aspergillus species or other filamentous fungi.
- Results: All-cause mortality through Day 42 in the overall population (ITT) was 18.6% in the CRESEMBA treatment group and 20.2% in the voriconazole treatment group. Overall success at End-of-Treatment was seen in 35% of CRESEMBA-treated patients compared to 38.9% of voriconazole-treated patients.

Mucormycosis:

Per UpToDate (accessed 6/20/15):

"Isavuconazole has not been studied in randomized trials, but it has been evaluated in an open-label non-comparative study that included 37 patients with proven or probable mucormycosis. Patients were treated with isavuconazole IV or orally. Median treatment duration was 102 days for patients with primary mucormycosis, 33 days for those with refractory mucormycosis, and 85 days for those with intolerance to other antifungal therapy. All-cause mortality through day 42 was 38 percent, and overall success rate at the end of treatment was 31 percent. These data suggest that isavuconazole has some clinical efficacy in treating mucormycosis, although how it compares to amphotericin B or posaconazole is unknown."

Recommendation:

1. Exclude due to lack of evidence justifying higher cost.

2. Cover with PA, allowing that patients get Cresemba for aspergillosis or mucormycosis infections after trying the standard of care.

References:

Cresemba package insert.
UpToDate accessed 6/20/15.

Outcome After EBRx meeting: EXCLUDED

Tiotropium/Olodaterol Respimat (Stiolto Respimat)
Holly Rowton
July 22, 2015

FDA Approved Uses: Maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema
Comparators:

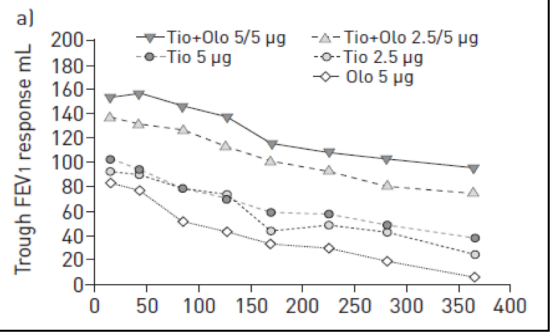
Drug name	COPD dosing	Form	AWP	Current Coverage	Proposed on 7/22/15	Coverage after 7/22/15
Tiotropium/olodaterol 5ug/5ug (Stiolto)	Two inhalations daily	Respimat	$378.82		Exclude	T3
Umeclindinium/vilanterol (Anoro Ellipta)	One inhalation daily	Dry powder inhaler	$357.37	T2	T2	T2
Fluticasone/vilanterol 100mcg/25mcg (Breo Ellipta)	One inhalation daily	Dry Powder inhaler				
Budesonide/Formoterol 80/4.5, 160/4.50 (Symbicort)	Two inhalations twice daily	Oral inhaler				
Fluticasone/Salmeterol 250mcg/50mcg (Advair Diskus)	One inhalation twice daily	Dry Powder inhaler				

Black Box Warning – asthma related death without other long-term asthma control medications.
Drug interactions: **category X**: aclidinium; anticholinergic agents, Beta-blockers (non-selective); eluxadoline; glucagon; lobenguane I 123; ipratropium (oral inhalation); Long-acting beta2 agonist; loxapine; potassium chloride; umeclindinium. **category D**: mifepristone; linezolid; high risk QTc-prolonging agents; pramlintide; secretin

Evidence:
Tiotropium and olodaterol fixed-dose combination versus mono-components in COPD (GOLD 2-4)

- **Design:** Two Multinational, R, 5 arm, parallel, DB, controlled phase 3 clinical trials. (TOnado 1 and TOnado 2) Combined N = 5162 randomized equally into the 5 arms (Olodaterol 5ug, Tiotropium 2.5ug, Tiotropium 5ug, Tiotropium 2.5ug/ Olodaterol 5ug, and Tiotropium 5ug/ Olodaterol 5ug). Baseline characteristics were similar across all arms. (Tiotropium 2.5/5 is not available in US).
- This study was Funded by Boehringer Ingelheim Pharma GmbH & Co.
- **Inclusion Criteria**: Pt ≥ 40 years old, Moderate to very severe COPD (GOLD 2-4), Post-bronchodilator FEV1 < 80% of predicted normal, capacity < 70%, Current or ex-smokers with history of > 10 pack-years.
- **Exclusion criteria**: clinically relevant abnormal baseline lab parameters or history of asthma, MI or hospitalized with HF within 1 year of screening, unstable or life-threatening arrhythmia, known active TB, bronchiectasis, CF or life threatening pulmonary obstruction, diagnosed thyrotoxicosis or paroxysmal tachycardia, previous thoracotomy with pulmonary resection, regular use of daytime oxygen, or currently enrolled (or completed within past 6 weeks) in a pulmonary rehabilitation program.
- **Results**: Primary endpoints were FEV1 AUC 0-3 h and trough FEV1 (response defined as change from baseline) at 24 weeks and 52 weeks and St. George's Respiratory Questionaire total score (SGRQ) (response defined as a decrease in total score by ≥ 4 units) at 12, 24, and 52 weeks. Secondary endpoint was the PFT's (performed 2, 6, 12, 18, 24, 32, 40 and 52 weeks), TDI score, and change in inhaled corticosteroid use.
- All arms showed statistically significant improvements in FEV1 AUC 0-3 h, trough FEV1, and SGRQ. Both fixed dose combinations (FDC) 5ug/5ug and 2.5ug/5ug had statistically significant improvements over the mono-components in FEV1 AUC and trough FEV1.

Adjusted mean FEV trough after 52 weeks.



- The SGRQ showed significant improvement in responder rates (those who met the minimally significant decrease in total score by ≥ 4 units) for the FDC's (57.5% 5ug/5ug) over the mono-components (44.8% olodaterol, 48.7% tiotropium 5ug). The difference between the improvements in SGRQ scores in responders between the mono-

components and the FDCs were not statistically significant. Those on the FDC used less rescue therapies than did those on the mono-components.

- *Buhl R, Maltais F, Abrahams R, et al. Tiotropium and olodaterol fixed-dose combination versus mono-components in COPD (GOLD 2–4). Eur Respir J. 2015; 45: 969–79*

Efficacy of Tiotropium + Olodaterol in Patients with Chronic Obstructive Pulmonary Disease by Initial Disease Severity and Treatment Intensity: A Post Hoc Analysis

- **Design**: Post Hoc Analysis of by initial disease severity and treatment intensity of TOnado 1 and TOnado 2 trials. Same as above for Design, inclusion and exclusion criteria. Also analyzed if prior treatment with LAMA or LABA maintenance therapy caused a difference in outcomes.
- **Results**: Patients categorized as GOLD 2 (50 – 80% predicted FEV1) had the best response for FEV1 AUC and trough FEV1 regardless of whether treated with mono-components or FDC, with the FDC showing statistically significant improvements over the mono-therapy. However, patients in the GOLD 3-4 categories still showed statistically significant improvements. Gold 3-4 patients actually reflected a better response if they had not been on prior maintenance therapy with a LAMA or LABA, while GOLD 2 did not reflect such a trend. The authors also looked at other patient subgroups including age, sex, and prior ICS usage. The FDC was found to be more effective statistically across all of these subgroups, except for the trough FEV1 in patients aged 75-85 years old when FDC 5ug/5ug was compared to Tiotropium 5ug.
- *Ferguson G., Flez˘ar M., Korn S. Efficacy of Tiotropium + Olodaterol in Patients with Chronic Obstructive Pulmonary Disease by Initial Disease Severity and Treatment Intensity: A Post Hoc Analysis Adv Ther (2015) 32:523–536*

Package Insert: According to the package insert, the Stiolto Respimat underwent 3 dosing range trials, two active controlled trials, three active- and placebo controlled trials and one placebo controlled trail, with the efficacy being based primarily on the two 4-week dosing trials and the two active controlled trials (discussed above). A subset of patients (n=521) completed an extended lung function measurements up to 12 hours post-dose. In this study, the STIOLTO RESPIMAT showed a significantly greater FEV1 response compared to tiotropium 5 mcg and olodaterol 5 mcg over the full 24-hour dosing interval.

Pending research: DYNAGITO study. It will assess the potential benefit of tiotropium + olodaterol Respimat FDC compared to Spiriva® (tiotropium) Respimat on reducing the risk of sudden worsening of symptoms (exacerbations) and improving survival in patients with COPD. The 52-week study aims to involve 7,800 patients in 59 countries. Results are expected in 2017. There are also trials underway regarding Stiolto and LAMA/ICS inhalers, and its benefits in exercise endurance.

Conclusion: Stiolto may have a role as add–on therapy in improving symptomatic breathlessness. We need more information to determine exact place in therapy. They may provide an effective and potentially safer alternative to a LABA/ICS combination in step up therapy in symptomatic patients especially in those who have contraindications to ICS use.

Recommendation: Do not cover at this time. Reconsider when the DYNAGITO study results are published.

Outcome: cover at Tier 3

Irenka (duloxetine) 40mg cap
Andrew Mullings, Pharm.D.
7/12/2015

Labeled Uses: Irenka (duloxetine) is a SNRI with similar indications as duloxetine including major depressive disorder, diabetic neuropathy, generalized anxiety disorder, and chronic musculoskeletal pain. Of note, it is not indicated to treat fibromyalgia unlike its counterparts.

Dosing:

Indication	Dose
Major Depressive Disorder	Initial: 40 to 60 mg QD; dose may be divided (ie, 20 or 30 mg BID) or given as a single 60mg daily dose. May start at 30 mg QD for 1 week before increasing to 60 mg QD. Maintenance: 60 mg once daily; maximum dose: 120 mg daily
Diabetic neuropathy	Initial: 60 mg QD; lower initial doses if tolerability is a concern and/or renal impairment is present; max dose: 60 mg QD
Generalized anxiety disorder	Initial: 60 mg QD; lower initial doses, 30 mg QD for 1 w before increasing to 60 mg QD. For doses >60 mg QD, titrate dose in increments of 30 mg QD over 1w (US labeling) as tolerated; max dose: 120 mg QD.
Chronic musculoskeletal pain	30 mg QD X1w, then increase to 60 mg QD as tolerated; max dose: 60 mg QD

Comparator Drugs:

Brand	Dose*	AWP	Cost Per Day
Irenka (duloxetine 40mg EC pellets capsule)	1 tablet	$8.724 Per tablet	$8.724
Cymbalta (duloxetine 20mg EC pellets capsule)	2 tablets	$466.56 / 30 day supply (#60)	$15.552
Duloxetine 20mg EC capsule	2 tablets	$419.44 / 30 day supply (#60)	$13.981

Analysis: The new Irenka tablet offers a single tablet alternative in place of taking two 20mg tablets to achieve a 40mg dose. The utility of this, would likely be beneficial in the treatment of MDD which contains an initial dosing range including 40mg. However, in other indications, this product does not offer any dosing advantages and is not indicated to treat fibromyalgia unlike its counterparts.
Additionally, according to current dosing instructions, patients on the 40mg would likely be titrated to a maintenance dose of at least 60mg, which is the therapeutic dose for the indication of major depressive disorder. Secondary to this, potential cost savings would be eroded in time.

Evidence: Clinical trial evidence supports a dose response relation of duloxetine. A R, DB, placebo and active controlled, multi-centered study in patients with MDD (n=353) demonstrated significantly higher remission rates for patients on the 80mg (50%) vs 40mg (35% p=0.045).

Recommendation: Given the limited utility of Irenka's 40mg dose, recommend excluding from coverage.

Outcome: Excluded by EBRx.

Goldstein DJ, Lu Y, Detke MJ, et al: Duloxetine in the treatment of depression: a double-blind placebo-controlled comparison with paroxetine. J Clin Psychopharmacol 2004; 24:389-399.

Panobinostat (Farydak)

FDA Labeled indication: Treatment of multiple myeloma (in combination with bortezomib and dexamethasone) in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.

Comparator Drugs: For relapsed or refractory multiple myeloma

Category 1 NCCN recommendations	Regimen	Dose and Price per Cycle
Bortezomib	IV, SubQ: 1.3 mg/m^2 twice weekly for 2 weeks on days 1, 4, 8, and 11 of a 21-day treatment cycle. Therapy extending beyond 8 cycles may be administered by the standard schedule or may be given once weekly for 4 weeks (days 1, 8, 15, and 22), followed by a 13-day rest (days 23 through 35).	B=$5601.52/10.192 mg **Total per cycle: $5,601.52**
Bortezomib/ Liposomal Doxorubicin	▪ Bortezomib: IV: 1.3 mg/m^2/day days 1, 4, 8, and 11 [total dose/cycle = 5.2 mg/m^2] ▪ Doxorubicin (liposomal): IV: 30 mg/m^2 day 4 [total dose/cycle = 30 mg/m^2] Repeat cycle every 21 days for **up to 8 cycles**	B=$5601.52/10.192 mg Lip.Dox.=$3418.63/58.8 mg **Total per cycle: $9,020.15**
Lenalidomide/ Dexamethasone	▪ Lenalidomide: Oral: 25 mg/day days 1 to 21 [total dose/cycle = 525 mg] ▪ Dexamethasone: Oral: 40 mg/day days 1, 8, 15, and 22 [total dose/cycle = 160 mg] Repeat cycle every 28 days	L=$11825.81/21 tabs (25mg) D=$25.60 / 40 tabs (4mg) **Total for cycle =$11,851.41**
Panobinostat/ Bortezomib/ Dexamethasone	▪ Panobinostat (20 mg; on days 1, 3, 5, 8, 10, 12, orally) ▪ Bortezomib (1.3 mg/m^2 on days 1, 4, 8, 11, intravenously) ▪ Dexamethasone (20 mg on days 1, 2, 4, 5, 8, 9, 11, 12, orally). **For up to 8 cycles.** Treatment may continue (at the same schedule) for an additional 8 cycles in patients experiencing clinical benefit and acceptable toxicity.	P=$8232 / 6 tabs (20mg) B=$5601.52/10.192 mg D=$25.60 /40 tabs (4mg) **Total for cycle=$13,859.12**
Carfilzomib/ Lenalidomide/ Dexamethasone	▪ Carfilzomib ○ Cycle 1: 20 mg/m^2 on days 1 and 2 followed by 27 mg/m^2 on days 8, 9, 15, and 16. ○ Cycles 2 to 12: 27 mg/m^2 on days 1, 2, 8, 9, 15, and 16. ○ Cycles 13 to 18: 27 mg/m^2 on days 1, 2, 15, and 16 ▪ Lenalidomide (25 mg) was given on days 1 through 21. ▪ Dexamethasone (40 mg) was administered on days 1, 8, 15, and 22.	C= Cycle1=$10,042.57 Cycles 2-12=$10,992.52 Cycles 13-18=$7,286.82 L=$11825.81/21 tabs (25mg) D=$25.60 / 40 tabs (4 mg) **Total for Cycle 1: $21,893.98** **Total for Cycle 2-12: $22,843.93** **Total for Cycle 13-18: $19,112.63** **Total Cycle 19+: $11,851.41**

*Based on patient ht 69 in, 80 kg, BSA 1.96m^2

MOA: Panobinostat is a histone deacetylase (HDAC) inhibitor; inhibits enzymatic activity of HDACs resulting in increased acetylation of histone proteins. Accumulation of acetylated histones and other proteins induces cell cycle arrest and/or apoptosis of some transformed cells. Panobinostat has minimal activity in multiple myeloma as a single-agent; however, synergistic activity is demonstrated when combined with bortezomib and dexamethasone

Contraindications: none

Adverse Reactions: Abnormal T waves, ST depression, arrhythmias, peripheral edema, fatigue, diarrhea, nausea, thrombocytopenia, increased serum creatinine

- BBW: Severe and fatal cardiac ischemic events, severe arrhythmias, and ECG.
- BBW: Severe diarrhea.

Drug Interactions: QT prolonging agents, immunosuppressants, CYP3A4/2D6 substrates.

Evidence:

<u>Panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma: a multicentre, randomised, double-blind phase 3 trial</u>

Design: PANORAMA1 (PANobinostat ORAl in multiple MyelomA 1) a placebo- controlled, phase 3 trial done at 215 centers, in 34 countries. Patients were randomly assigned (1:1) to receive either panobinostat, bortezomib, and dexamethasone or placebo, bortezomib and dexamethasone. The 1` endpoint of PFS and was defined as the time from randomization until documented disease progression, relapse from complete response, or death, whichever came first. The 2` endpoint was OS, which was defined as the time from randomization to death from any cause.

Results: An improved median PFS with panobinostat containing regimen compared with the control arm (11.99 months [95% CI; 10.33– 12.94 months] vs. 8.08 months [95% CI; 7.56–9.23 months]; HR= 0.63, 95% CI; 0.52–0.76; *P* <. 0001) along an increased depth of response. The regimen containing panobinostat is associated with significant toxicity. Serious adverse events were reported in 228 (60%) of 381 patients in the panobinostat group and 157 (42%) of 377 patients in the placebo group such as thrombocytopenia 67% vs. 31%), lymphopenia (53% vs. 40%), diarrhea (26% vs. 8%), fatigue (4% vs. 2%), and peripheral neuropathy (18% vs. 5%). OS was unable to estimate yet.

San-Miguel, Jesús F., Vânia T M Hungria, Sung-Soo Yoon, Meral Beksac, Meletios Athanasios Dimopoulos, Ashraf Elghandour,et. All. "Panobinostat plus Bortezomib and Dexamethasone versus Placebo plus Bortezomib and Dexamethasone in Patients with Relapsed or Relapsed and Refractory Multiple Myeloma: A Multicentre, Randomised, Double-blind Phase 3 Trial." The Lancet Oncology. (2014)15(11): 1195-206. Web. 21 Apr. 2015.

<u>Carfilzomib, Lenalidomide, and Dexamethasone for Relapsed Multiple Myeloma</u>

Design: 792 patients with relapsed multiple myeloma were randomly assigned to carfilzomib with lenalidomide and dexamethasone (carfilzomib group) or lenalidomide and dexamethasone alone (Rd)(control group). The 1` endpoint was PFS.

Results: When compared with Rd alone, Rd plus carfilzomib resulted in an improved ORR (87% versus 67%). Rd plus carfilzomib resulted in improved PFS (median 26 versus 18 months; hazard ratio 0.69; 95% CI 0.57-0.83), a trend towards superior overall survival (73% versus 65% at 24 months; hazard ratio 0.79; 95% CI 0.63-0.99) and an improved quality of life as measured by the QLQ-C30 Global Health Status and Quality of Life scale (difference 5.6 points). Rd plus carfilzomib also showed higher rates of adverse events (84% versus 81%), but no increase in drug discontinuation due to toxicity 15% versus 18%.

Stewart, Keith A., M.B, Vincent S. Rajkumar, M.D., and Meletios A. Dimopoulos. "Carfilzomib, Lenalidomide, and Dexamethasone for Relapsed Multiple Myeloma." New England Journal of Medicine 372.2 (2015): 142-52. Massachusetts Medical Society, 8 Jan. 2015. Web. 22 Apr. 2015.
****unable to view full article****

<u>Phase 2 dose-expansion study (PX-171-006) of carfilzomib, lenalidomide, and low-dose dexamethasone in relapsed or progressive multiple myeloma</u>

Design: PX-171-006 is a multicenter, single-arm, open-label, phase 1b/2 study. The objectives of the phase 2 portion of the study were to assess safety and secondary efficacy end points, ORR; defined as ≥partial response, PFS, and DOR.

Results: In the MPD (maximum planned dose) cohort (n=52), the ORR was 76.9% with a median time to response of 0.95 month (range, 0.5-4.6) and median DOR of 22.1 months (95% confidence interval [95% CI], 9.5-38.0). After a median follow-up of 24.4 months (95% CI, 10.6-37.3), median PFS was 15.4 months (95% CI, 7.9–34.1). The most common AEs of any grade (in the MPD cohort) were fatigue (69.2%) and diarrhea (57.7%), lymphopenia (51.9%), neutropenia (36.5%), and anemia (32.7%).

Wang, M., T. Martin, W. Bensinger, M. Alsina, D. S. Siegel, E. Kavalerchik, M. Huang, R. Z. Orlowski, and R. Niesvizky. "Phase 2 Dose-expansion Study (PX-171-

006) of Carfilzomib, Lenalidomide, and Low-dose Dexamethasone in Relapsed or Progressive Multiple Myeloma." Blood 122.18 (2013): 3122-128. Web. 22 Apr. 2015.

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NCCN Guidelines Version 4.2015
Multiple Myeloma

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Multiple Myeloma Table of Contents
Discussion

MYELOMA THERAPY[1,2,3,8]

Exposure to myelotoxic agents (including alkylating agents and nitrosoureas) should be limited to avoid compromising stem-cell reserve prior to stem-cell harvest in patients who may be candidates for transplants.

	Preferred Regimens	Other Regimens
Therapy for Previously Treated Multiple Myeloma	• Repeat primary induction therapy (if relapse at >6 mo) • Bortezomib (category 1) • Bortezomib/dexamethasone • Bortezomib/lenalidomide/dexamethasone • Bortezomib/liposomal doxorubicin (category 1) • Bortezomib/thalidomide/dexamethasone • Carfilzomib • Carfilzomib/lenalidomide/dexamethasone (category 1) • Cyclophosphamide/bortezomib/dexamethasone • Cyclophosphamide/lenalidomide/dexamethasone • Dexamethasone/cyclophosphamide/etoposide/cisplatin (DCEP) • Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide (DT-PACE) ± bortezomib (VTD-PACE) • High-dose cyclophosphamide • Lenalidomide/dexamethasone[9] (category 1) • Panobinostat/bortezomib/dexamethasone[10] (category 1) • Pomalidomide[11]/dexamethasone • Thalidomide/dexamethasone[9]	• Bendamustine • Bortezomib/vorinostat • Lenalidomide/bendamustine/dexamethasone

[1]Selected, but not inclusive of all regimens.
[2]Recommend herpes zoster prophylaxis for patients treated with bortezomib and carfilzomib. Consider using subcutaneous bortezomib for patients with pre-existing or high-risk peripheral neuropathy.
[3]Prophylactic anticoagulation recommended for patients receiving thalidomide-based therapy or lenalidomide with dexamethasone.
[8]Consideration for appropriate regimen is based on the context of clinical relapse.
[9]Consider single-agent lenalidomide, pomalidomide, or thalidomide for steroid-intolerant individuals.
[10]Indicated in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.
[11]Indicated for patients who have received at least two prior therapies including bortezomib and an immunomodulatory agent and have demonstrated disease progression on or within 60 days of completion of the last therapy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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Recommendation: Panobinostat/Bortezomib/Dexamethasone is better than Bortezomib/Dexamethasone alone at improving PFS (12 vs. 8 months), but without known OS improvement to date, and with added ADE and BBW.

Outcome: Exclude from coverage due to lack of OS data. PFS was only 4 m.

EBRx Arkansas Employee Benefits Division
Prior Authorization Criteria
for ivacaftor (Kalydeco) 150mg tablets

Initial approval criteria:

1. Does the patient have a diagnosis of cystic fibrosis with gene positive testing for the *G551D-CFTR* mutation OR one of these mutations: G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, R117H?	**□Yes □ No**
2. Is the patient 2 years of age or older?	**□Yes □ No**
3. Is the patient currently demonstrating compliance with the evidence-based standard of care for inhaled therapies for cystic fibrosis?[1] (Or does the patient experience intolerance to dornase alfa &/OR bronchospasm or irritability with inhaled hypertonic saline and therefore cannot use it?—This must be documented in the medical record and represented to the call pharmacists.)	**□Yes □ No**
4. Has the patient had transaminases (ALT and AST) drawn prior to beginning the drug and will they be monitored every 3 months during the 1st year of treatment and then annually thereafter? [Ivacaftor should be interrupted if ALT or AST is greater than 5xs ULN and benefits/risks should be reconsidered.]	**□Yes □ No**
5. Does the patient smoke tobacco products?	**□Yes □ No**
If "yes" to 1-4 and "no" to 5, approve for 1 year. Otherwise, deny coverage.	

***Quantity limit of 62/31 days; normal dose is 150 mg BID**

In a NEJM 2011 article, ivacaftor at a dose of 150 mg BID was compared to placebo in pulmonary function improvement in patients aged 12 years and up with cystic fibrosis with at least one *G551D-CFTR* gene mutation. The trial was run for 48 weeks; by week 2, pulmonary improvements could be seen with ivacaftor. The primary endpoint was the mean change from baseline by week 24 in percent of predicted forced expiratory volume in 1 second (FEV_1). Ivacaftor, on average, raised the FEV_1 over placebo by 10.6% reflecting a mean increase in FEV1 of 367 mL (P,0.001); this was maintained through week 48.

Continuation criteria:

1. Is the patient currently demonstrating compliant with the evidence-based standard of care for inhaled therapies for cystic fibrosis? (or does the patient experience intolerance to dornase alfa &/OR bronchospasm or irritability with inhaled hypertonic saline and therefore cannot use it)?	**□Yes □ No**
2. Has the patient had transaminases (ALT and AST) drawn prior to beginning the drug and will they be monitored every 3 months during the 1st year of treatment and then annually thereafter?	**□Yes □ No**
3. Does the patient smoke tobacco products?	**□Yes □ No**
4. Has the patient experienced a clinical benefit with ivacaftor as shown by lung function (FEV1), weight gain, or reduction in CF exacerbations or CF hospitalizations?	**□Yes □ No**
5. Has the member been compliant with therapy as determined by refill history or reported by physician?	**□Yes □ No**
If "yes" to 1-4 and "no" to 5, approve for 1 year. Otherwise, deny coverage.	

***Quantity limit of 62/31 days; normal dose is 150 mg BID**

References:

1. **Mogayzel PJ, Naureckas ET, Robinson KA, Mueller G, et al. cystic Fibrosis Pulmonary Guidelines: Chronic medications for maintence of lung health. Am J Respir Crit Care Med. 2013;187(7):680-689.**
2. Ramsey, B et al. A CFTR Potentiator in Patients with Cystic Fibrosis and the *G551D* Mutation. N Engl J Med 2011; 365: 1663-72

Date	What changed?	Pharmacist's initials
3/6/13	Criteria created	JB
3/6/13	Jill added standard of care criteria and transaminase monitoring requirement	JJ
6/30/14	Jill added other gene mutations to be allowed.	JJ
12/30/14	Jill inserted the requirement that CF patients on ivacaftor must be tobacco free; introduced continuation criteria; and changed the language for demonstrating adherence to evidence-based SOC therapies. Also added reference for current CF guidelines.	JJ

Mircera® (methoxy polyethylene glycol-epoetin beta)
2015 Nghia Tran

Maintenance treatment of renal anemia in HD patients with IV Mircera qm vs IV darbepoetin alfa qm: a randomized comparative trial

- Phase III, R, multi-national, parallel group, prospective trial from 82 centers in Europe, Canada and Australia
- N=490, included: aged≥18 years, had stable chronic renal anemia (Hb range of 11–13 g/dL), and on regular HD
- N=245 received IV Mircera QM for 26 w w/ dose adjustment for Hb target (11–13 g/dL; max decrease from baseline 1 g/dL)
- N=245 received IV darbepoetin alfa q 2 w for 26 w with dose adjustment for Hb target (11–13 g/dL; max decrease from baseline 1 g/dL)
- Primary endpoint: proportion of patients who maintained average Hb≥10.5 g/dL, with a decrease from baseline≤1 g/dL
- Results:
  - Response rate in 157 of 245 (64.1%) of Mircera pts
  - Response rate in 99 of 245 (40.4%) of darbepoetin alfa pts
  - Absolute difference of 23.7% (95% CI 14.9–32.5; P < 0.0001)
  - RR of response with Mircera vs darbepoetin alfa 1.59 (95% CI 1.33–1.90)
  - Most common A/E included: HTN, procedural hypotension, nasopharyngitis and muscle spasms
    - No differences between groups
- Authors concluded: treatment with Mircera administered IV QM was superior to darbepoetin alfa IV at the same dosing interval for maintaining Hb concentrations in patients with CKD and renal anemia (P < 0.0001) despite dose increases with darbepoetin alfa

Carrera F, Lok CE, et al. Maintenance treatment of renal anemia in HD patients with methoxy polyethylene glycol-epoetin beta versus darbepoetin alfa administered monthly: a randomized comparative trial. *Nephrol Dial Transplant* 2010; 25:4009–4017

Efficacy of IV Mircera q2w compared with epoetin 3 times weekly in HD or PD patients: a randomized trial

- Phase III, R, MC, open-label, parallel study at 42 centers in 10 countries from March 2004 to December 2005
- N=181, included: age ≥18 years with CKD stage 5 on HD or PD for ≥2 w
- N=135 received IV C.E.R.A. (methoxy polyethylene glycol-epoetin beta) q 2 w at an initial dose of 40 mcg/kg
- N=46 received IV epoetin (epoetin alfa, N=5; epoetin beta, n=41) 3x/week
- Primary Endpoint: Hb level response rate (increase in Hb level ≥1 g/dL vs baseline and Hb level ≥11 g/dL without blood transfusion during the 24-week correction period) in the ITT population
- Results:
  - Hb response rates ITT population were
    - C.E.R.A. pts 93.3% (95% CI; 87.72-96.91)
    - Epoetin pts 91.3% (95% CI; 79.21-97.58)
  - Hb response rates per-protocol population
    - Peak mean Hb levels
      - C.E.R.A pts 12.28±1.13 (SD) g/dL
      - Epoetin pts 12.19+1.24 g/dL
    - Mean change in Hb levels from baseline to the end of the correction period
      - C.E.R.A pts 2.70±1.45 g/dL
      - Epoetin pts 2.56±1.31 g/dL
    - Median times to Hb level response
      - C.E.R.A pts ~8 weeks (57 days; 95% CI, 50 to 64)
      - Epoetin pts ~4.4 weeks (31 days; 95% CI, 27 to 38)
  - Both treatments were generally well tolerated; most AEs were not considered to be treatment related and were consistent with those commonly associated with this patient population
  - Authors concluded: IV C.E.R.A. q 2 weeks may be as safe and effective as 3x/week epoetin for correcting anemia in dialysis patients

Klinger M, Arias M, et al. Efficacy of intravenous Mircera administered q2w compared with epoetin TIW in HD or PD patients: a randomized trial. *Am J Kidney Dis* 2007; 50: 989–100O

Recommendations: Include Aranesp® b/c cost is comparable with other ESAs; less dosing frequency than epoetin; effective in patients with CKD and certain types of cancer; recommended in the KDIGO and NCCN guidelines. Include Mircera® b/c cost is comparable with other ESAs; less dosing frequency; phase III studies show superiority to darbepoetin alfa and as safe and effective as epoetin (alfa and beta).

Deferasirox (Jadenu)
90mg, 180mg, 360mg tablets
Casey Jones
6/25/15

Labeled Uses:

- Treatment of chronic iron overload due to blood transfusions in patients 2 years of age or older
  - Exjade: Initial 20 mg/kg/day, then up to 40 mg/kg/day
  - Jadenu: Initial 14 mg/kg/day, then up to 28 mg/kg/day
- Treatment of chronic iron overload in non-transfusion-dependent thalassemia syndromes in patients 10 years or over.
  - Exjade: Initial 10 mg/kg/day, then up to 20 mg/kg/day
  - Jadenu: Initial 7 mg/kg/day, then up to 14 mg/kg/day

Comparators:

Drug Name	Jadenu (oral tablet)	Exjade (tablet for oral suspension)
Dosage	Initial: 14 mg/kg once daily Maint: Titrate up to goal	Initial: 20 mg/kg once daily Maint: Titrate up to goal
AWP	90 mg (30): $1019.90 180 mg (30): $2039.76 360 mg (30): $4079.45	125 mg (30): $1019.90 250 mg (30): $2039.76 500 mg (30): $4079.45
Conversion	Exjade to Jadenu: 30% lower rounded to the nearest whole tablet due to improved bioavailability w/ Jadenu.	

Pharmacokinetics: "The absolute bioavailability (AUC) of deferasirox tablets for oral suspension is 70% compared to an IV dose. The bioavailability (AUC) of JADENU was 36% > with deferasirox tablets for oral suspension. After strength-adjustment, JADENU (i.e., 360 mg strength) was equivalent to deferasirox tablets for oral suspension (i.e., 500 mg strength) with respect to the mean AUC under fasting conditions, however the mean Cmax was increased by 30%. The exposure-response analysis for safety indicated that 30% increase in JADENU Cmax is not clinically meaningful."

Pricing example with 60 kg patient:

Drug	AWP per tablet	AWP per mg	Initial Dose: 60 kg pt	Maintenance Dose: 60 kg pay
Exjade	125mg: $39.997 250mg: $67.992 500mg: $135.982	125mg: $0.32 250mg: $0.27 500mg: $0.27	20mg/kg/day:1200 mg 5-250 mg tabs: $396.96	40mg/kg/day:2400 mg 5-500 mg tabs: $679.91
Jadenu	90mg: $39.997 180mg: $67.992 360mg: $135.982	125mg: $0.44 250mg: $0.38 500mg: $0.38	14mg/kg/day: 840 mg 5-180 mg tabs: $396.96	28mg/kg/day:1680 mg 5-360 mg tabs: $679.91

Contraindications:

- Hypersensitivity to deferasirox
- CrCl <40 mL/min
- SCr ≥ 2 ULN
- High risk myelodysplatic syndromes
- Advanced malignancies
- Platelet counts < 50,000 mm^3

Drug Interactions:

- Aluminum containing antacids, CYP3A4 (Jadenu is an inducer), SSRIs, Tricyclics, Antipsychotics, Benzodiazepines, Statins, Calcium Channel Blockers, CYP2C8 (Jadenu is an inhibitor), Repaglinide, Paclitaxel , CYP1A2 (Jadenu is an inhibitor), Bile Acid Sequestrants

Black Box Warnings:

- Can cause Renal failure, Hepatic failure, Gastrointestinal bleeding,

Benefits:

- Once-daily oral tablet that can be swallowed whole with water or other liquid and does not require to be dissolved in liquid like Exjade (also QD).
- Jadenu can be taken without regards to food, while Exjade must be taken on an empty stomach

Recommendation: Cover Jadenu with PA criteria as it has better bioavailability than Exjade and is priced the same. Exjade and Jadenu could be available with a PA.

Outcome: Cover Jadenu with current Exjade PA requirement. Continue to cover Exjade as well.

References:

Deferasirox. National Institutes of Health MedlinePlus website. http://www.nlm.nih.gov/medlineplus/druginfo/meds/a606002.html. Updated on October 1, 2010. Accessed on June 4, 2015.

Jadenu [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2013

Note: All data from Jadenu package insert used the clinical trials for Exjade tablet for oral suspension.

Parathyroid Hormone (Natpara)
25, 50, 75, 100mcg cartridge, SC using the Q-cliq pen
Jill Johnson, Pharm.D.

FDA Indication: Hypoparathyroidism as an adjunct to calcium and vitamin D to control hypocalcemia. Because of risk of osteosarcoma, it is recommended only for pts who cannot be controlled on Ca+VitD supplements alone. The drug has not been studied in pts w/ hypoparathyroidism caused by Ca-sensing receptor mutations or in pts w/ acute postsurgical hypoparathyroidism.

REMS is in place for assuring safe use.

Dosing:
***Must make sure serum Ca (adjusted for serum albumin) is >7.5mg/dL and 25-hydroxyvitamin D stores are sufficient AND IF NOT, they must be corrected prior to initiating PTH.
Initial: 50mcg QD
Adjustment: increase every 4w by 25mcg/d increments, max dose is 100mcg/d

Cost:
$4750 (AWP) per cartridge of 1 each regardless of mcg cartridge.

31ds=$147,250

Per UpToDate (accessed 5/28/15):
"The addition of recombinant human parathyroid hormone (1-84) is an option for patients with chronic hypoparathyroidism who cannot maintain stable serum and urinary calcium levels with calcium and vitamin D supplementation. **However, parathyroid hormone (PTH) 1-84 is not yet initial therapy because of high cost, the necessity for subcutaneous administration, and uncertainty about long-term safety of dosing for primary hypoparathyroidism.**

Hypoparathyroidism is treated 1st line with Ca 1-2g of elemental daily in divided doses, and Vit D (although PTH is required for the renal conversion of calcidiol, aka 25-hydroxyvitamin D, to the active metabolite calcitriol, aka 1,25-dihydroxyvitamin, therefore calcitriol is the treatment of choice). Calcitriol 0.25 mcg BID-2mcgQD.

The goals of therapy in patients with hypoparathyroidism are to relieve symptoms, to raise and maintain the serum calcium concentration in the low normal range (eg, 8.0 to 8.5 mg/dL [2.0 to 2.1 mmol/l]), and to prevent iatrogenic development of kidney stones. Attainment of higher values is not necessary and is usually limited by the development of hypercalciuria due to the loss of renal calcium-retaining effects of PTH.

Second-line therapy — In view of the fact that hypoparathyroidism is a hormonal deficiency, replacement of the missing hormone, ie, PTH 1-84, is a potentially attractive intervention. For patients with chronic hypoparathyroidism who cannot maintain stable serum and urinary calcium levels with calcium and vitamin D supplementation, the addition of recombinant PTH 1-84 is an option [30]. In small trials, it has been shown to maintain serum calcium levels while reducing the need for large doses of calcium and vitamin D. It is not considered first-line therapy, however, primarily since the long-term safety of dosing for primary hypoparathyroidism (relative to its skeletal effects) has not been established (particularly in growing children who may be at greater risk of osteosarcoma). In addition, recombinant PTH is much more expensive than standard therapy with calcitriol and calcium.

Recommendation:
Exclude parathyroid hormone (Natpara). Until a controlled trial comparing Ca+calcitriol vs rhPTH shows a clinical benefit with rhPTH over the 1st-line therapy, it should not be covered. There are no cost-effectiveness studies in PubMed to date (5/28/15).