AGENDA

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

April 8, 2013 – 1:00 PM

1. **Call to Order** ..... *Dr. Matthew Hadley, Chairman*
2. **Approval of Minutes** ..... *Dr. Matthew Hadley, Chairman*
3. **Tabled Items**..... *Jill Johnson, UAMS*
4. **Second Review Drugs** ..... *Jill Johnson, UAMS*
5. **New Drugs** ..... *Jill Johnson, UAMS*
6. **Antidepressant Class Review** ..... *Jill Johnson, UAMS*
7. **PPI / H2 Antagonist Class Review** ..... *Jill Johnson, UAMS*
8. **Director's Report** ..... *Jason Lee, EBD*

Next Meeting
August 5th

State and Public School Life and Health Insurance Board Clinical and Fiscal Drug Utilization and Evaluation Committee
Minutes
February 4, 2012

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday, February 4, 2013 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Little Rock, AR.

Members present:
Matthew Hadley
Kat Neill
Dr. William Golden
Larry Dickerson/Proxy
Scott Pace
Dr. Hank Simmons
Dr. Joe Stallings

Members absent:
Kelly Chaney
Mark McGrew

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

OTHERS PRESENT
Jill Johnson, UAMS College of Pharmacy/EBRx; Connie Bennett, Informed Rx; John Kirtley, State Board of Pharmacy; Jordan Brazeal, Pharm.D. Evidence-based Medicine Pharmacy Practice Resident ; Doug Shackleford; Michelle Hazelett, Sherri Saxby, Sherry Bryant, Melida Vasquez, Cathy Harris, EBD; Janna Keathley, AHH; Bridget Johnson, Pfizer, Dwight Davis, David Keisner, Allison Hollis, Amy Chiaro, UAMS; Warren Tyes, Merck; Rhonda Walthall, AHTD; Barbara Melugin, Tonya Rogers, Health Advantage; Gary Riordan, NovoNordisk; John Harris, Abbott; Charlene Kaiser, Amgen; David Williams, Forest Pharmaceuticals; Bruce Valentine, Accordia Pharmaceuticals

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

APPROVAL OF MINUTES
The motion was made by Dr. Hadley to approve the November 5, 2012 minutes. Neill made the motion to approve. Dr. Simmons seconded. All were in favor. Minutes were approved.

TESTOSTERONE REVIEW-CLINICAL DISCUSSION *by Jill Johnson*
The committee reviewed the Endocrine Society's clinical guidelines for Testosterone therapy in adult men with Androgen Deficiency Syndromes.

Committee discussion: Testosterone replacement therapy is primarily indicated for the treatment of male hypogonadism.

Recommendation: Cover the injectable Testosterone and not the topical - Communicate to current users the transition period. Continue to require PA.

CONSIDERATION OF REFERENCE PRICING OF NASAL STEROIDS-CLINICAL DISCUSSION *by Jordan Brazeal*
Nasal corticosteroids (NCs) are a diverse group of agents available as treatment options for allergic and non-allergic rhinitis (AR).

In a drug class review by the Oregon Health & Science University, NCs were systematically evaluated based on efficacy and adverse event profiles. The differences in efficacy were found in mometasone and budesonide in the treatment of two different types of AR. While mometasone was associated with a reduction in severity of rhinitis symptoms when compared to beclomethasone in the prophylaxis of seasonal AR, the mometasone arm had a lower mean nasal symptoms score at baseline, and thus may have overinflated the differences between the arms. Brazeal explained how the scores were evaluated.

Recommendation: Reference price nasal corticosteroids (NCs)

CONSIDERATION OF REFERENCE PRICING OF OVERACTIVE BLADDER AGENTS *by Jordan Brazeal*
The mainstay of pharmacologic treatment of overactive bladder (OAB) lies in the antispasmodic actions of the numerous anticholinergic agents currently available for relief of incontinence. In a drug class review published by the Oregon Health & Science University, the agents for OAB were evaluated based upon efficacy and adverse event profiles

Recommendation: Reference price overactive bladder agents except for the generic products oxybutynin and oxybutynin ER, which will remain covered with a Tier 1 copayment.

ALZHEIMER'S DRUGS *by Jill Johnson*
The medications include: Razadyne® (galantamine), Exelon® (rivastigmine), Aricept® (donepezil) and Namenda® (memantine).

Recommendation: Continue 31-day fill limit in the above listed drugs and look for therapeutic duplication.

REVIEW OF BID VS XR ADDERALL/STIMULANTS *by Jill Johnson*

The committee reviewed the Cochrane Collaboration review: Amphetamines for Attention Deficit Hyperactivity Disorder (ADHD) in adults.

Recommendation: For adults age 26 year and older. Reimburse for immediate release Amphetamines products only. Cover the extended release products but at no more cost for the plan than what we would have reimbursed for immediate release products. (Extended release products will be referenced priced for adults age 26 and over.) Notify current users of price change.

FIRST REVIEW MEDICATIONS *by Jill Johnson*

Drug Name	Tier Status
Eliquis (apixaban)	**T2 w/PA, QL**

Indication- anticoagulant
Similar therapies on Formulary/tier/ AWP - warfarin, Pradaxa (PA), Xarelto (PA and QL)

Aubagio tabs (Teriflunomide) **T3 w/PA, QL**
Indications– Oral treatment for relapsing forms of multiple sclerosis.
Similar therapies on Formulary/tier/ AWP - Gilenya - also oral therapy. Currently covered w/PA. Arava

Juxtapid (lomitapide) **T3 w/PA**
Indications- (tx for homozygous familial hypercholesterolemia. Will only be available through one specialty pharmacy – Centric Health)
Similar therapies on Formulary/tier/ AWP- N/A

Xeljanz (tofacitinib citrate) **T3 w/PA**
Indications- For adults with moderately to severely active rheumatoid arthritis who have an inadequate response or intolerance to methotrexate

Bosulif (bosutinib) **T3 w/PA**
Indications- Oral treatment of adults w/chronic, accelerated, or blast phase Philadelphia chromosome-positive chronic myelogenous leukemia w/ resistant or intolerance to prior therapy
Similar therapies on Formulary/tier/ AWP- Bosulif is the fourth product approved in its therapeutic class, behind Gleevec, Tasigna, and Sprycel.

Prepopik Pak **T3**
Indications- Bowel preparation prior to colonoscopy
Similar therapies on Formulary/tier/ AWP – Golytely/Colyte /MoviPrep /PEG 3350 (Generics - $10 copay and Brand $30 copay)

Flucelvax **Free w/PA**

Indications- cell based flu vaccine
Similar therapies on Formulary/tier/ AWP - currently cover flu vaccine through pharmacy

Kalydeco (ivacaftor) **T3 w/PA**
Indications- Cystic Fibrosis

- **Cometriq (cabozantinib)** was **tabled** until the next meeting.
  Indications- Tx of patients w/progressive, metastatic medullary thyroid carcinoma (140mg/daily).

- **Oxtellar XR was tabled until the next meeting.**
  Indications- extended release form of oxcarbazepine (Trileptal) for the tx of partial seizures
  Similar therapies on Formulary/tier/AWP – N/A

Excluded Drugs

Linzess Caps (145mcg and 290mcg caps)
Indications - Treatment of irritable bowel syndrome w/constipation (IBS-C) and idiopathic constipation in adults Dose= 145mcg/day for idiopathic constipation.
290mcg/day for IBS-C
Similar therapies on Formulary/tier/ AWP - Amitiza

Lovaza (Omega-3-Acid Ethyl Esters)
Indications- hypertriglyceridemia
Similar therapies on Formulary/tier/ AWP - Never reviewed by DUEC but was covered. Send letters to members to notify of exclusion.

Vascepa (icosapent ethyl)
Indications - Approved as an adjunct to diet to reduce triglyceride concentrations in adults w/hypertriglycederidemia
Similar therapies on Formulary/tier/ AWP- Lovaza

Stivarga (regorafenib)
Indications- Treatment of metastatic colorectal cancer for patients should have been previously treated w/ currently available therapies. Dose: 160mg PO daily for first 21 days of each 28 day cycle
Similar therapies on Formulary/tier/ AWP
Review in 6 months

Iclusig (ponatinib)
Indications- Treatment of acute lymphocytic leukemia and chronic myelogenous leukemia (45mg/day) carcinoma (140mg/daily)
Similar therapies on Formulary/tier/ AWP- N/A

Episil (Exclude review in 6 mos)
Indications – Treatment for intra-oral pain caused by oral mucositis
Similar therapies on Formulary/tier/AWP – No info

Pliaglis Cream ((lidocaine & tetracaine) Cream 7%/7%Generic-
Indications- - Local/topical anesthesia
Similar therapies on Formulary/tier/ AWP – Local/topical anesthesia - Synera and Emla cream

Lotemax Ophth gel
Indications- Treatment of steroid responsive ophthalmic diseases.
Similar therapies on Formulary/tier/ AWP – Lotemax Ophth Ointment is currently covered by the plan

Quillivant Suspension XR (methylphenidate HCl for extended release suspension.
Indications- Max dose is 60mg/day given once daily in the morning for treatment of ADHD
Similar therapies on Formulary/tier/ AWP- Quillivant Susp is the only oral liquid extended release methylphenidate. Daytrana is available as a topical patch applied once daily

Dr. Golden requested the committee review class of drug used for treatment of severe hypertriglyceridemia.

NO QUORUM –

GENERIC METFORMIN VS GLUMETZA
AND OTHER ITEMS.

Meeting adjourned.

DUEC 4/2/2013

DUEC 4/2/2013				
GPI	**DRUG NAME**	**INDICATION**	**SIMILAR THERAPIES ON FORMULARY/ TIER**	Consultant's Notes
Tabled from last meeting				
215340131064**	Cometriq (cabozantinib)	Tx of patients w/progressive, metastatic medullary thyroid carcinoma (140mg/daily)	Caprelsa (300mg/day) also for thyroid cancer. Currently non-formulary on plan.	Discuss. See attachment. The alternative, Caprelsa (vandetanib) is excluded for similar reason 10/11/11 Insurance Board meeting. Exclude.
726000460075**	Oxtellar XR (oxcarbazepine)	extended release form of oxcarbazepine(Trileptal) for the tx of partial seizures		Delayed release tablet, not crushable/chewable. FDA-approved for adjunctive tx only. Per Lexicomp, most pts cannot tolerate CNS side effects from doses >2400mg/d. 3/25/13--still no clinical trials in PubMed with XR form. In PI, 1200mgXR/d did not reach statistical significance at reducing seizure frequency vs placebo. 2400mg/d did. From last mtg: T3. Adverse event profile scores and QOL improved significantly. (Review article available, original trial N/A). 85% of pts reported improved QOL. N=27 for entire trial. Not sure if trial was blinded which, if not, could have influenced the improved QOL scores.
215330500003**	Stivarga (regorafenib)	Treatment of metastatic colorectal cancer for patients who have been previously treated w/ currently available therapies. Dose: 160mg PO daily for first 21 days of each 28 day cycle	N/A	Drug with limited medical benefit. FDA-approval: Treatment of metastatic colorectal cancer in patients previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, anti-VEGF therapy, or anti-EGFR therapy (if KRAS wild type). **Median OS was 6.4m for regorafenib and 5m for placebo,** (95%CI 5.9-7.3; 4.4-5.8, respectively.) Grothey X, et al. Results of a phase 3 R, DB, PC multicenter trial of regorafenib + best supportive care vs placebo plus BSC. J Clin ONco. 2012 30(4supplement) LBA 385. Discuss median OS issue.
2nd review				

66100060107520	Naprelan (naproxen sodium)	pain, osteoarthritis.	see nsaids on PDL	3 trials available in abstract form only showed Naprelan was not different from IR naproxen. Lisse JR, Clinical efficacy and safety of naprelan versus naprosyn in the treatment of rheumatoid arthritis. Am J Orthop. 1996; Sep9;25(9suppl):21-9. Schiff MH. A comparison of naprelan and naprosyn in the treatment of osteoarthritis of the knee. Am J Orthop. 1996 Sep;25(9 Suppl):14-20. Hawkey C, et la. Two comparative endoscopic evaluations of Naprelan. Am J Orthop. 1996 Sep;25(9 Suppl):30-6.
613530301075**	Intuniv (guanfacine)	ADHD	guanfacine (T1)	This trial showed reduced tics but used IR guanfacine. Scahill L, Chappell P, Kim Y, Schultz R, Katsovich L. A placebo controlled study of guanfacine in the treatment of children with tic disorders and ADHD. American Journal of Psychiatry. 2001;158:1067–74. There are no comparative trials of XR vs IR in ADHD. Exclude,
215340351003**	Gleevec (imatinib)	CML, ALL	Sprycel (T2 PA), Tasigna (T3PA), Bosulif (T3 PA), Iclusig (excluded)	See attached PA criteria.
525570500001**	Linzess (linactolide)	IBS		Amitiza (lubipristone) is the alternative; in amitiza trials, they, too, required DC of all laxatives.
new drugs				
525330700064**	Gattex (teduglutide)	short bowel syndrome	Zorbtive (somatropin) PA, T3. Nutrestore(glutamine) is T2	ted 0.05mg/kg/d (not 0.1mg/kg/d) significantly improved graded response score (GRS) vs placebo; GRS accounted for the weekly TPN volume & whether it was reduced by ≥20%, and the duration during wks 16 & 20, and 20&24. Neither tx arm resulted in reduced days on TPN. Jeppesen PB, et al. *Gut* 2011;60:902-14.
275500101003**	Nesina (alogliptin) 6.25mg 12.5mg, 25mg--usual dose is 25 mg daily (dose determined by CrCl)	Type 2 diabetes	Januvia(T3 PA), Janumet (T3 PA),Kombiglyze XR (T3 PA), Onglyza (T3 PA), Tradjenta (T3 PA)	T3PA, QL 31/31--follow current DM criteria--pts must be on/ or intolerant to Metformin at the max dose. Decreases HbA1C 0.5% in T2DM; not studied in T1DM. (Defronzo R, et al. Efficacy and safety of the DPP-4 inhibitor in T2DM in inadequate glycemic control. Diab Care. 2008;31(12):315-17.) As add on to metformin, SU, insulin, or TZD, alogliptin has data in the PI, not PubMed.
279925021003**	Kazano (alogliptin + metformin)	Type 2 diabetes	Januvia(T3 PA), Janumet (T3 PA),Kombiglyze XR (T3 PA), Onglyza (T3 PA), Tradjenta (T3 PA)	T3PA, QL 31/31--follow current DM criteria--pts must be on/ or intolerant to Metformin at the max dose.

279940021003**	Oseni (alogliptin + pioglitazone)	Type 2 diabetes	Januvia(T3 PA), Janumet (T3 PA),Kombiglyze XR (T3 PA), Onglyza (T3 PA), Tradjenta (T3 P	T3PA, QL 31/31--follow current DM criteria--pts must be on/ or intolerant to Metformin at the max dose.
221000120075**	Uceris (budesonide tab SR 24HR 9mg)	UC	budesonide (T1)	From PL 3/13: Uceris is budesonide like Entocort EC...but not interchangeable. Both work locally in the GI tract to reduce systemic steroid effects...but they target different areas. Entocort EC targets the ileum and right colon for Crohn's disease...Uceris targets the entire colon for ulcerative colitis. UC tx is based on disease location and severity...patient preferences...and cost. Pts w/ distal disease may achieve remission w/ rectal mesalamine (Rowasa, etc) or hydrocortisone (Cortenema, etc)...but pts w/ more extensive disease usu need oral therapy. 5-ASA products (mesalamine, etc) are still first-line for inducing and maintaining remission in mild-mod dz. Uceris will be used as an alternative to oral prednisone if 5-ASA products aren't effective. Uceris will cost about $1200/m; vs as little as $4 per month for prednisone. But adrenal suppression is unlikely when Uceris is used short-term. T3PA. 1. Dx of UC, 2. failure of or intolerant to sulfasalazine, 3. failure of or intolerance of mesalamine oral or rectal.
52500030006530	DELZICOL (mesalamine 400mg delayed release, gastro-resistant capsule)	UC	Asacol (T2), Pentasa (T2). Rowasa (T3),	
214500800001**	POMALYST (POMALIDOMIDE)	multiple myeloma	Revlimid (T3 PA), Velcade (T2 -SC, IV) , Kyrpolis (T3 PA). Thalomid (T3, specialty network required)	NCCN Multiple Myeloma 2.2013: Pomalyst is salvage tx. T3PA.
309080300009**	Ravicti Liquid	urea cycle disorders	buphenyl tab (T2)	Ravicti is glycerol phenylbutyrate oral liquid for long-term management, not treatment of, hyperammonemia in pts with urea cycle disorder. Neurotoxicity. 17.4mL glyPBA=40 tabs NaPBA, the maximal approved daily dose. $112.50/mL=$1957.5/d, $714,488/y. Neuropsychological tests improved more w/ Ravicti vs NaPBA. (Diaz et al. Hepatology. 2012.)

472500250006**	Fulyzaq		antidiarrheal indicated for the symptomatic relief of non-infectious diarrhea in adults w/ HIV AIDS on antiretroviral therapy	FDA-approved dose:125mg delayed-release tab taken BID; for noninfectious diarrhea for HIV/AIDS on ART tx age ≥18. 17.6% vs 8% had <2 watery BMs/w during at least 2 of the 4 weeks of the trial. Efficacy not yet established for IBS-D predominant. Exclude. No peer-reviewed published data. PI analyzed efficacy data with all doses (125, 250, 500mg BID lumped together; no further info for critiquing.)
592500150019**	Abilify Maintena		Abilify oral (T2 PA) Abilify IM (T3). Other INJ (Risperdal Consta, Invega sustena) T2	Exclude.
395000401020**	KYNAMRO	homozygous familial hypercholesterolemia	Juxtapid (T3 PA)	Exclude due to: the effect on CV mortality/morbidity not yet determined. Reconsider Juxtapid. Consider excluding for the same reason. Juxtapid was on top of apheresis. Kynamro PI states it should not be used with apheresis. If cover, consider enforcing non-smoking, healthy lifestyle.
Other Topics				
SNRI, SSRI class review.				
Prescription coverage of Rx/OTC PPI's and H2 antagonists				
Drugs not reviewed. Likely administerd through Medical				
868010600020**	Jetrea	symptomatic vitreomacular adhesion	physician administered	Intravitreal injection; medical
25200050005310	Skyla	Contraception/IUD	Currently IUD's (Mirena ect) excluded through pharmacy beneifit. Provided through medical.	procedure-related; medical
213550703021**	Kadcyla	HER2-positive, late stage (metastatic) breast cancer.	IV infusion	Infusion; Should require a PA.
191000700021**	Varizig	varicella (chickenpox) infection prophylaxis	IM injection	Physician office administered. Varicella zoster immune globulin for post-exposure prophylaxis in high risk groups. 1 or 2 IM doses.

Thyroid Carcinoma—NCCN.org guidelines 1.2013:

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Medullary Thyroid Carcinoma

MEDU-1

- Additional Workup:
  - Seventh Bullet: "Consider lateral neck ultrasound" changed to "Thyroid and neck ultrasound (including central and lateral compartments); if not previously done".
  - Eight Bullet was modified: "Consider evaluation of vocal cord mobility".

MEDU-2

- This page was revised to address the concept of incomplete thyroidectomy if sporadic disease, no imaging evidence of disease, and calcitonin negative.

MEDU-3

- Germline mutation of RET proto-oncogene; Additional Workup for MEN 2B and MEN2A/Familial medullary: "Neck ultrasound" changed to "Central and lateral neck compartments ultrasound, if not previously done".

MEDU-5

- Basal calcitonin undetectable or CEA within reference range; Observe; Surveillance: Second Bullet: "Consider neck ultrasound" changed to "Consider central and lateral neck compartments ultrasound".

MEDU-6

- Recurrent or Persistent Disease
  - Locoregional:
    - The following recommendation was revised as follows: "Consider EBRT ~~or vandetanib for unresectable symptomatic or structurally progressive disease~~".
    - "Consider cabozantinib (category 1) for unresectable disease that is symptomatic or structurally progressive" was added as an option. Vandetanib changed from category 2A to a category 1 recommendation. Due to these changes, the following recommendation was added: "Consider vandetanib (category 1) or cabozantinib (category 1) for unresectable disease that is symptomatic or structurally progressive".

MEDU-6—continued

- Symptomatic, distant metastasis
  - Vandetanib changed from category 2A to a category 1 recommendation, and the recommendation was modified as follows: "Consider vandetanib (category 1)".
  - The following recommendation was added: "Consider cabozantinib (category 1)".
- Asymptomatic, distant metastases:
  - The recommendation was revised as follows: Consider resection (if possible), ablation (eg, RFA, embolization, or other regional therapy), or vandetanib (category 1), or cabozantinib (category 1) if structurally progressive disease". (vandetanib changed from category 2A to category 1 recommendation)
- Disseminated symptomatic disease
  - Vandetanib changed from category 2A to a category 1 recommendation.
  - Cabozantinib (category 1) was added as a treatment option.

- Footnote "k" is new to the page: "Increasing tumor markers, in the absence of structural disease progression, are not an indication for treatment with vandetanib or cabozantinib.
- Footnote "m" was revised as follows: "While not FDA approved for treatment of thyroid cancer, other commercially available small molecule kinase inhibitors (such as sorafenib or sunitinib) can be considered if clinical trials, vandetanib, or cabozantinib are not available or appropriate, or if the patient progresses on vandetanib or cabozantinib."

Continued

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RECURRENT OR PERSISTENT DISEASE

Locoregional →
- Surgical resection ± postoperative EBRT
- or
- Consider EBRT
- or
- Consider vandetanib[k,l] (category 1) or cabozantinib (category 1)[k] for unresectable disease that is symptomatic or structurally progressive

Symptomatic, distant metastases →
- Consider palliative resection, ablation (eg, radiofrequency [RFA], embolization, or other regional therapy), or other regional treatment
- or
- Consider vandetanib[k,l] (category 1)
- or
- Consider cabozantinib[k] (category 1)

Asymptomatic, distant metastases →
- Observe
- or
- Consider resection (if possible), ablation (eg, RFA, embolization, or other regional therapy), or vandetanib[k,l] (category 1), or cabozantinib[k] (category 1) if structurally progressive disease

→ **Disseminated symptomatic disease** →
- Vandetanib[l] (category 1)
- or
- Cabozantinib[k] (category 1)
- or
- Clinical trial
- or
- Consider other small molecule kinase inhibitors[m]
- or
- Dacarbazine (DTIC)-based chemotherapy

- EBRT for focal symptoms
- Consider bisphosphonate or denosumab[n] therapy for bone metastases
- Best supportive care

[k] Increasing tumor markers, in the absence of structural disease progression, are not an indication for treatment with vandetanib or cabozantinib.

[l] Only health care professionals and pharmacies certified through the vandetanib Risk Evaluation and Mitigation Strategy (REMS) program, a restricted distribution program, will be able to prescribe and dispense the drug.

[m] While not FDA approved for treatment of thyroid cancer, other commercially available small molecule kinase inhibitors (such as sorafenib or sunitinib) can be considered if clinical trials, vandetanib or cabozantinib are not available or appropriate, or if the patient progresses on vandetanib or cabozantinib.

[n] Denosumab can be associated with severe hypocalcemia; patients with hypoparathyroidism and vitamin D deficiency are at increased risk.

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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a phase III randomized trial in unresectable, locally advanced, or metastatic MTC (n = 331), vandetanib increased progression-free survival when compared with placebo (hazard ratio [HR], 0.46; 95% CI, 0.31 to 0.69; $P < .001$); overall survival data are not available yet.[294,297] The FDA recently approved the use of vandetanib for adult patients with metastatic MTC who are not eligible for surgery and whose disease is causing symptoms or growing (http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/022405s003lbl.pdf). However, access is restricted through a vandetanib Risk Evaluation and Mitigation Strategy (REMS) program because of potential cardiac toxicity (see boxed warning in the prescribing information). The NCCN panel recommends vandetanib for patients with recurrent or persistent MTC. Currently, vandetanib is the only drug that is approved for metastatic MTC.

When locoregional disease is identified in the absence of distant metastases, surgical resection is recommended with or without postoperative external-beam RT. If there is symptomatic progressive or unresectable locoregional disease, then external-beam RT or vandetanib can be considered. Distant metastases that are causing symptoms (eg, those in bone) could be considered for palliative resection, ablation (eg, radiofrequency, embolization), or other regional treatment or vandetanib. These interventions may be considered for asymptomatic distant metastases (especially for progressive disease) but observation is acceptable, given the lack of data regarding alteration in outcome.

In the setting of disseminated symptomatic metastases, the guidelines recommend the following: (1) clinical trial (preferred); (2) external-beam RT for focal symptoms; (3) vandetanib;[295,296] (4) consider other small molecule kinase inhibitors (ie, sorafenib or sunitinib) if clinical trials or vandetanib are not available or appropriate;[298-302] or if the patient progresses on vandetanib; or (5) systemic chemotherapy can be administered, using dacarbazine or combinations including dacarbazine.[109,303] Bisphosphonate therapy or denosumab can be considered for bone metastases.[249-251] Best supportive care is also recommended.

In patients with metastatic MTC, sorafenib reduces symptoms due to hypercalcitonemia and metastases.[300] Recently, stable disease rates of about 50% and clinical benefit rates of approximately 70% have been seen with motesanib diphosphate (AMG-706).[295,304] In addition, clinical response was seen in 6 of 8 patients with MTC who were treated with a combination of sorafenib and the farnesyltransferase inhibitor, tipifarnib.[305] Sunitinib was associated with clinical response in several case reports.[301,306,307] Clinical trials are assessing the effectiveness of novel multitargeted therapies including sunitinib,[210,301] sorafenib,[305,308] XL 184 (cabozantinib),[309-311] and pazopanib (GW786034). Severe or fatal side effects from kinase inhibitors include bleeding, hypertension, and liver toxicity; however, many side effects can be managed.[222] Because some patients may have indolent and asymptomatic disease, toxic therapy may not be appropriate.

Several recent reviews have been published that examine novel therapies and the therapeutic approach to the management of aggressive MTC.[198,312-314] Of interest, calcitonin levels decreased dramatically after vandetanib therapy, which did not directly correlate with changes in tumor volume; thus, calcitonin may not be a reliable marker of tumor response in patients receiving RET inhibitor therapy.[295] A study in patients with progressive metastatic MTC assessed treatment using pretargeted anti–CEA radioimmunotherapy with ^{131}I;[315] overall survival was improved in the subset of patients with calcitonin doubling times less than 2 years.

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Oncol 2007;25(Suppl 18):Abstract 14065. Available at: http://meeting.ascopubs.org/cgi/content/abstract/25/18_suppl/14065.

301. Kelleher FC, McDermott R. Response to sunitinib in medullary thyroid cancer. Ann Intern Med 2008;148:567. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18378960.

302. Sherman SI. Advances in chemotherapy of differentiated epithelial and medullary thyroid cancers. J Clin Endocrinol Metab 2009;94:1493-1499. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19258410.

303. Nocera M, Baudin E, Pellegriti G, et al. Treatment of advanced medullary thyroid cancer with an alternating combination of doxorubicin-streptozocin and 5 FU-dacarbazine. Groupe d'Etude des Tumeurs a Calcitonine (GETC). Br J Cancer 2000;83:715-718. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10952773.

304. Schlumberger MJ, Elisei R, Bastholt L, et al. Phase II study of safety and efficacy of motesanib in patients with progressive or symptomatic, advanced or metastatic medullary thyroid cancer. J Clin Oncol 2009;27:3794-3801. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19564535.

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Discussion update in progress

Proposed Imatinib PA Criteria DUEC 4/2/13

EBRx PA Criteria

Imatinib (Gleevec), 100mg, 400mg tablets

Imatinib requests will be approved for patients requesting use for an FDA-approved use or in the case a physician (oncologist) provides adequate literature deemed appropriate that supports the use for an unlabeled use. Access will be limited to 31 days supply and quantity limits will apply according to use.

Imatinib is FDA-approved for:

Use	Dose
1. Gastrointestinal stromal tumors (GIST) that are kit-positive (CD117), including unresectable and/or metastatic malignant and adjuvant treatment following complete resection	Max: 800mg daily; Usual: 400mg daily
2. Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (newly-diagnosed) in children and adults	Max: 800mg daily; Usual: 400mg daily
3. Ph+ CML in blast crisis, accelerated phase, or chronic phase after failure of interferon therapy	Max: 800mg daily; Usual: 600mg daily
4. Ph+ acute lymphoblastic leukemia (ALL), relapsed or refractory	600mg daily
5. Ph+ ALL (newly diagnosed; in combination with chemotherapy), in children	340 $mg/m^2/day$; max of 600mg daily
6. Aggressive systemic mastocytosis (ASM) without D816V c-Kit mutation (or c-Kit mutation status unknown)	400mg daily
7. Dermatofibrosarcoma protuberans (DFSP), unresectable, recurrent and/or metastatic	400mg twice daily
8. Hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL)	400mg daily
9. Myelodysplastic/myeloproliferative disease (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements	600mg daily

Imatinib is **experimental** for: treatment of desmoid tumors or chordoma (soft tissue sarcomas); post-stem cell transplant (allogeneic) follow-up treatment for recurrence in CML; treatment of advanced or metastatic melanoma (C-KIT mutated tumors)

Quantity Limits will apply. Quantities will be limited to the maximum daily dose for the indication, supported in the patient's medical record.

- Patients with severe hepatic impairment : 300 mg/day maximum daily dose.

- Patients taking concurrent strong CYP 450-3A4 inducers: **Dosage adjustment with concomitant strong CYP3A4 inducers:** Avoid concomitant use of strong CYP3A4 inducers (eg, dexamethasone, carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin); **if concomitant use cannot be avoided, increase imatinib dose by at least 50% with careful monitoring.**

Revision History:

Date	What changed	Pharmacist's initials
3/26/13	Criteria written	JJ

Delzicol (mesalamine 400mg delayed release capsules)—From Drug Facts & Comparisons
4/2/13 DUEC meeting

Product Name View Selected	Labeler Name	Generic Name	Route	Doseform	Strengths View Selected	Market Status	Current coverage
Apriso	SALIX PHARMACEUTICALS, INC.	Mesalamine	Oral	Capsule Extended Release 24 Hour	0.375 GM	Active	Tabled, 3/3/09 DUEC
Asacol	WARNER CHILCOTT PHARMA	Mesalamine	Oral	Tablet Delayed Release	400 MG	DCd	
Asacol HD	WARNER CHILCOTT PHARMA	Mesalamine	Oral	Tablet Delayed Release	800 MG	DCd	
Asacol HD	WARNER CHILCOTT PROF PROD DIV	Mesalamine	Oral	Tablet Delayed Release	800 MG	Active	Excluded, 2009
Canasa	APTALIS PHARMA	Mesalamine	Rectal	Suppository	1,000 MG	Active	
Delzicol	WARNER CHILCOTT PROF PROD DIV	Mesalamine	Oral	Capsule Delayed Release	400 MG	Active	
Lialda	SHIRE US, INC.	Mesalamine	Oral	Tablet Delayed Release	1.2 GM	Active	T3, 4/17/07
Mesalamine	Various	Mesalamine	Rectal	Enema	4 GM	Active	T1
Mesalamine-Cleanser	Various	Mesalamine w/ Cleanser	Rectal	Kit	4 GM	Active	
Pentasa	SHIRE US, INC.	Mesalamine	Oral	Capsule Extended Release	250 MG	Active	T2
					500 MG	Active	T2
Rowasa	ALAVEN PHARMACEUTICAL, LLC	Mesalamine w/ Cleanser	Rectal	Kit	4 GM	Active	T2
SfRowasa	MEDA PHARMACEUTICALS	Mesalamine	Rectal	Enema	4 GM/60ML	Active	

Delzicol PI states, "The data presented in Section 14 are from clinical trials conducted with mesalamine delayed-release tablets. Delzicol is bioequivalent to these mesalamine delayed-release tablets."

14.1 Mildly to Moderately Active Ulcerative Colitis

2 PC studies showed the efficacy of mesalamine DR tabs in pts with mild-mod ulcerative colitis. A R, DB, PC, MC trial of 158 pts, mesalamine DR doses of 1.6 g/day and 2.4 g/day for 6 w used the scoring system for determination of tx efficacy included assessment of stool frequency, rectal bleeding, sigmoidoscopic findings, patient's functional assessment, and physician global assessment. At the dose of 2.4 g/day, 21 of 43 (49 percent) pts on mesalamine DR tabs showed an improvement in sigmoidoscopic appearance of the bowel compared to 12 of 44 (27 percent) patients using placebo ($p = 0.048$). In addition, significantly more pts in mesalamine DR tablets 2.4 g/day group showed improvement in rectal bleeding and stool frequency. The 1.6 g/day dose did not produce consistent evidence of effectiveness.

In a second R, DB, PC clinical trial of 6 w duration in 87 pts, mesalamine DR tablets, at a dose of 4.8 g/day, for 6 w, resulted in sigmoidoscopic improvement in 28 of 38 (74%) pts compared to 10 of 38 (26%) placebo patients ($p < 0.001$). Also, more patients in the mesalamine DR tablets 4.8 g/day group showed improvement in overall symptoms.

14.2 Maintenance of Remission of Ulcerative Colitis

A 6-month, R, DB, PC, MC study involved 264 pts txd w/ mesalamine DR tablets 0.8 g/day (n = 90), 1.6 g/day (n = 87), or placebo (n = 87). In the 0.8g/day arm, pts were dosed twice daily; in the 1.6 g/day arm, patients were dosed four times daily. The proportion of patients treated with 0.8 g/day who maintained endoscopic remission was not statistically significant compared to placebo. The proportion of patients using mesalamine delayed-release tablets 1.6 g/day who maintained endoscopic remission of ulcerative colitis was in 61 of 87 (70.1 percent) compared with 42 of 87 (48.3 percent) of placebo patients ($p = 0.005$).

A pooled efficacy analysis of 4 maintenance trials compared mesalamine delayed-release tablets, at doses of 0.8 g/day to 2.8 g/day, in divided doses ranging from twice daily to four times per day, with sulfasalazine, at doses of 2 g/day to 4 g/day. Treatment success was seen in 59 of 98 (59 percent) patients using mesalamine delayed-release tablets and 70 of 102 (69 percent) of patients using sulfasalazine, a non-significant difference.

Antidepressants (AD)
DUEC April 2, 2013
Jill Johnson, Pharm.D., BCPS

EBD March 2013

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

Summary:

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

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

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

Adverse Effects:

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

Fibromyalgia

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

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Proposal:

Implement reference pricing for second generation antidepressants.