State and Public School Life and Health Insurance Board Clinical and Fiscal Drug Utilization and Evaluation Committee
Minutes
April 9, 2012

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday, April 9, 2012 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Little Rock, AR.

Members present:
Matthew Hadley
Dr. William Golden
Kat Neill
Larry Dickerson/proxy
Dr. Hank Simmons
Mark McGrew

Members absent:
Kelly Chaney
Dr. Joe Stallings
Scott Pace

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

OTHERS PRESENT
Jill Johnson, UAMS College of Pharmacy/EBRx; Connie Bennett, Informed Rx; Rhonda Walthall, AHTD; Michelle Hazelett, Lori Eden, Amy Tustison, Sherri Saxby, Latryce Taylor, Cathy Harris, EBD; Bridget Johnson, Pfizer, Dwight Davis, Alan Hickman, UAMS; Bryan Meldrum, Novasys; Frances Baumen, Novo Nordisk; Warren Tyes, Merck; Mark DeClark, Lilly; Janie Huff, Takeda; BJ Himes, QualChoice

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

APPROVAL OF MINUTES
The motion was made by Dr Golden to approve the October 4, 2011 minutes. Neil made the motion to approve. Dr. Simmons seconded. All were in favor. Minutes were approved.

SECOND REVIEW MEDICATIONS, *Jill Johnson*

a. Vibryd (vilazodone) indicated use for major depressive disorder.

Vibryd is currently excluded from coverage.

Johnson reported there are still no head-to-head trials comparing vilazodone to other selective serotonin reuptake inhibitors (SSRIs*)* and serotonin/norepinephrine reuptake inhibitors (SNRIs*)* to know relative efficacy.

Recommendation: continue to exclude. Neil seconded. Motion carried.

b. Incivek (telaprevir tabs)

The committee reviewed information about the formulary management of the Protease Inhibitors Boceprevir and Telaprevir for Chronic Hepatitis C Virus, and the study regimen and comparator for "Previous partial response" (reduction of >2log10 after 12 w of tx but with detectable HCV RNA thereafter), and "Relapse" (undetectable at end of tx but then detectable thereafter).

Johnson reported Telaprevir has been shown to be effective in treatment-naïve patients, relapsers, partial responders, and null responders. Boceprevir has been shown to be effective in treatment-naïve patients, relapsers, and partial responders, but it has not been studied in prior null responders."Both drugs have data that show efficacy in treatment naïve patients. Each also has data for previous partial responders.

Recommendation: Continue to exclude telaprevir (Incivek). Cover Boceprevir for non-responders. Liver biopsy required.

FIRST REVIEW MEDICATIONS *by Jill Johnson*

Drug Name	Tier Status

Conzip caps **Exclude**
Tx of moderate to severe pain

Firazyr inj **Exclude**
used to treat attacks of hereditary angioedema (an immune system disorder).

Xalkori **T3 w/PA**
*Available from select specialty pharmacies
For the tx of patients with locally advanced or metastatic non-small cell lung cancer that is anaplastic lymphoma kinase-positive.

Lazanda Spray **T3 w/PA**
Initiate w/100mcg - 1 spray in 1 nostril for breakthrough cancer pain. Is only available through the Lazanda REMS program - prescribers (who prescribe for outpatient use) and dispensing pharmacies must enroll in REMS

Juvisync **Exclude**
For the combined treatment of type 2 diabetes mellitus and hypercholesterolemia, hyperlipoproteinemia, and/or hypertriglyceridemia and for myocardial infarction prophylaxis, and/or stroke prophylaxis in patients for whom treatment with both sitagliptin and simvastatin is appropriate.

Ferriprox **T3 W/ PA**
Oral treatment for transfusional iron overload

Jakafi **T3 W/PA**
Tx of myelofibrosis

Onfi tabs 5, 10, 20mg tabs **Exclude**
Oral benzodiazepine for adjunct treatment to other anticonvulsants for Lennox-Gastaut syndrome

Medrox-Rx Oint **Exclude**
Pain relief oint for temporary relief of minor aches/pains of the muscles and joints

Dutoprol **Exclude**
Hypertension

Aurstat Kit **Exclude-kit**
For itch/pain from minor skin irritations, lacerations, abrasions & minor burns. Alternative to "bleach baths"

Edarbyclor **Exclude**
*Angiotensin receptor blocker (*ARB) + diuretic combination for hypertension

Oxecta **Exclude**
Immediate release oxycodone (5 or 7.5mg) in a dosage form designed to discourage common methods of tampering associated with opioid abuse and misuse

Picato Gel **T3**
Used to treat actinic keatosis

Bydureon **Exclude**
Once weekly injection for treatment of Type 2 diabetes.

Erivedge caps **Exclude /** *review in 6 mos.*
Basal cell carcinoma

Inlyta **Exclude /** *review in 6 mos.*
Advanced renal cell cancer after failure of one prior systemic therapy.

Jentadueto **Exclude**
Once daily oral treatment for Type 2 diabetes. Combination of Tradjenta and metformin.

Kalydeco **Exclude /** *review in 6 mos.*
Treatment of cystic fibrosis

Rectiv **Exclude**
Treatment of moderate to severe pain associated with chronic anal fissures

Janumet XR tabs **Exclude**
Oral once daily treatment for Type 2 diabetes

Zithranol Shampoo **T3 /***check utilization in 1yr*
Medicated shampoo for treatment of psoriasis

Zioptan Drops **Exclude**
Treatment of glaucoma, increased intraocular pressure, ocular hypertension

Dr. Golden requested information (results of implementation of step therapy for diabetes- were there any member push back. Lee said they will bring back info at next meeting.

DIRECTORS REPORT *by Jason Lee*

Chair & Co-Chair nominations

Meeting adjourned.

AGENDA

State and Public School Life and Health Insurance Board

Drug Utilization and Evaluation Committee

EBD Board Room - 501 Building, 5th Floor

April 9, 2012 1:00 p.m.

1. **Call to Order** ..... *Dr. Matthew Hadley, Chairman*
2. **Approval of Minutes** ..... *Dr. Matthew Hadley, Chairman*
3. **Second Review Medications**..... *Jill Johnson, UAMS*
    a. **Vibryd**
    b. **Incivek**
4. **First Review Medications** ..... *Jill Johnson, UAMS*
5. **Director's Report**..... *Jason Lee, Executive Director*

Next Meeting: **July 9th**

Vilazodone (Viibryd) Reconsideration
4/9/12 DUEC Meeting

DUEC April-Aug 2011 Vote:

Drug	Generic Name	Other Drugs in Same Class (AWP Pricing)		AWP per unit	Estimated AWP/month	Indications	PBM Notes	Consultant's Notes	DUEC Vote	Insurance Vote
Viibryd	vilazodone	citalopram fluoxetine, Lexapro, paroxetine, sertraline	$73.00 - 130.00	$4.74	$142.00	Major deprssive disorder	Tier 3 (ST). Tier 3 w/ step therapy. Doesn't appear to have any significant efficacy over existing antidepressants	**Exclude.** Reevaluate in 6 months. There is only 1 clinical trial in Pub Med and it is vs placebo.	exclude	exclude

4/5/12: There are still no head-to-head trials comparing vilazodone to other SSRIs or SNRIs to know relative efficacy.

Recommendation:

Continue to exclude.

Recommendation for approving telaprevir (Incivek) for Hep C, Genotype 1, Null responders

DUEC Meeting 4/9/12

Jill Johnson, Pharm.D., BCPS

The DUEC and Board Decision, 2011

Drug	Generic Name	Other Drugs in Same Class (AWP Pricing)		AWP per unit	Estimated AWP/month	Indications	PBM Notes	Consultant's Notes	DUEC Vote	Insurance Vote
Incivek 375mg tablet	telaprevir tabs	Victrelis	$5,655/mo. Entire tx $31,000 to 53,000	$111.14 /tab	$19,680/4 weeks ($4920/w) Entire course of tx about $59,000.	Chronic Hep C genotype 1 in combination w/ peginterferon alfa and ribavirin in adults 18 and older with compensated liver disease	FDA approval based on sustained virologic response of 45-80% in patients new to therapy. PA/specialty **Specialty w/PA, QL, and duration limits based on response.**	2 tabs TID=6/d; 666.84/d x 12w=$56K	Exclude	Exclude
Victrelis 200mg caps	boceprevir capsules 200mg	Incivek	Entire course of about $59,000	$15.71	$5,655/mo. Entire tx $31,000 to 53,000	Chronic Hep C genotype 1 in combination w/ peginterferon alfa and ribavirin in adults 18 and older with compensated liver disease	FDA approval was based on clinical trials that showed a sustained virologic response from around 40% to about 65% PA specialty. Specialty w/PA,QL, and duration limits based on response	T3 PA. Criteria for tx-naive: 1. Dx of chronic HCV, genotype 1, with a quantitative plasma HCV RNA of at least 10,000 IU/mL, 2. is the patient without decompensated cirrhosis, coinfection with HBV or HIV, or active cancer, or pregnancy, 3. will concomitantly receive peginterferon and ribavirin therapy with boceprevir. If approved, the PA would provide 20 weeks of boceprevir. If after 20 weeks of boceprevir (week 24 of total therapy including the first 4 w of lone peginterf/ribavirin) Criteria for previously treated: 1. Dx of chronic HCV, genotype 1, 2. Pt must have received at least 12 w of peginterferon and ribavirin and failed to have at least a 2 log10 decrease in the HCV RNA level, AND 3. absence of decompensated cirrhosis, coinfection with hepatitis B virus infection or HIV, or active cancer, or pregnancy. 12 capsules/d X 32 w=$42K	T3PA	T3PA

From UpToDate: " Telaprevir has been shown to be effective in treatment-naïve patients, relapsers, partial responders, and null responders. Boceprevir has been shown to be effective in treatment-naïve patients, relapsers, and partial responders, but it has not been studied in prior null responders."Both drugs have data that show efficacy in treatment naïve patients. Each also has data for previous partial responders.

Author, year	Sample Size	Study regimen and comparator
Re-treatment		
⌧Bacon, 2011	N=54	A: PR4, then BPR32, then PR12 if no SVR (if SVR, then all drugs were stopped)—Response-guided therapy Results: Prior relapse, SVR=69%; prior nonresponse, SVR=40% B: PR4, then BPR44 Results: Prior relapse, SVR=75%; prior nonresponse, SVR=52%, NS from Group A. C: PR44 Results: Prior relapse, SVR=29%; prior nonresponse, SVR=7%
		Boceprevir dosing was 800mg TID in four capsules of 200mg each. Peginterferon was SC 1.5ug/kg/week. Ribavirin dose was 600mg to 1400mg/d based on body weight.
‡McHutchison, 2010	N=453	A: TPR12, then PR24 Results: Previous nonresponse, SVR 39 %; Relapse, SVR=69%; Breakthrough, SVR =57% B: TPR24, then PR24 Results: Previous nonresponse, SVR 11 %; Relapse, SVR=42%; Breakthrough, SVR =36% C: PR48 Results: Previous nonresponse, SVR 9 %; Relapse, SVR=20%; Breakthrough, SVR =40%
		Telaprevir dose was 1125mg once then 750mg q8h. Peginterferon was SC 180ug/w. Ribavirin was 1000mg daily f or <75kg, or 1200mg daily for ≥75kg.
€Zeuzem, 2011	N=453	A: TPR12, PR48 Results: Previous No response, SVR 29%; Previous Partial response, SVR 59%;Relapse, SVR 83% B: PR4, then TPR12, PR32 Results: Previous No response, SVR 33%;Previous Partial response, SVR 54%; Relapse, SVR 88% C: PR48 Results: Previous No response, SVR 5%;Previous Partial response, SVR 15%;Relapse, SVR 24%
		Telaprevir dose was oral 750mg q8h. Peginterferon was SC 180ug/w. Ribavirin was oral 1000-1200mg daily.

B=boceprevir, P=peginterferon, R=ribavirin, T=telaprevir, SVR=sustained viral response

⌧Included patients with previous treatment stratified to:

"Prior relapse" (undetectable HCV RNA at end of treatment but without attaining SVR).

"Prior nonresponse" (decrease in the HCV RNA level of at least 2 log 10 by 12 w but with detectable HCV RNA during the therapy period), and

‡Included patients with previous treatment stratified to:

"Previous nonresponse" (never undetectable),

"Relapse" (undetectable for 42 w, but then detectable), and

"Breakthrough"(undetectable during treatment but then detectable before end of treatment).

€Included patients with previous treatment stratified to:

"Previous No response" (reduction of <2log10 after 12 w of tx),

"Previous partial response" (reduction of >2log10 after 12 w of tx but with detectable HCV RNA thereafter), and
"Relapse" (undetectable at end of tx but then detectable thereafter).

Proposal:

1. Cover telaprevir (Incivek) for previously treated HCV-genotype 1 patients who were previous non-responders when they took at least 12 w of peginterferon and ribavirin.

DUEC New Drugs Sept 2011 through February 2012

Drug	Generic Name	Other Drugs in Same Class	Indications	Consultant's Notes	DUEC Vote	Insurance Vote
Conzip caps	tramadol SR	Tramadol immediate release tab 50mg (cov'd at T1). Tramadol ER tab 100mg (cov'd at T1)	Tx of moderate to severe pain	Exclude		
Firazyr inj	icatibant	Berinert, Kalbitor (both are not labeled for self administration) Cinryze (cov'd at T3)	Dose: 30mg SC,may repeat every 6 hours. No more than 3 injections in 24 hours for treatment of acute attacks of hereditary angioedema. Labeled for self administration.	PA		
Xalkori *Available from select specialty pharmacies	crizotinib	None	For the tx of patients with locally advanced or metastatic non-small cell lung cancer that is anaplastic lymphoma kinase-positive. Dose	T3 PA		
Lazanda Spray	fentanyl nasal spray	Fentanyl patch (cov'd at T1) Actiq (cov'd at T3 w/PA). May not substitute fentanyl products on a mcg per mcg basis.	Initiate w/100mcg - 1 spray in 1 nostril for breakthrough cancer pain. Is only available through the Lazanda REMS program - prescribers (who prescribe for oupatient use) and dispensing pharmacies must enroll in REMS	T3 PA, under fentanyl		
Juvisync	sitagliptin /simvastatin	Januvia 100mg tab / simvastatin (cov'd at T3 w/PA); Simvastatin (cov'd at T1)	For the combined treatment of type 2 diabetes mellitus and hypercholesterolemia, hyperlipoproteinemia, and/or hypertriglyceridemia and for myocardial infarction prophylaxis, and/or stroke prophylaxis in patients for whom treatment with both sitagliptin and simvastatin is appropriate.	Exclude; considered a convenience kit and more expensive than the individual components separately.		
Ferriprox	deferiprone	Exjade (deferasirox) - must be mixed in liquid prior to administration.	Oral treatment for transfusional iron overload	T3 PA using Exjade criteria.		

Jakafi	ruxolitinib phosphate	None	Tx of myelofibrosis	T3 PA		
Onfi tabs 5,10,20mg tabs	clobazam	Clonazepam (cov'd at T1)	Oral benzodiazepine for adjunct treatment to other anticonvulsants for Lennox-Gastaut syndrome	T3 PA (See clobazam in your handout)		
Medrox-Rx Oint	Capsaicin-menthol-methyl-salicylate oint	Similar OTC products	Pain relief oint for temporary relief of minor aches/pains of the muscles and joints	Methyl salicylate 20%, menthol 7%, capsaicin 0.05%; T3 or exclude; Capsaicin available OTC, this combo is available OTC called Pain Doctor with MS 25%, menthol 10%, Capsaicin 0.025%.		
Dutoprol	metoprolol & hydrochlorothiazide SR 24 hr	Metoprolol XR 50mg ; Hydrochlorothiazide	Hypertension	T3		
Aurstat Kit	emollient cream & wound dressing gel kit		For itch/pain from minor skin irritations, lacerations, abrasions & minor burns. Alternative to "bleach baths"	Exclude-kit		
Edarbyclor	azilsartan medoxomil & chlorthalidone	Edarbi; Chlorothalidone	ARB + diuretic combination for hypertension	T3 ARB ST		
Oxecta	oxycodone -abuse deterrent	Oxycodone 5mg/aspirin ; oxycodone 7.5mg/APA	Immediate release oxycodone (5 or 7.5mg) in a dosage form designed to discourage common methods of tampering associated with opioid abuse and misuse.	Exclude		
Picato Gel	ingenol mebutate gel 0.015% and 0.05%	Fluorouracil; Imiquimod; Levulan; Metvixia; Solaraze	Used to treat actinic keatosis	T3 or exclude; Usual tx is liquid nitrogen or surgery (curative)--pain and nonasthetic outcomes. If not feasible, can use field therapies which eradicate surrounding potential Aks (4 week topical 5-FU-overall efficacy is 50% in hypertrophic AK or >90% in nonhypertrophic AKs; or topical diclofenac or imiquimod X 4w. Picato used for 3 days led to a >75% reduction in AKs.		
Bydureon	extended release exenatide	Byetta BID inj; Victoza once daily injection	Once weekly injection for treatment of Type 2 diabetes.	Exclude. See Bydureon Discussion in your handout.		

Erivedge caps	vismodegib	none	Basal cell carcinoma	Limited medical evidence. Single arm trial only. Alternatives are surgical resection and radiotherapy. Investigational is cetuximab.		
Inlyta	axitinib	n/a	Advanced renal cell cancer after failure of one prior systemic therapy.	This drug has limited known medical benefit. Awaiting overall survival data. The only Phase III trial measured PFS vs sorafenib. Axitinib PFS=6.7m vs sorafenib PFS=4.7m. T3PA. Criteria: 1. diagnosis of advanced renal cell cancer, clear cell type and had failure of one prior systemic treatment (sunitinib, temsirolimus, bevacisumab + interferon, high dose interleukin-2, or sorafenib. Consider the published trial was conducted by Pfizer including collection and analysis of data. Also consider they enrolled only ECOG performance status 0-1 patients (fully ambulatory patients)		
Jentadueto	linagliptin-metformin combination	Tradjenta 5mg (once daily); Metformin 500mg XR	Once daily oral treatment for Type 2 diabetes. Combination of Tradjenta and metformin.	T3PA: Criteria: 1. Dx of T2DM (not T1DM), 2. No insulin claims in the past 30 days, 3. Metformin together with either a sulfonylurea or pioglitazone (not in combination with a DPP-4 antagonist) must be on the profile for 90 or the past 120d at the maximum or near-maximum dose without reaching HbA1C goal (unless contraindicated due to renal function, HF, edema, or fracture risk). The only data measured A1C, not clinical endpoints.		

Kalydeco	ivacaftor	none	Treatment of cystic fibrosis	T3 PA: Criteria: 1. Gene testing positive for G551D mutation in the CFTR gene; AND 2. currently receiving and compliant for 6 months on standard treatment protocol for inhaled therapies, at a minimum to include inhaled hypertonic saline and dornase alfa; AND 3. Transaminases alanine transaminase (ALT) and aspartate transaminase (AST) tests required at baseline and every 3 months during 1st year of treatment and then annually thereafter; AND 4. QL of 62/31 days' supply		
Rectiv	nitroglycerin oint 0.4%	Has been available through compounding pharmacies	Treatment of moderate to severe pain associated with chronic anal fissures	T3. From UpToDate: Topical nitroglycerin — The observation that the posterior commissure of the internal anal sphincter is less perfused than the other sections led to the concept that ischemia could be contributing to the persistence of anal fissures [3,4]. Topical nitroglycerin increases local blood flow and reduces pressure in the internal anal sphincter, which may further facilitate healing. It is applied as a 0.2 to 0.4 percent ointment. In 2011, the US Food and Drug Administration approved a 0.4 percent nitroglycerin ointment (Rectiv, ProStrakan Group). Prior to that, the commercially available nitroglycerin ointments in the United States were 2 percent, a concentration that may not be well tolerated [13]. A 0.2 percent concentration can be custom-made by a pharmacist.		

Janumet XR tabs	sitagliptin-metformin 24hour sustained release tab	Januvia 100mg tab; Metformin 1000mg	Oral once daily treatment for Type 2 diabetes	T3PA: Criteria: 1. Dx of T2DM (not T1DM), 2. No insulin claims in the past 30 days, 3. Metformin together with either a sulfonylurea or pioglitazone (not in combination with a DPP-4 antagonist) must be on the profile for 90 or the past 120d at the maximum or near-maximum dose without reaching HbA1C goal (unless contraindicated due to renal function, HF, edema, or fracture risk). The only data measured A1C, not clinical endpoints.		

Zithranol Shampoo	anthralin 1%	n/a	Medicated shampoo for treatment of psoriasis	T3. Other agents seem to be better. Per the 2009 Guidelines (current): While anthralin used to be a mainstay for the topical treatment of psoriasis, typically in the inpatient setting, its use has declined in recent years because of the availability of more cosmetically acceptable alternatives. Although the exact mechanism of action of anthralin is not fully understood, recent studies suggest that its ability to prevent T-lymphocyte activation and normalize keratinocyte differentiation may occur by a direct effect on mitochondria. In the two small placebo-controlled studies of the efficacy of anthralin as monotherapy for 12 and 27 patients, a totally aqueous gel formulation of dithranol, in increasing conc as tolerated up to 2%, when applied twice daily after 4 weeks, and 1 min of treatment with 2% dithranol ointment daily for 3 w both demonstrated significantly better results than placebo in the treatment of psoriasis. Several doses and preps of anthralin are available; however, owing largely to issues of cosmesis and convenience, anthralin is most commonly used as short contact (20-30 minutes) therapy in the outpatient setting, starting at 1% concentration with increasing concentration over time as tolerated.		
Zioptan Drops	tafluprost	Latanoprost	Treatment of glaucoma, increased intraocular pressure, ocular hypertension	Overall efficacy not different from latanoprost.		

For Crizotinib - Xalkori®
Prior Authorization Criteria

1. Has the patient been diagnosed with locally advanced or metastatic non small cell lung cancer‡?	☐ Yes ☐ No
2. Is the patient's cancer anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test?	☐ Yes ☐ No If yes, please provide chart notes documenting the patient is ALK positive.
3. Does the patient maintain a performance status of ECOG[1] 0-3* or Karnofsky score[2] ≥60?	( ) YES ( ) NO
If yes to both questions, approve PA for 3 months, then re-evaluate. No 90 day fills on specialty drugs.	

‡ Crizotinib is not approved for adjuvant therapy.
Clinical trials included only ECOG PS 0-2 patients.

ECOG Performance Status

These scales and criteria are used by doctors and researchers to assess how a patient's disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis. They are included here for health care professionals to access.

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

Credit to the Chair of the ECOG Committee: *Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.*

KARNOFSKY PERFORMANCE STATUS SCALE DEFINITIONS RATING (%) CRITERIA[2]

Able to carry on normal activity and to work; no special care needed.	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent.
	20	Very sick; hospital admission necessary; active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead

References:
1. ECOG. http://www.ecog.org/general/perf_stat.html
2. Karnofsky. http://www.hospicepatients.org/karnofsky.html
3. Kwak EL, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. N Engl J Med. 2010;363:1693-703.
4. Shaw AT, Year BY, Solomon J, Riely GJ, et al. Impact of crizotinib on survival in patients with advanced, ALK positive NSCLC compared with historical controls. 2011 ASCO Annual Meeting. J Clin Oncol 29:2011 (Supl:abstr7507).

Ruxolitinib (Jakafi)
EBRx
Prior Authorization Criteria

1. Has the patient been diagnosed with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis?	☐ Yes ☐ No
PA is good for 6 months.[4] QL is 25mg twice daily (60 units/30 days).	

If "yes" to question 1, approve for 6 months. Otherwise, deny coverage.

Notes:

1. Ruxolitinib was shown to reduce spleen size and was not a durable response. Only Phase 1 & Phase 2 trials are available in peer-reviewed published literature.
2. In a sponsor-independent analysis from Mayo Clinic, there was a 92% discontinuation rate primarily for loss of treatment benefit after 9.2months, but also because of drug AEs. The "ruxolitinib withdrawal syndrome" is manifested by acute relapse of disease symptoms, accelerated splenomegaly, worsening of cytopenias, and occasional hemodynamic decompensation including septic shocklike syndrome.
3. No survival benefit has been shown with Jakafi. However it was effective in reducing constitutional symptoms in the majority of patients with myelofibrosis. Side effects such as thrombocytopenia, worsening anemia, and the withdrawal syndrome should be communicated with the patients before beginning therapy.
4. The package insert directs the physician to discontinue after 6 months if no spleen reduction or symptom improvement.

References

1. Verstovsek S, et al. Safety and efficacy of INCB018424, a JAK1 and JAK2 inhibitor, in myelofibrosis. N Engl J Med. 2010;363:1117-27.
2. Tefferi A, Pardanani A. Serious adverse events during ruxolitinib treatment discontinuation in patients with myelofibrosis. Mayo Clin Proc. 2011;86(12):1188-1191.
3. Tefferi A, Litzow MR, Pardanani A. Longterm outcome in treatment with ruxolitinib in myelofibrosis. N Engl J Med. 365;15:1455-57.
4. Jakafi PI. http://www.incyte.com/products/uspi_jakafi.pdf Accessed 2/2/12.

Clobazam (Onfi)
EBRx
Prior Authorization Criteria

1. Has the patient been diagnosed with Lennox-Gastaut seizure disorder?	□ Yes □ No
2. Does the patient seek to use clobazam as add-on anti-seizure therapy to other anti-seizure medications?	□ Yes □ No

If questions 1-2 are answered "yes" approve for 1 year

Notes:

1. There is no consensus by any national neurology group as to practice guidelines to date (2/2/12).
2. FDA approved for adjuvant treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years of age or older.
3. Onfi is a benzodiazepine, scheduled IV, abusable, and can lead to a withdrawal syndrome upon stopping.

References

1. Onfi PI. http://www.lundbeck.com/upload/us/files/pdf/Products/Onfi_PI_US_EN.pdf Accessed 2/2/12.
2. Arzimanoglou A, et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. Lancet Neurol. 2009;8:82-93.
3. Hancock EC, Cross HJ. Treatment of Lennox-Gastaut syndrome. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD003277. DOI: 10.1002/14651858.CD003277.pub2.
4. Van Rijckevorsel K. Treatment of Lennox-Gastaut syndrome: overview and recent findings. Neuropsychiatric Disease and Treatment 2008;4(6):1001–1019.

Bydureon Discussion
4/9/13 DUEC Meeting
Jill Johnson, Pharm.D., BCPS

Proposal: Exclude from coverage.

One industry-sponsored trial, Blevins, et al., showed QW exenatide(-1.6%) reduced HbA1C by 0.7% more than BID exenatide (-0.9%) over 24 weeks. No clinical outcomes were measured. In this short term trial, patients in the BID group had more nausea and vomiting than the QW group. The QW group had more diarrhea and injection site erythema although no stats were shown for any adverse events.

The other issue is long-term adverse effects. A study by Elashoff M, et al., examined the US FDA database of reported adverse events for those associated with GLP-1 agonists (exenatide). They found an increased risk of pancreatitis (almost 11 fold), pancreatic cancer (2.57 fold), and thyroid cancer (almost 5 fold) with the drug. (Please see table below.)

Table 1. Test and Control Events for Exenatide and Sitagliptin vs Control Drugs

PANCREATITIS				
Drug	Pancreatitis events	Control events	Odds ratio vs control drugs	*P*-value vs control drugs
Exenatide	971	1433	10.68	2×10^{-16}
Sitagliptin	131	306	6.74	2×10^{-16}
Controls	43	678	—	—
PANCREATITIS (2006 AND PRIOR)				
Drug	Pancreatitis events	Control events	Odds ratio vs control drugs	*P*-value vs control drugs
Exenatide	152	748	2.57	8×10^{-7}
Sitagliptin	2	15	1.69	.37
Controls	32	405	—	—
PANCREAS CANCER				
Drug	Pancreas cancer events	Control events	Odds ratio vs control drugs	*P*-value vs control drugs
Exenatide	81	1433	2.95	9×10^{-5}
Sitagliptin	16	306	2.72	.008
Controls	13	678	—	—
THYROID CANCER				
Drug	Thyroid cancer events	Control events	Odds ratio vs control drugs	*P*-value vs control drugs
Exenatide	30	1433	4.73	4×10^{-3}
Sitagliptin	2	306	1.48	.65
Controls	3	678	—	—
ALL OTHER CANCERS				
Drug	All cancer events	Control events	Odds ratio vs control drugs	*P*-value vs control drugs
Exenatide	375	1433	1.08	.47
Sitagliptin	59	306	0.8	.2
Controls	164	678	—	—

The Byetta package insert contains warnings pertaining to pancreatitis. The subsequent advice is to discontinue Byetta promptly.

----------WARNINGS AND PRECAUTIONS----------

 Pancreatitis: Postmarketing reports with exenatide, including fatal and nonfatal hemorrhagic or necrotizing pancreatitis. *Discontinue BYETTA promptly. BYETTA should not be restarted.* Consider other antidiabetic therapies in patients with a history of pancreatitis (5.1).

Bydureon carries a boxed warning.

WARNING: RISK OF THYROID C-CELL TUMORS

See full prescribing information for complete boxed warning.

☐ Exenatide extended-release causes thyroid C-cell tumors at clinically relevant exposures in rats. It is unknown whether BYDUREON causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be determined by clinical or nonclinical studies (5.1).

☐ BYDUREON is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) (5.1).

Bydureon carries a warning for pancreatitis as well.

5.2 Acute Pancreatitis

Based on postmarketing data, exenatide has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. After initiation of BYDUREON, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back, which may or may not be accompanied by vomiting). If pancreatitis is suspected, BYDUREON should promptly be discontinued and appropriate management should be initiated. If pancreatitis is confirmed, BYDUREON should not be restarted. Consider antidiabetic therapies other than BYDUREON in patients with a history of pancreatitis.

Conclusion:

Together with the lack of longterm safety data with extended exposure Bydureon, the lack of clinical endpoint data, the known 11-fold odds for an association of pancreatitis with exenatide (the short acting), and the package insert advisement to discontinue promptly if pancreatitis occurs in a patient taking this pharmacokinetically prolonged drug, I recommend waiting to cover Bydureon until further long term safety data is released.

References:

1. Blevins T, Pullman J, Malloy J, Yan P, et al. Duration-5: Exenatide once weekly resulted in greater improvements in glycemic control compared with exenatide twice daily in patients with type 2 DM. *J Clin Endocrinol Metab*. 2011; 96:1301-10.

2. Elashoff M, Matveyenko AV, Gier B, Elashoff R, Butler PC. Pancreatitis, pancreatic, and thyroid cancer with glucagon-like peptide-1-based therapies. *Gastroenterology*. 2011;141:150-156.

3. Byetta PI. http://documents.byetta.com/Byetta_PI.pdf. Accessed 4/5/12.

4. Bydureon PI. http://documents.bydureon.com/Bydureon_PI.pdf. Accessed 4/5/12.

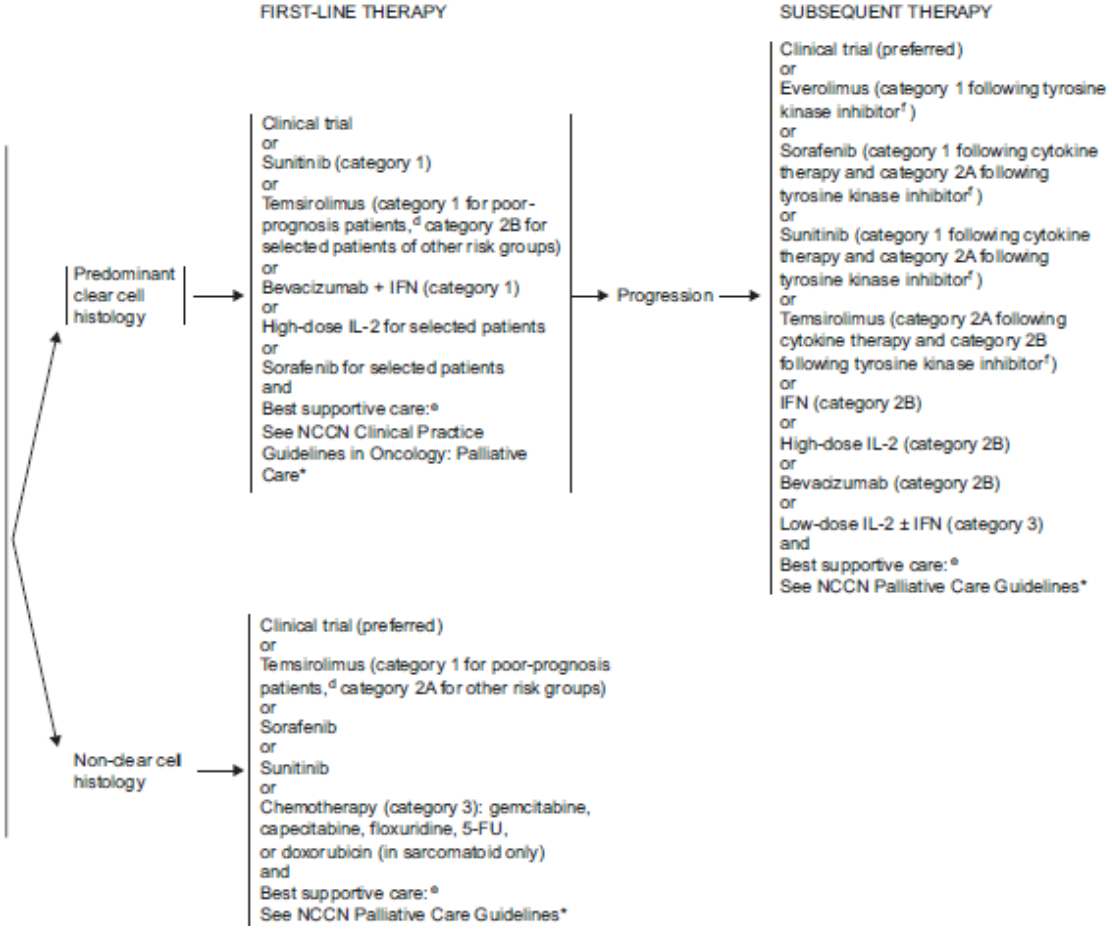
Axitinib (Inlyta®) 1mg, 5mg tablets
PA Criteria

1. Does the patient have a diagnosis of advanced renal cell cancer, clear cell type and had failure of one prior systemic treatment (sunitinib, temsirolimus, bevacisumab + interferon, high dose interleukin-2, or sorafenib)?	( ) YES ( ) NO
Initial dose is 5mg twice daily, increased to 10mg twice daily if tolerated. Dose may be reduced due to toxicity to 3mg twice daily or further reduced to 2mg twice daily.	
Quantity edits: 5 mg= 4:1 (124 tabs/31 days); 1 mg = 6:1 and 186/31 days' supply; (1 mg packaged in bottles of 180)	

If the question is answered yes, PA is approved for one year.

References:
1. Motzer RJ, et al. NCCN Guidelines for Kidney Cancer. **2009;7:618-630** ***J Natl Compr Canc Netw*** http://www.jnccn.org/content/7/6/618.full
2. Rini BJ, Escudier B, et al. Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomized phase 3 trial. Lancet. 2011;378:1931-39.

Notes:
From NCCN (Kidney Cancer 2009)



Deferiprone (Ferriprox)
DUEC 4/9/12
Cheryl Kaye, Pharm.D.

1. Diagnosis of iron overload due to blood transfusions in pts with thalassemia
2. Inadequate response to or contraindication to deferoxamine (Desferal)
   *inadequate response = serum ferritin concentrations >2500mcg/L

A Cochrane systemic review concluded that Ferriprox is indicated for the treatment of iron overload due to blood transfusions if Desferal is inadequate or contraindicated. [1]

"Approval of Ferriprox was based on an unpublished, prospective, pooled analysis (summarized in the package insert) of 12 trials in a total of 236 patients with transfusional iron overload who had an inadequate response (serum ferritin concentrations remained above 2500 mcg/L) to, or were unable to tolerate, other iron chelation therapy. "[2]

A RCT comparing deferiprone (Ferriprox) to deferoxamine (Desferal) found a statistically significant difference in the primary outcome of myocardial T2 levels favoring deferiprone (Ferriprox). Participants were 18 years or older without HF and previously taking deferoxamine (Desferal). They were randomized to either a higher dose of Desferal or switching to Ferriprox. While it is stated that cardiac measurements were made in London by 2 reviewers who were blinded to treatment arms, it does not state whether pts and physicians were blinded. There was a statistically significant difference in baseline serum ferritin levels, with the deferiprone (Ferriprox) arm having a lower baseline level. Several of the authors have financial interest in Apotex, which produces deferiprone (Ferriprox).[4]

No meaningful RCT comparing Exjade to Ferriprox.

Dosage: 25 -33 mg/kg body weight PO TID for a total daily dose of 75 - 99mg/kg body weight.

Supplied: 500 mg film-coated tablets with a functional score.

References:

1. Roberts D, Brunskill S, Doree C, Williams S, Howard J, Hyde C. Oral deferiprone for iron chelation in people with thalassaemia. *CochraneDatabase of Systematic Reviews* 2007, Issue 3. Art.No.: CD004839. DOI: 10.1002/14651858.CD004839.pub2.
2. The Medical Letter. Deferiprone (Ferriprox) for iron overload. The Medical Letter, 2012, Issue 1384, Volume 54.
3. Ferriprox prescribing information. http://www.ferriprox.com/us/pdf/ferriprox_full_pi.pdf
4. Pennell DJ, Berdoukas V, Karagiorgia M, et al. Randomized Controlled trial of deferiprone or deferoxamine in beta-thalassemia major patients with asymptomatic myocardial siderosis. Blood, 2006;107(9): 3738-3744.