State and Public School Life and Health Insurance Board Clinical and Fiscal Drug Utilization and Evaluation Committee
Minutes
June 25, 2012

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday, June 25, 2012 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Little Rock, AR.

Members present:	**Members absent:**
Matthew Hadley	Kelly Chaney
Dr. Joe Stallings	Mark McGrew
Kat Neill	Dr. William Golden
Larry Dickerson	
Dr. Hank Simmons	
Scott Pace/Proxy	

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

OTHERS PRESENT
Eric Crumbaugh, AR Pharmacist Association; Jill Johnson, UAMS College of Pharmacy/EBRx; Connie Bennett, Informed Rx; John Kirtley, State Board of Pharmacy; 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

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 April 9, 2012 minutes. Neil made the motion to approve. Dr. Simmons seconded. All were in favor. Minutes were approved.

UAMS-COLLEGE OF PHARMACY REVIEW *by Jill Johnson*

1. **HEPATITIS C**
   The committee discussed triple therapy for Hepatitis C virus; whether and/or in which situations double therapy would be covered for genotype 1.

   Johnson informed the committee it is assumed that genotypes other than type 1 would continue to have access to double therapy. Addition of protease inhibitor therapy is not indicated at this time. For exceptions, drug intolerance or hypersensitivity should be considered. Additionally, total lifetime access limitations should be discussed for all genotypes. Johnson suggested the committee review for lifetime max on peginterferon/ribavirin.

   The committee decided to table the discussion and work on a coverage policy and communication strategy for the next meeting.

2. **XYREM** (sodium oxybate) is a central nervous system depressant that reduces excessive daytime sleepiness and cataplexy in patients with narcolepsy.

   Johnson explained the indications, dosage, side effects and drug interactions. Johnson suggested the committee consider adding PA requirement for Xyrem.

   The committee reviewed member utilization data for March 2012 through May 2012.

   Recommendation: Cover with prior authorization (PA): Existing & New member must have appropriate diagnosis as evaluated by Neurologist. Maximum FDA quality limit applies.

   The committee agreed by consensus to approve recommendations for Xyrem.

3. **SUBOXONE & ORAL BUPRENORPHINE**
   Suboxone contains a combination of buprenorphine and naloxone. Buprenorphine is an opioid medication.

   Johnson suggested the committee determine whether to place QL or PA or automated ST on Suboxone and buprenorphine (generic Subutex, which is no longer marketed in the brand but is still available generically).

   The committee reviewed member utilization data for March 2012 through May 2012 and also discussed the Medicaid coverage policy for Suboxone.

Recommendation: To require PA for oral Buprenorphine containing products; similar to Medicaid PA criteria. Current users will be covered through the end of the plan year in accordance with the formulary management rule.

The committee agreed by consensus to approve recommendation.

4. **KETEK** (telithromycin) is a ketolide antibiotic. Telithromycin helps the body fight infection that is caused by bacteria.

   The DUEC placed PA on the drug in 2006 due to FDA toxicity warning.

   Johnson informed the committee there was no utilization for this agent during March 2012 through May 2012.

   Recommendation: Remove the PA from Ketek.

   The committee agreed by consensus to approve recommendation for Ketek.

5. **ISENTRESS** (raltegravir) is an antiviral medication that prevents human immunodeficiency virus.

   Johnson reported that recently the drug received indications for use in treatment-naïve patients. Johnson proposed they remove the PA from raltegravir (Isentress). The criteria call for failure of other HIV drugs before allowing raltegravir.

   The committee reviewed the current PA and member utilization data for March 2012 through May 2012.

   Recommendation: Edit current PA to allow for use in treatment –naive HIV patients and require automated step therapy (Truvada filled in last 30 days).

   The committee agreed by consensus to approve recommendation for Isentress.

6. **BOTOX-LIKE DRUGS**
   Onabotulinumtoxin A (Botox), Abobotulinumtoxin A, (Dysport), Incobotulinumtoxin A (Xeomin), RimabotulinumtoxinB (Myobloc)

   Recommendation: Adopt Prior authorization (PA) criteria for botulinum toxins, and include PA for Migraine HA.

   The committee agreed by consensus to approve recommendation for Botox-like drugs.

7. **TARGETED IMMUNE MODULATORS REVIEW**
   Enbrel Products, Humira Products, Simponi and Remicade

   Johnson reported Humira (Adalimumab) appears to have an advantage over other TIMs with efficacy for RA. It also appears to have a safety advantage over several other effective TIMs regarding adverse effects.

   The committee discussed a possible move from requiring PA to only requiring ST.

   The committee decided by consensus to table the discussion.

   Johnson will consult with Rheumatologist and bring back current guidelines for treatment of Rheumatoid Arthritis (RA) in the next meeting.

FIRST REVIEW MEDICATIONS *by Jill Johnson*

Drug Name	**Tier Status**
POTIGA TAB (EZOGABINE TAB) FDA-approved for partial onset seizures in pts age 18 and older	**T3 w/PA**
REVLIMID CAP 2.5MG (LENALIDOMIDE CAPS 2.5 MG) Restricted to FDA approved indication	**T3 w/PA**
INTELENCE TAB 25MG (ETRAVIRINE TAB 25 MG)	**T2 w/PA**
SKLICE LOT 0.5% (IVERMECTIN LOTION 0.5%)	**T3w/PA**
BAL-CARE DHA MIS ESSNTIAL	**Exclude**
GELNIQUE GEL 3% (OXYBUTYNIN TD GEL 3% (28MG/ACT METERED-DOSE PUMP)	**Exclude**
PRENATE MINI CAP	**Exclude**
OMECLAMOX MIS –PAK (AMOXICILLIN CAP-CLARITHRO TAB W/ OMEPRAZ CAP DR THERAPY PACK)	**Exclude**
RA LUTEIN CAP 20MG	**Exclude**
RIBAPAK MIS 600/DAY (RIBAVIRIN TAB 200 MG & RIBAVIRIN TAB 400 MG DOSE PACK)	**Exclude**

Drug Name	Tier Status
VASCAZEN CAP 1GM (OMEGA-3-ACID ETHYL ESTERS (DIETARY MANAGEMENT) CAP 1 GM	**Exclude**
VIVA CT CHW 28-1MG	**Exclude**
ELELYSO INJ 200UNIT (TALIGLUCERASE ALFA FOR INJ 200 UNIT)	**Exclude**
HYDROCO/APAP TAB 2.5-325 (HYDROCODONE-ACETAMINOPHEN TAB 2.5-325 MG)	**Exclude**
AMYVID INJ (FLORBETAPIR F 18 IV SOLN 500- 1900 MBQ/ML (13.5-51 MCI/ML**)**	**Exclude**
CITRANATAL MIS B-CALM	**Exclude**
HISTOACRYL LIQ	**Exclude**
SORILUX AER 0.005% (CALCIPOTRIENE FOAM 0.005%)	**Exclude**
DYMISTA SPR 137-50 (AZELASTINE HCL-FLUTICASONE PROP NASAL SPRAY 137-50 MCG/ACT)	**Exclude**
ZETONNA AER 37MCG (CICLESONIDE NASAL AEROSOL SOLN 37 MCG/ACT (50 MCG/VALVE)	**Exclude**
KORLYM (MIFEPRISTONE TAB 300 MG)	**Exclude**
OMONTYS (PEGINESATIDE)	**Exclude** ***Review in 6 mos***
REDICHEW CHW Rx	**Exclude**

The committee agreed by consensus to approve recommendations for new drugs.

Meeting adjourned.

DUEC Meeting Agenda

6/25/2012

1. New Drugs
2. Hepatitis C
3. Xyrem
4. Suboxone & oral buprenorphine
5. Ketek
6. Isentress
7. Botox-like drugs
8. Targeted Immune Modulators

GPI	Product Name	Generic Name	Pkg Sz	Notes	DUEC Vote	IB Vote
	DUEC 6/25/2012					
	Drugs New to Market: April 23, 2012 to June 11, 2012, Rxs, no Kits					
72600026000330	POTIGA TAB 200MG	EZOGABINE TAB 200 MG	90.000EA	**T3PA.** FDA-approved for partial onset seizures in pts age 18 and older. 538 refractory partial epilepsy patients (placebo, n = 179; 600 mg, n = 181; 900 mg, n = 178), 471 of whom (placebo, n = 164; 600 mg, n = 158; 900 mg, n = 149) entered the maintenance phase. Median percentage seizure reductions were greater in EZG-treated patients (600 mg, 27.9%, p = 0.007; 900 mg, 39.9%, p < 0.001) compared with placebo (15.9%). Responder rates were higher in EZG-treated patients (600 mg, 38.6%, p < 0.001; 900 mg, 47.0%, p < 0.001) than with placebo (18.9%). Treatment discontinuations due to adverse events (AEs) were more likely with EZG than with placebo (placebo, 8%; 600 mg, 17%, 900 mg, 26%). Neurology. 2010 Nov 16;75(20):1817-24. Epub 2010 Oct 13. More evidence in Neurology. 2011 May 3;76(18):1555-63. Epub 2011 Mar 30.		
7260	POTIGA TAB 300MG	EZOGABINE TAB 300 MG	90.000EA			
7260	POTIGA TAB 400MG	EZOGABINE TAB 400 MG	90.000EA			
7260	POTIGA TAB 50MG	EZOGABINE TAB 50 MG	90.000EA			
9939	REVLIMID CAP 2.5MG	LENALIDOMIDE CAPS 2.5 MG	100.000EA	T3PA. Restricted to FDA approved indication, currently: Multiple myeloma, In combination with dexamethasone, first-line therapy: (high-dose dexamethasone) 25 mg ORALLY daily on days 1 to 21 of a 28-day cycle; co-administer dexamethasone 40 mg ORALLY daily on days 1 to 4, 9 to 12, and 17 to 20 of each 28-day cycle Multiple myeloma, In combination with dexamethasone, first-line therapy: (low-dose dexamethasone) 25 mg ORALLY daily on days 1 to 21 of a 28-day cycle; co-administer dexamethasone 40 mg ORALLY on days 1, 8, 15, and 22 of each 28-day cycle Multiple myeloma, in combination with dexamethasone, in patients who have received at least 1 prior therapy: initial, 25 mg ORALLY daily with water (as a single 25 mg capsule) on days 1 to 21 of a 28-day cycle; co-administer dexamethasone 40 mg/day ORALLY on days 1 to 4, 9 to 12, and 17 to 20 of each 28-day cycle for the first 4 cycles, then 40 mg/day ORALLY on days 1 to 4 every 28 days; continue therapy, with dose adjustments for toxicities, until disease progression Myelodysplastic syndrome, Transfusion-dependent, deletion 5q abnormality, low or intermediate-1 risk: 10 mg ORALLY once daily with water . *Also requires a high dollar override.		
9939	REVLIMID CAP 2.5MG	LENALIDOMIDE CAPS 2.5 MG	28.000EA			
###	BAL-CARE DHA MIS ESSNTIAL	*PRENAT W/FE POLY-NA FERED-FA TAB 27-1 & OMEGA CAP DR 374MG*	60.000EA	exclude		

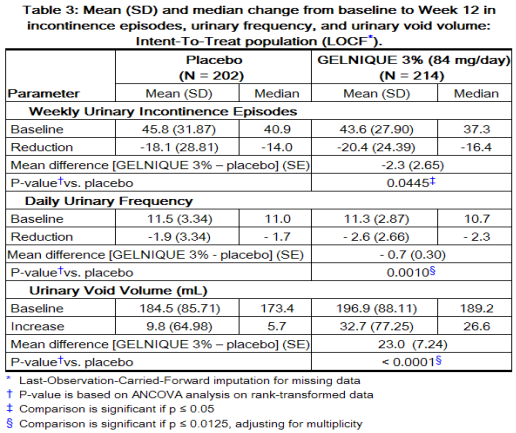
###	GELNIQUE GEL 3%	OXYBUTYNIN TD GEL 3% (28 MG/ACT METERED-DOSE PUMP)	92.000GM	Exclude. No published trials comparing topical to po urinary antispasmodics. 		
###	PRENATE MINI CAP	*PRENAT W/O A W/FECBN-METHYLF-FA-DHA CAP 29-0.6-0.4-350 MG**	30.000EA	exclude		
1210	INTELENCE TAB 25MG	ETRAVIRINE TAB 25 MG	120.000EA	T2 w/ PA: require 1. Dx of HIV, 2.genotyping/phenotyping to show viral susceptibility to this agent.		
4999	OMECLAMOX MIS -PAK	AMOXICILLIN CAP-CLARITHRO TAB W/ OMEPRAZ CAP DR THERAPY PACK	8.000EA	exclude kit		
4999	OMECLAMOX MIS -PAK	AMOXICILLIN CAP-CLARITHRO TAB W/ OMEPRAZ CAP DR THERAPY PACK	8.000EA			
9599	RA LUTEIN CAP 20MG	LUTEIN-ZEAXANTHIN CAP 20-1 MG	30.000EA	T3. One study demonstrated that lutein supplementation increases macular pigment optical density (MPOD), as assessed with an objective method. The correlation between the change in MPOD and the change in visual acuity (VA) and mean differential light threshold (MDLT) indicates that patients who show a pronounced increase in MPOD also benefit in terms of visual function. Gu¨nther Weigert, Semira Kaya, Berthold Pemp, et al. Effects of Lutein Supplementation on Macular Pigment Optical Density and Visual Acuity in Patients with Age-Related Macular Degeneration. *Invest Ophthalmol Vis Sci* . 2011;52:8174–8178.		
1235	RIBAPAK MIS 600/DAY	RIBAVIRIN TAB 200 MG & RIBAVIRIN TAB 400 MG DOSE PACK	14.000EA	exclude kit		
1235	RIBAPAK MIS 600/DAY	RIBAVIRIN TAB 200 MG & RIBAVIRIN TAB 400 MG DOSE PACK	56.000EA			
8125	VASCAZEN CAP 1GM	OMEGA-3-ACID ETHYL ESTERS (DIETARY MANAGEMENT) CAP 1 GM	60.000EA	exclude		

Table 3: Mean (SD) and median change from baseline to Week 12 in incontinence episodes, urinary frequency, and urinary void volume: Intent-To-Treat population (LOCF*).

Parameter	Placebo (N = 202)		GELNIQUE 3% (84 mg/day) (N = 214)	
	Mean (SD)	Median	Mean (SD)	Median
Weekly Urinary Incontinence Episodes				
Baseline	45.8 (31.87)	40.9	43.6 (27.90)	37.3
Reduction	-18.1 (28.81)	-14.0	-20.4 (24.39)	-16.4
Mean difference [GELNIQUE 3% – placebo] (SE)			-2.3 (2.65)	
P-value†vs. placebo			0.0445‡	
Daily Urinary Frequency				
Baseline	11.5 (3.34)	11.0	11.3 (2.87)	10.7
Reduction	-1.9 (3.34)	- 1.7	- 2.6 (2.66)	- 2.3
Mean difference [GELNIQUE 3% - placebo] (SE)			- 0.7 (0.30)	
P-value†vs. placebo			0.0010§	
Urinary Void Volume (mL)				
Baseline	184.5 (85.71)	173.4	196.9 (88.11)	189.2
Increase	9.8 (64.98)	5.7	32.7 (77.25)	26.6
Mean difference [GELNIQUE 3% – placebo] (SE)			23.0 (7.24)	
P-value†vs. placebo			< 0.0001§	

* Last-Observation-Carried-Forward imputation for missing data
† P-value is based on ANCOVA analysis on rank-transformed data
‡ Comparison is significant if p ≤ 0.05
§ Comparison is significant if p ≤ 0.0125, adjusting for multiplicity

7851	VIVA CT CHW 28-1MG	*PRENATAL W/O A VIT W/ FE FUM-FA TAB CHEW 28-1 MG***	30.000EA	exclude		
8270	ELELYSO INJ 200UNIT	TALIGLUCERASE ALFA FOR INJ 200 UNIT	1.000EA	Exclude for now. This one is IV infusion q2w. From UpToDate: Several enzyme replacement therapies are available for Gaucher's Disease currently. Imiglucerase (Cerezyme) is produced by recombinant DNA technology in a Chinese hamster ovary cell system and velaglucerase alfa (VPRIV) is produced by gene activation technology in a human cell line. The purified enzyme imiglucerase is a monomeric glycoprotein composed of 497 amino acids. Recombinant enzyme differs from the native form and the therapeutic placental form (alglucerase or Ceredase) by a His for Arg substitution at position 495. Alglucerase has been largely replaced by imiglucerase. Oligosaccharide chains at the glycosylation sites are modified by sequential deglycosylation [23] to terminate in mannose moieties. Mannose groups are specifically recognized by endocytic receptors, allowing uptake of the enzyme by the cell and trafficking to the lysosome. Velaglucerase differs from imiglucerase insomuch as the enzyme protein sequence is the native human sequence and greater mannose display is achieved. Imiglucerase seems to have the most data. There is currently only one taliglucerase trial in PubMed and it is not comparative.		
6599	HYDROCO/APAP TAB 2.5-325	HYDROCODONE-ACETAMINOPHEN TAB 2.5-325 MG	100.000EA	exclude; non-novel		
9435	AMYVID INJ	FLORBETAPIR F 18 IV SOLN 500-1900 MBQ/ML (13.5-51 MCI/ML)	1.000EA	N/A for brain PET scans		
7851	CITRANATAL MIS B-CALM	*PRENAT W/O A W/FECBN-FEGLU-FA TAB 20-1 MG & VIT B6 TAB PAK*	90.000EA	exclude		
9736	HISTOACRYL LIQ	*SKIN ADHESIVES - LIQUID***	1.000EA	Alternative to Dermabond		
9025	SORILUX AER 0.005%	CALCIPOTRIENE FOAM 0.005%	60.000GM	exclude. Generic calcipotriene solution and ointment 0.005% are available.		
9025	SORILUX AER 0.005%	CALCIPOTRIENE FOAM 0.005%	120.000GM			
4299	DYMISTA SPR 137-50	AZELASTINE HCL-FLUTICASONE PROP NASAL SPRAY 137-50 MCG/ACT	23.000GM	exclude		
9090	SKLICE LOT 0.5%	IVERMECTIN LOTION 0.5%	117.000GM	T3PA		
4220	ZETONNA AER 37MCG	CICLESONIDE NASAL AEROSOL SOLN 37 MCG/ACT (50 MCG/VALVE)	6.100GM	RP with nasal steroids; otherwise T3. Alvesco (T3) is an oral inhaler for asthma-not relevant here. Omnaris (T3) is a intranasal suspension for allergic rhinitis available in 50mcg/actuation, #120 actuations/cannister given 2 sprays each nostril once daily. Zetonna is for allergic rhinitis, available in aerosol spray given 1 spray each nostril once daily. No comparisons with Omnaris published. Consider cost.		
27304050003**	Korlym	MIFEPRISTONE TAB 300 MG		EXCLUDE. Korlym (mifepristone) is a cortisol receptor blocker indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery. No trials peer-reviewed and published in PubMed. The one trial in the package insert states it was uncontrolled and open label and the results were unable to discern whether any improvement in Cushing's syndrome could be attributed to Korlym.	Excluded	

824 010 601 020 **	Omontys	Peginesatide	**Exclude and reevaluate in 6 months.** Initial tx: 0.04mg/kg SC or IV monthly for anemia due to chronic kidney disease in adult patients on dialysis. Dose varies depending on individual patient response. There are no trials indexed in Pubmed. Also no phase 3 trials in Ovid/DARE/IPA. 3 inhouse trials listed on the package insert are not indexed. This once-monthly-administered drug induces erythropoiesis in CKD adult patients on dialysis. In the PI, Omontys vs Epo yielded inconsistent results. Ref: www.omontys.com		
785 100 200 005 **	Redichew Chw RX		Exclude. Not indexed in Drug Facts & Comparisons currently. Once daily - prenatal chewable vitamin		
540 003 000 40**	Gelnique Gel 3% (oxybutynin)		**Table 3: Mean (SD) and median change from baseline to Week 12 in incontinence episodes, urinary frequency, and urinary void volume: Intent-To-Treat population (LOCF*).** Placebo (N = 202) / GELNIQUE 3% (84 mg/day) (N = 214) Parameter: Mean (SD) / Median / Mean (SD) / Median **Weekly Urinary Incontinence Episodes** Baseline: 45.8 (31.87) / 40.9 / 43.6 (27.90) / 37.3 Reduction: -18.1 (28.81) / -14.0 / -20.4 (24.39) / -16.4 Mean difference [GELNIQUE 3% – placebo] (SE): -2.3 (2.65) P-value†vs. placebo: 0.0445‡ **Daily Urinary Frequency** Baseline: 11.5 (3.34) / 11.0 / 11.3 (2.87) / 10.7 Reduction: -1.9 (3.34) / - 1.7 / - 2.6 (2.66) / - 2.3 Mean difference [GELNIQUE 3% - placebo] (SE): - 0.7 (0.30) P-value†vs. placebo: 0.0010§ **Urinary Void Volume (mL)** Baseline: 184.5 (85.71) / 173.4 / 196.9 (88.11) / 189.2 Increase: 9.8 (64.98) / 5.7 / 32.7 (77.25) / 26.6 Mean difference [GELNIQUE 3% – placebo] (SE): 23.0 (7.24) P-value†vs. placebo: < 0.0001§ * Last-Observation-Carried-Forward imputation for missing data † P-value is based on ANCOVA analysis on rank-transformed data ‡ Comparison is significant if p ≤ 0.05 § Comparison is significant if p < 0.0125, adjusting for multiplicity		
499 930 032 653 **	Omeclamox(amoxicillin,clarithromycin,omeprazole)		Exclude Kits		

DUEC
July 2012
Jill Johnson, Pharm.D., BCPS

1. DUEC should discuss triple therapy for Hepatitis C virus. Specifically, determine whether and/or in which situations double therapy would be covered for genotype 1. It is assumed that genotypes other than type 1 would continue to have access to double therapy. Addition of protease inhibitor therapy is not indicated at this time. For exceptions, drug intolerance or hypersensitivity should be considered. Additionally, total lifetime access limitations should be discussed for all genotypes. (Have DUEC review for lifetime max on peginterferon/ribavirin)

Utilization: March 1, 2012 – May 31, 2012

Ribavirin Products: (ribavirin, Ribapak, Ribasphere)
Utilizing Members: 13
Rxs: 45
Plan Paid: $19,887

Interferon Products: (Pegasys, Infergen, Peg-Intron)
Utilizing Members: 19
Rxs: 41
Plan Paid: $ 109,241

Protease Inhibitors (Victrelis, Incivek)
Victrelis:
Utilizing Members: 9
Rxs: 21
Plan Paid: $99,500

Incivek:
No utilization during this timeframe

2. DUEC/IB should determine whether to PA Xyrem. (Have DUEC review for adding PA requirement.)

Utilization: March 1, 2012 – May 31, 2012
Xyrem Sol 500mg/ml
Utilizing Members: 7
Rxs: 15
Plan Paid: $76,415

3. DUEC/IB should determine whether to place QL or PA or automated ST on suboxone and buprenorphine (generic Subutex, which is no longer marketed in the brand but is still available generically). (Have DUEC review for adding PA requirement.)

Utilization: March 1, 2012 – May 31, 2012

Suboxone (all strengths)
Utilizing Members: 49
Rxs: 153
Plan Paid: $62,127

Buprenorphine Sublingual 8mg
Utilizing Members: 5
Rxs: 11
Plan Paid: $2,549

4. Consider removing the PA from Ketek. (Have DUEC review for possible removal of PA requirement.)

Utilization: March 1, 2012 – May 31, 2012
No utilization for this agent during this time period.

5. DUEC/IB should remove the PA from raltegravir (Isentress). The criteria call for failure of other HIV drugs before allowing raltegravir. Recently it received the indication for use in treatment-naïve patients. (Have DUEC review for possible removal of PA requirement.)

Utilization: March 1, 2012 – May 31, 2012
Utilizing Members: 15
Rxs: 37
Plan Paid: $39,522

6. Need to look at the Botox-like drugs to determine which uses they will be covered for. Consider negotiating the lowest net-cost drug from the class. (Have DUEC review to determine which uses these products will be covered for.)

Utilization: March 1, 2012 – May 31, 2012
Botox:
Utilizing Members: 4
Rxs:3
Plan Paid: $3,684

Dysport:
No utilization during this timeframe

7. RA Drug Class Review. (Have DUEC review for possible move from requiring PA to now only requiring ST.)

Utilization: March 1, 2012 – May 31, 2012

Enbrel Products:
Utilizing Members: 152
Rxs: 358
Plan Paid: $812,572

Humira Products:
Utilizing Members: 149
Rxs: 323
Plan Paid: $808,757

Simponi
Utilizing Members: 20
Rxs: 45
Plan Paid: $101,530

Remicade
Utilizing Members: 3
Rxs: 4
Plan Paid: $15,506

8. MS Drug Class Review. (Have DUEC review for possible move of beta interferon (Extavia) and Avonex to Tier 3. Review to determine if Betaseron and/or Rebif should remain in Tier 2.) (Have DUEC review for ST requirement for Gilenya instead of PA.)
Utilization: March 1, 2012 – May 31, 2012

Copaxone:
Utilizing Members: 71
Rxs: 156
Plan Paid: $746,969

Avonex:
Utilizing Members: 22
Rxs: 53
Plan Paid: $210,212

Rebif:
Utilizing Members: 20
Rxs: 51
Plan Paid: $196,716

Betaseron:
Utilizing Members: 12
Rxs: 32
Plan Paid: $124,807

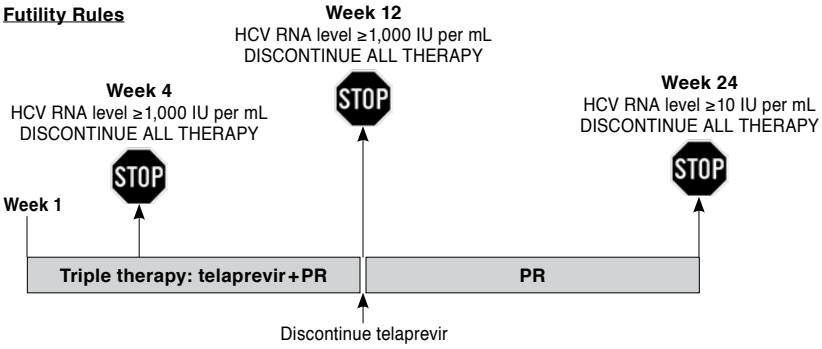
Gilenya:
Utilizing Members: 11
Rxs: 30
Plan Paid: $119,856

Extavia:
No utilization during this timeframe

FIGURE 2 Hepatitis C Treatment Algorithm: Telaprevir[a] and Boceprevir[b]

Telaprevir

Futility Rules



Continuation Rules

Treatment-naïve* and prior-relapse patients:

Week 24 | Week 48

Not detectable at week 4 and week 12–continue PR through week 24

***for patients with cirrhosis**–continue PR through week 48 unless detectable at week 24

Detectable at week 4 and/or week 12 – continue PR through week 48 unless detectable at week 24

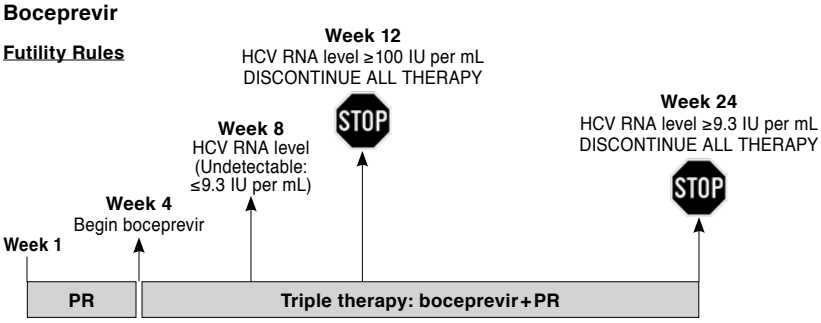
Prior partial- and null-responder patients:

Week 48

Not detectable at week 4 and week 12–continue PR through week 48 unless detectable at week 24

Boceprevir

Futility Rules



Continuation Rules

Treatment-naïve patients:

Week 24

Not detectable at week 8 and week 24–continue triple therapy with boceprevir + PR through week 24

Week 48

Detectable at week 8 and not detectable at week 12–complete boceprevir at week 36 and continue PR through week 48

Prior-relapse and partial-responder patients:

Week 36

Not detectable at week 4 and week 24–continue triple therapy with boceprevir + PR through week 36

Week 48

Detectable at week 8 and not detectable at week 12–complete boceprevir at week 36 and continue PR through week 48

Patients with cirrhosis:

Week 48

4 weeks of PR followed by 44 weeks of triple therapy with boceprevir + PR

[a]*Source: Telaprevir (Incivek) prescribing information.*[11]
[b]*Source: Boceprevir (Victrelis) prescribing information.*[10]
HCV = hepatitis C virus; IU = international units; mL = milliliter; PR = peginterferon + ribavirin; RNA = ribonucleic acid.

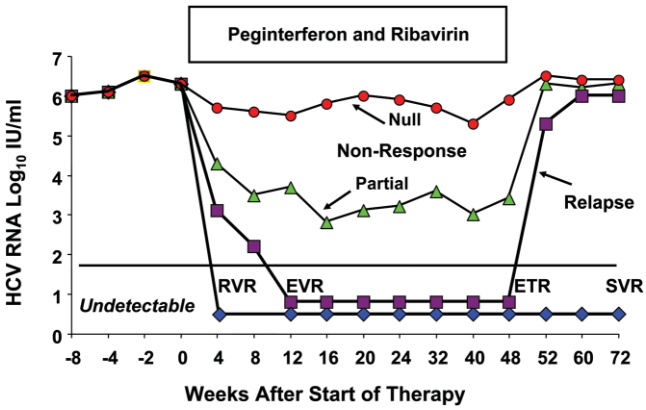


Fig. 1. Graphic display of virological responses. RVR, rapid virological response (clearance of HCV from serum by week 4 using a sensitive PCR-based assay); EVR, early virological response (≥2 log reduction in HCV RNA level compared to baseline HCV RNA level or HCV RNA negative at treatment week 12); SVR, sustained virological response (HCV RNA negative 24 weeks after cessation of treatment); relapse, reappearance of HCV RNA in serum after therapy is discontinued; nonresponder, failure to clear HCV RNA from serum after 24 weeks of therapy; partial nonresponder , 2 log decrease in HCV RNA but still HCV RNA positive at week 24; null nonresponder, failure to decrease HCV RNA by < 2 logs after 24 week of therapy.

those whose HCV RNA levels decrease by ≤2 logs IU/mL but never become undetectable are referred to as partial nonresponders.

The Optimal Treatment of Chronic HCV: Peginterferon Alfa and Ribavirin

The currently recommended therapy of chronic HCV infection is the combination of a pegylated interferon alfa and ribavirin. The choice of this regimen was based upon the results of three pivotal, randomized, clinical trials that demonstrated the superiority of this combination treatment over standard interferon alfa and ribavirin.[71-73] While not directly comparable, these three trials defined several key components of therapy, namely the appropriate dose of the drugs, the optimal duration of therapy and the need for a different regimen for patients with genotype 1 and genotype 2 and 3 infections.

There are two licensed pegylated interferons in the United States, peginterferon alfa-2b (Peg-Intron, Schering Plough Corp., Kenilworth, NJ), with a 12-kd linear polyethylene glycol (PEG) covalently linked to the standard interferon alfa-2b molecule, and peginterferon alfa-2a (Pegasys, Hoffmann-La Roche, Nutley, NJ) with a 40-kd branched PEG covalently linked to the standard interferon alfa-2a molecule.[108] The doses of these two forms of pegylated interferons differ.

The optimal dose of peginterferon alfa-2b, based on the original registration trial, is 1.5 μg/kg/week dosed according to body weight (Fig. 2). Although the dose of ribavirin used in the original registration trial was fixed at 800 mg daily, a subsequent community-based study of patients with genotype 1 infection demonstrated that weight-based ribavirin (800 mg for patients <65 kg; 1,000 mg for patients weighing 65 to 85 kg; 1,200 mg for patients weighing 85 to 105 kg; and 1,400 mg for patients weighing >105 kg but <125 kg) was more effective.[71,109]

Peginterferon alfa-2a is administered at a fixed dose of 180 μg/week given subcutaneously together with ribavirin 1,000 to 1,200 mg daily, 1,000 mg for those who weigh ≤75 kg and 1,200 mg for those who weigh >75 kg (Fig. 2).[72] The registration trial highlighted the two beneficial effects of ribavirin, an improvement in the ETR but, more importantly, a significant decrease in the relapse rate as compared to peginterferon monotherapy treatment.

A third randomized trial determined that the optimal duration of treatment should be based on the viral genotype. The study established that patients with genotype 1 should be treated for 48 weeks with peginterferon alfa-2a plus standard weight-based ribavirin, whereas patients with genotypes 2 and 3 could be treated with peginterferon alfa-2a plus low dose ribavirin (800 mg) for 24 weeks.[73]

For patients with HCV genotype 4 infection, combination treatment with pegylated interferon plus weight-based ribavirin administered for 48 weeks appears to be the optimal regimen, as concluded in a meta-analysis of six randomized trials.[110] While data from another randomized trial of treatment with combination peginterferon alfa-2b plus a fixed dose of ribavirin (10.6 mg/kg per day) has suggested that 36 weeks duration of therapy is sufficient provided an EVR is achieved, these results need to be confirmed.[111]

Patients with genotypes 5 and 6 are underrepresented in trials of peginterferon and ribavirin due to their limited worldwide frequency. A recent retrospective analysis of

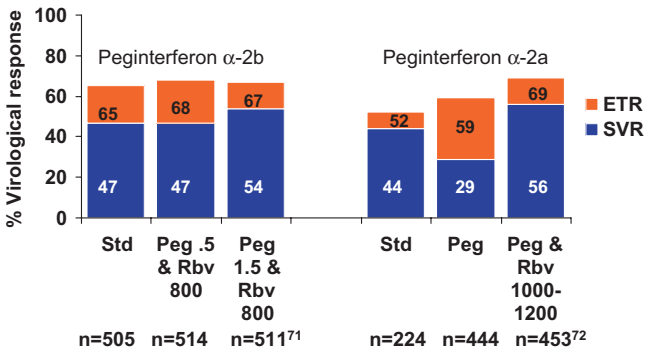


Fig. 2. Virological responses to pegylated interferon and ribavirin in the two U.S. Registration trials.[71,72] ETR, end-of-treatment response; SVR, sustained virological response.

the treatment of patients with HCV genotype 6 concluded that treatment with peginterferon alfa plus ribavirin for 48 weeks was effective and preferable to treatment for 24 weeks.[112] There are insufficient data to make recommendations on the specific doses of medications or durations of treatment for persons with genotype 5 infection.

Currently, the major challenge with regard to therapy is what new approaches are needed to increase the SVR rates in (1) patients with genotype 1 infection and a high viral load; (2) HCV-infected African-American patients (see below); and (3) persons who fail to achieve an SVR using the currently approved treatment regimens.

Pretreatment Predictors of Response. Pretreatment predictors of response are useful for advising patients on their likelihood of an SVR. Absence of favorable factors should not be used, however, to deny therapy. Data on predictors of an SVR come from several sources: registration trials which have strict inclusion and exclusion criteria and may not accurately reflect the general population infected with HCV; community-based trials that may not be conducted with the same rigor as registration trials; and Veterans Affairs databases which involve men predominantly and therefore do not reflect the general population with HCV infection. Despite these caveats, multivariate analyses have identified two major predictors of an SVR among all populations studied: the viral genotype and pretreatment viral load.[71-73] Sustained virological response rates were higher in patients infected with genotype non-1 infection (mostly genotype 2 and 3) and in those with a viral load of less than 600,000 IU/mL.[73] Other less consistently reported baseline characteristics associated with a favorable response include the doses of peginterferon (1.5 μg/kg/week versus 0.5 μg/kg/week) and ribavirin (>10.6 mg/kg), female gender, age less than 40 years, non–African-American race, lower body weight ($\leq$75 kg), the absence of insulin resistance, elevated ALT levels (three-fold higher than the upper limit of normal), and the absence of bridging fibrosis or cirrhosis on liver biopsy.[71,72,113]

Viral Kinetics

Measuring the rate of viral clearance from serum is helpful in predicting the likelihood of a response to therapy, for determining the optimal duration of therapy and as a stopping rule for patients with CHC. Accordingly, there has been intense interest in tailoring treatment regimens for individual patients using viral kinetics. This approach may have the benefit of limiting exposure to peginterferon and ribavirin, thus potentially leading to reduced toxicity and a cost savings.

Early Virological Response (EVR)

The absence of an EVR is the most robust means of identifying non-responders. Data from two retrospective analyses of multicenter trials indicated that failure to decrease serum HCV RNA by 2 logs or more at treatment week 12 correlated strongly with non-response in treatment-naive subjects with genotype 1 infection.[72,105] Ninety-seven to 100% of treatment-naive patients with HCV genotype 1 infection who did not reach an EVR failed to achieve an SVR. Thus, patients who do not have an EVR can discontinue therapy early without compromising their chance to achieve an SVR. In contrast, an EVR is less accurate in predicting an SVR since only 65% to 72% of subjects who achieved an EVR ultimately attained an SVR. A completely negative test for HCV RNA at week 12 (complete EVR) is a better predictor of an SVR than a 2-log reduction in HCV RNA, 83% versus 21%.[105] The clinical utility of an EVR is less helpful in persons with HCV genotype 2 and 3 infection since a majority of such individuals clear virus by week 12 and respond to therapy.

Rapid Virological Response (RVR)

Earlier time points have also been examined in the hope of limiting exposure to and the side effects of therapy. Achieving an RVR is highly predictive of obtaining an SVR independent of genotype and regardless of the treatment regimen.[107] However, only 15% to 20% of persons with HCV genotype 1 infection and 66% with HCV genotype 2 and 3 infections achieve an RVR.[107,114] In a retrospective analysis of the predictive value of an RVR in persons with HCV genotype 1 treated with peginterferon alfa-2a, those who achieved an RVR had an SVR rate of 91%, those who achieved a complete EVR had an SVR rate of 75%, and those who achieved an undetectable HCV RNA at week 24, had an SVR rate of 45%.[107]

Because of the rapid clearance of virus from serum, patients who achieve an RVR may be able to shorten the duration of treatment.[104,107] In contrast, because of a poor negative predictive value, the absence of an RVR should not be a basis for discontinuing treatment.

Utility of RVR in Patients with Genotype 1 Infection. Two analyses suggest that patients with HCV genotype 1 who achieve an RVR may be able to shorten the duration of therapy from 48 to 24 weeks. A *post hoc* analysis was conducted of a trial in which patients with chronic HCV infection were treated with peginterferon alfa-2a plus ribavirin either with a fixed dose (800 mg per day) or a weight-based dose (800-1,200 mg per day) for 24 or 48 weeks.[73] Overall, 24% of patients with HCV

Table 9. Summary of Studies Comparing Short Versus Standard Therapy Stratifying Based Upon RVR in Genotype 2 and 3 Patients

Trial/ Regimen	[a]PegIFN α-2b 1 μg/kg/wk & Rbv 1,000-1,2000 mg daily[117]			[b]PegIFN α-2a 180 μg/wk & Rbv 800-1,200 mg daily[118]			[c]PegIFN α-2a 180 μg/wk & Rbv 1,00-1,200 mg daily[119]		[d]PegIFN α-2a 180 μg/wk & Rbv 800 mg daily[114]	
N	283			153			150		1,469	
Gt 2	76%			26%			100%		50%	
Gt 3	24%			74%			0%		50%	
Rx duration/	12^{I} wks	24^{II} wks	24^{III} wks	16^{1} wks	24^{2} wks	24^{3} wks	16 wks	24 wks	16 wks	24 wks
n	113	80	70	71	71	11	50	100	732	731
RVR	100	0	64	100	100	0	86	87	67	64
ETR	95	68	79	94	85	72	100	98	89	82
SVR	85	64	76	82	80	36	94	95	62	70
REL	9	6	4	13	5	50	6	3	30	13

[a]Patients were randomized at baseline to a standard 24 week regimen (Group III), or a variable-duration regimen depending on results of HCV RNA testing at week 4: HCVRNA negative-treatment duration 12 weeks (Group I) or HCV RNA positive-treatment duration 24 weeks (Group II).

[b]All patients treated for 4 weeks, patients with an RVR (HCV RNA $<$ 600 IU/ml) were randomized to 16 (Group 1) or 24 weeks (Group 2). Patients with HCV RNA $\geq$600 IU/ml were treated for 24 weeks (Group 3).

[c]Patients randomized 1:2 to either 16 or 24 weeks.

[d]Patients randomized to 16 or 24 weeks.

Abbreviations: Gt, genotype; n, number; Rx, Treatment; REL, Relapser.

genotype 1 infection in the two 24-week treatment arms achieved an RVR. The SVR rate was 89% in patients who achieved an RVR and 19% in those who did not achieve an RVR, and was similar among those treated for 24 or 48 weeks.[104] Features predictive of an RVR were a low baseline viral load ($\leq$200,000 IU/mL) and HCV subtype 1b.

In another study, patients with HCV genotype 1 infection and a low viral load ($<$600,000 IU/mL) were treated with peginterferon alfa-2b, 1.5 μg/kg/week plus ribavirin 800 to 1,400 mg daily for 24 weeks.[115] Overall an SVR occurred in 50% of patients.[115] However, a subanalysis of patients who achieved an RVR, 47%, reported an SVR rate of 89% compared to 20% among those who did not achieve an RVR. These results suggest that HCV genotype 1 patients who achieve an RVR can be successfully treated with a 24-week course of therapy.

Utility of an RVR in Persons with Genotypes 2 and 3 Infections. Four trials have evaluated the usefulness of an RVR in shortening the duration of therapy from 24 weeks to 12 to 16 weeks in patients with chronic HCV genotypes 2 and 3 infection.[116-119] Although not directly comparable because of the use of different inclusion criteria, treatment regimens and trial designs, the data from these trials suggest that patients with genotypes 2 and 3 infection who achieve an RVR can shorten their treatment duration to 12 to 16 weeks, because the SVR rates at 12 to 16 weeks (62%-94%) were comparable to the SVR rates at 24 weeks (70%-95%), (Table 9). The one shortcoming of this approach is that the relapse rate more than doubles from 3% to 13% in those treated for 24 weeks, to 10% to 30% for those treated for 12 to 16 weeks. Importantly, patients with HCV, genotypes 2 and 3 who relapse after a short course of treatment almost always achieve an SVR when re-treated with a standard 24-week course of therapy. No predictors of an RVR were identified in multivariate analysis in the single study that performed this analysis.[117] Predictors of an SVR among these studies were HCV genotype 2 infection, a low baseline HCV RNA level ($\leq$800,000 IU/mL), and the absence of bridging fibrosis or cirrhosis.[118] Patients with genotype 2 and 3 infections who fail to achieve an RVR (mostly patients with HCV genotype 3 infection with high viral loads and bridging fibrosis or cirrhosis) have poor SVR rates with 24 weeks of therapy and may benefit from longer duration of treatment, but this has not been prospectively evaluated.

Based on these results, it appears that patients with HCV genotype 2 or 3 infections who achieve an RVR can shorten their duration of therapy to 12 to 16 weeks. However, a recent large multicenter, multinational trial that included 1,469 patients with genotype 2 and 3 infection has challenged this concept. Patients were randomized to receive peginterferon alfa-2a, 180 μg / week plus 800 mg of ribavirin for either 16 or 24 weeks without stratification based upon RVR. In contrast to previous studies, the results demonstrated that treatment for 24 weeks was superior to treatment for 16 weeks (SVR rate 76% versus 65%, respectively, P $<$0.001), even in those who achieved an RVR (85% versus 79%, respectively).[114] One possible explanation for this varying result was that a fixed dose of ribavirin (800 mg) was used in this trial whereas weight-based ribavirin was used in the other trials.

Thus, patients with HCV genotypes 2 and 3 who are intolerant of a planned 24-week course of therapy can have their therapy discontinued between weeks 12 and 16 if they had achieved an RVR. However, patients should be informed of the higher relapse rate associated with this

strategy and be advised that re-treatment with a 24 to 48 week course of therapy may be required. Patients with HCV genotype 3 and a high viral load have lower response rates than do patients with HCV genotype 3 and a low viral load and patients with genotype 2 infections. Therefore, a longer duration of therapy should be considered for such patients. Comparable data are not available in difficult-to-treat populations such as African Americans, those with cirrhosis and those with HIV-HCV coinfection, and therefore this strategy cannot be recommended for these patient populations.

Utility of RVR in Persons with HCV Genotype 4 Infection. The role of RVR has also been assessed in patients with HCV genotype 4 infection. Patients with this genotype were treated with pegylated interferon, alfa-2b 1.5 μg/kg/week plus ribavirin 10.6 mg/kg/day for a fixed duration of 48 weeks or a variable duration based upon time to viral clearance (24 weeks if an RVR was achieved, 36 weeks if a complete EVR was achieved and 48 weeks for viral clearance beyond 12 weeks).[111] The SVR rate among those who achieved an RVR was 86%, 76% in those who achieved a complete EVR, 56% in those who had undetectable HCV RNA after 12 weeks, and 58% in those randomly assigned to 48 weeks. These results suggest that patients with HCV genotype 4 infection who achieve an RVR may be able to be treated for a shorter duration.

Effects of Higher Doses and Extended Duration of Treatment. Strategies to improve SVR rates in difficult-to-treat patients have included the use of higher doses of peginterferon and/or ribavirin or of longer durations of therapy. High dose interferon induction regimens have generally been unsuccessful. In one trial, high dose peginterferon alfa-2b induction therapy (3 μg/kg weekly for 1 week, 1.5 μg/kg/weekly for 3 weeks and 1 μg/kg weekly for 44 weeks) was compared to low dose peginterferon alfa-2b (0.5 μg/kg weekly for 48 weeks).[120] The high dose induction regimen was associated with a faster rate of viral clearance compared with the standard regimen, 22% versus 7% at week 4, but the proportion with undetectable HCV RNA was similar at the end of therapy, 71% versus 61.5%.[120] Unfortunately, SVR data were not provided.

High dose ribavirin (1,600 to 3,600 mg per day) given together with standard dose peginterferon was evaluated in a small pilot study of 10 patients with genotype 1 infection and a baseline viral load >800,000 IU/mL.[121] Ninety percent of patients achieved an SVR. While these results are compelling, safety issues are the major concern for this approach since significant anemia developed in all patients, requiring the use of growth factors in all and blood transfusions in two patients.

The strategy of extending therapy in naive subjects with delayed virological responses, defined as clearance of HCV RNA between weeks 12 and 24, was evaluated in two studies.[122,123] One study randomized subjects to either 48 or 72 weeks of treatment at week 12 if HCV RNA remained detectable,[123] and the other was a *post hoc* analysis of a study in which randomization of treatment duration occurred at baseline.[122] The study populations were not homogeneous, differing in their baseline characteristics and the regimens utilized were different. Nevertheless, the results showed a trend toward a higher SVR rate by extending therapy from 48 to 72 weeks. The SVR rate increased from 18% for 48 weeks treatment to 38% for 72 weeks of treatment in one study[123] and 17% to 29% in the other study.[122] The increased SVR was primarily due a lower relapse rate in the patients treated for 72 weeks. An additional study demonstrated that patients who failed to achieve an RVR (HCV RNA detectable at treatment week 4) also seemed to benefit from extending therapy from 48 to 72 weeks.[124] The SVR rates were significantly higher in patients who received treatment for 72 (45%) compared to those treated for 48 weeks (32%).[124] It is clear that not all patients will benefit from extended therapy judging from the results of the trial in which randomization to 48 or 72 weeks of therapy occurred at baseline.[122] No difference in SVR rates was observed between those treated for 48 compared to 72 weeks (53% versus 54%, respectively).[122] Thus, prolonging therapy can be considered in patients who are slow to respond (clearance of HCV RNA between weeks 12 and 24). Further studies are needed to determine whether extended therapy would be beneficial to patients who fail to clear virus between weeks 4 and 12.

Adverse Events. Almost all patients treated with peginterferon and ribavirin experience one or more adverse events during the course of therapy. Adverse events are a major reason that patients decline or stop therapy altogether. In the registration trials of peginterferon alfa-2a and 2b plus ribavirin, 10% to 14% of patients had to discontinue therapy due to an adverse event.[71,72] The most common adverse events in these trials were influenza-like side effects such as fatigue, headache, fever and rigors, which occurred in more than half of the patients, and psychiatric side effects (depression, irritability, and insomnia), which occurred in 22% to 31% of patients.

Laboratory abnormalities are the most common reasons for dose reduction. Among these, neutropenia (absolute neutrophil count [ANC] of 1500 mm^3) was a frequent laboratory abnormality, occurring in 18% to 20% in the two large phase III clinical trials where the dose was reduced 50% for an ANC of 750 mm^3 and permanently discontinued for an ANC of <500

Xyrem
(sodium oxybate, aka GHB Sodium, GBH Sodium, oxybate sodium, gamma-hydroxybutyrate)
DUEC Discussion 6/25/12

Sodium oxybate is used to prevent attacks of cataplexy (episodes of muscle weakness that begin suddenly and last for a short time) in patients who have narcolepsy (a sleep disorder that may cause extreme sleepiness, sudden uncontrollable urge to sleep during daily activities, and cataplexy). Sodium oxybate is a CNS depressant for which the mechanism of action to treat cataplexy is unknown.

It is a solution to mix with water and take by mouth twice each night because sodium oxybate wears off after a short time and the effects of one dose will not last for the entire night. The first dose is taken at bedtime, and a second dose is taken 2 1/2 to 4 hours after the first dose. The 1st dose should not be taken until you are in bed and are ready to go to sleep for the night. Sodium oxybate begins to work very quickly and you may have an upset stomach or feel dizzy or lightheaded if you take the medication before you go to bed for the night. An alarm clock must be used to administer the 2nd dose. This is not a cure.

The drug causes drowsiness, therefore, no driving or operating machinery or other dangerous activities should take place for at least 6hours after taking Xyrem.

Xyrem is contraindicated in patients who take other sedative hypnotics and in patients with succinic semialdehyde dehydrogenase deficiency.

Proposal:

1. Require prior authorization for Xyrem.
2. PBM should place a quantity limit of at or below the FDA-labeled maximum dose of 9g/night (540mL/30 days).

References:

1. http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0000315/
2. Xyrem website. Accessed 6/20/12. http://www.xyrem.com/

Suboxone (buprenorphine/naloxone), generic buprenorphine Issue

buprenorphine 2mg/ naloxone 0.5mg SL tablet and film

buprenorphine 16mg/naloxone 4mg tablet and film

plain buprenorphine sublingual tablet 8mg, 2mg (generic only, previously marketed as Subutex)

Suboxone is a sublingual tablet and FDA-approved for the maintenance treatment of opioid dependence. Prescription use is limited under the Drug Addiction Treatment Act.

> **The Drug Addiction Treatment Act of 2000** (**DATA 2000**), Title XXXV, Section 3502 of the Children's Health Act of 2000, permits physicians who meet certain qualifications to treat opioid addiction with Schedule III, IV, and V narcotic medications that have been specifically approved by the Food and Drug Administration for that indication. Such medications may be prescribed and dispensed by waived physicians in treatment settings other than the traditional Opioid Treatment Program (methadone clinic) setting.
>
> Since there is only one narcotic medication approved by the FDA for the treatment of opioid addiction within the Schedules given, DATA 2000 basically refers to the use of buprenorphine for the treatment of opioid addiction. Methadone and levomethadyl acetate (LAAM) are Schedule II narcotics approved for the same purpose within the highly regulated methadone clinic setting.

The buprenorphine injection and patch are FDA-approved for management of moderate to severe pain. The tablets and film are for opioid dependence and are dosed once daily due to the long duration of action of oral forms.

In 1 year, EBD had 32 unique utilizers of oral buprenorphine who also used other opioid pain medications. These 32 had multiple prescribers, multiple pharmacies, and utilized oral buprenorphine multiple times per day, a dosing regimen inconsistent with opioid dependence.

From June 2011 to May 2012, EBD spent over $98,000 on buprenorphine. Using oral buprenorphine for pain is off-label and there are many alternative opiates for this use. AR Medicaid prior authorizes oral buprenorphine products and limits their uses to opioid dependence. Additionally, they will allow only 24 months of suboxone/oral buprenorphine use for 24 months lifetime max for each member.

Proposal:

1. Require prior authorization for oral buprenorphine-containing products.
2. Communicate with current utilizers allowing a 3 month period of lead time for them to visit their physician to be prescribed an alternative pain med. (This point may be moot anyway because all 32 had other pain meds on their profiles.) No grandfathering.

CURRENT PA-6/25/12

EBRx Arkansas Employee Benefits Division
Prior Authorization Criteria
for Ketek® (telithromycin)

1. Does the prescriber suspect a resistant gram positive organism causing community acquired pneumonia because of recent antibiotics use or because of susceptibility results?	**□ Yes □ No**
2. Does this patient have ABSENCE of any known liver disease?	**□ Yes □ No**
If "yes", then allow coverage. If "no", then deny coverage.	

Note: This drug was voted by the Insurance Board 10-16-06 to require PA due to the boxed warning by the FDA warning of serious hepatoxicity.

Boxed warning: Telithromycin should be avoided in patients with pre-existing liver disease. Patients should be instructed to contact their healthcare provider immediately if symptoms of hepatic disease are noted, including scleral icterus, jaundice, pruritus, dark urine, pale stools, or abdominal pain develop.

Revision history:

Date	What changed?	Pharmacist's initials
10/16/06	IB voted to require PA due to the boxed warning by the FDA warning of serious hepatotoxicity.	JJ
5/17/12	Revision history added	JJ

ISENTRESS (raltegravir) tablets
PA Criteria, updated 6/4/08

1. Has the patient failed two (2) first line highly active antiretroviral therapy (HAART) regimens* due to: a. failure to suppress the virus, b. a drug interaction that precludes the use of the first line HAART, OR c. drug intolerance	( ) YES ( ) NO
2. Will Isentress be used in combination with other HAART medications?	( ) YES ( ) NO

If the question above is answered yes, approve PA for one year.
Quantity limit: 62 tablets for 31 days

Call center Info: The recommended dose of Isentress (raltegravir) is 400 mg twice daily.

References:
1. Product Package Insert, Isentress (raltegravir). Merck and Company, Inc. October 2007.
2. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. January 29, 2008; 1-128. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf Accessed June 4, 2008, Table 6.
It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the **AIDS*info* Web site** (**http://AIDSinfo.nih.gov**).

*

Table 6. Antiretroviral Components Recommended for Treatment of HIV-1 Infection in Treatment-Naïve Patients (Updated **January 29, 2008**)

A combination antiretroviral regimen in treatment-naïve patients generally contains 1 NNRTI + 2 NRTIs or a single or ritonavir-boosted PI + 2 NRTIs.
Selection of a regimen for an antiretroviral-naïve patient should be individualized based on virologic efficacy, toxicities, pill burden, dosing frequency, drug-drug interaction potential, and comorbid conditions. Components listed below are designated as preferred when clinical trial data suggest optimal and durable efficacy with acceptable tolerability and ease of use. Alternative components are those that clinical trial data show efficacy but that have disadvantages, such as antiviral activity or toxicities, compared with the preferred agent. In some cases, for an individual patient, a component listed as alternative may actually be the preferred component. Clinicians initiating antiretroviral regimens in the HIV-infected pregnant patient should refer to "*Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States*" at http://aidsinfo.nih.gov/guidelines/.

To Construct an Antiretroviral Regimen, Select 1 Component from Column A + 1 from Column B

	Column A (NNRTI or PI Options – in alphabetical order)		Column B (Dual-NRTI Options)
Preferred Components	NNRTI or PI efavirenz[1] (AII) atazanavir + ritonavir (AIII) fosamprenavir + ritonavir (2x/day) (AII) lopinavir/ritonavir[2] (2x/day) (AII) (coformulated)	+	Preferred Components (alphabetical order) abacavir/lamivudine[3] (for patients who test negative for HLAB*5701) (coformulated) (AII)[6]; or tenofovir/emtricitabine[3] (coformulated) (AII)
Alternative to Preferred Components	NNRTI or PI nevirapine[4] (BII) atazanavir[5] (BII) fosamprenavir (BII) fosamprenavir + ritonavir (1x/day) (BII) lopinavir/ritonavir (1x/day) (BII) (coformulated) saquinavir + ritonavir (BII)		Alternative to Preferred Components (order of preference) zidovudine/lamivudine[3] (coformulated) (BII); or didanosine + (emtricitabine or lamivudine) (BII)

[1] Efavirenz is not recommended for use in the first trimester of pregnancy or in sexually active women with childbearing potential who are not using effective contraception.
[2] The pivotal study that led to the recommendation of lopinavir/ritonavir as a preferred PI component was based on twice-daily dosing *[141]*. A smaller study has shown similar efficacy with once-daily dosing but also showed a higher incidence of moderate to severe diarrhea with the once-daily regimen (16% vs. 5%) *[148]*. In addition, once-daily dosing may be insufficient for those with viral loads >100,000 copies/mL *[151]*.
[3] Emtricitabine may be used in place of lamivudine and vice versa.
[4] Nevirapine should not be initiated the following treatment-naïve patients: women with CD4 count >250 cells/mm^3 or in men with CD4 count >400 cells/mm^3 because of increased risk for symptomatic hepatic events in these patients.
[5] Atazanavir must be boosted with ritonavir if used in combination with efavirenz or tenofovir.
[6] Please refer to "*DHHS Adults and Adolescents Antiretroviral Treatment Guidelines Panel's Communication Regarding Abacavir – April 4, 2008*" at http://www.aidsinfo.nih.gov/guidelines.

EBRx Arkansas Employee Benefits Division
Prior Authorization Criteria
for botulinum toxins

Onabotulinumtoxin A (Botox), Abobotulinumtoxin A, (Dysport), Incobotulinumtoxin A (Xeomin), RimabotulinumtoxinB (Myobloc)

Indication	Drug
Blepharospasm	☐ Botox ☐ Xeomin (for pts previously tx with Botox) ☐ Dysport
Strabismus ☐ Cannot have 6th nerve palsy or adult horizontal strabismus as botulinum toxin does not appear effective for these	☐ Botox
Cervical dystonia (spasmodic torticollis)	☐ Botox ☐ Myobloc ☐ Xeomin (for pts previously tx with Botox & toxin naïve pts) ☐ Dysport(for pts previously tx & toxin-naive) ☐ Dysport
Other Focal Dystonias (writer's cramp, occupational dystonias, etc) ☐ For upper extremities only; inadequate data for use in LE	☐ Botox
Hemifacial Spasm (a VII nerve disorder)	☐ Botox ☐ Dysport
Spasmodic dystonia (larangeal dystonia) ☐ must also undergo voice therapy	☐ Botox
Focal Spasticity (adult and child – MS, CP, brain injury, etc) ☐ must undergo physical or occupational therapy	☐ Botox ☐ Myobloc
Hyperhidrosis (primary axillary or palmer) ☐ unresponsive to treatment with aluminum chloride hexahydrate (Drysol) ☐ hyperhidrosis is interfering with activities of daily living or is causing skin maceration or infections (fungal, bacterial) ☐ must be administered as injection, not used in iontophoresis machine for paler hyperhyidrosis	☐ Botox
Detrusor overactivity associated with a neurologic condition ☐ Prescribed by a urologist ☐ Failure or contraindication to at least one anticholinergic medication for OAB. (failure is defined as one or more incontinent episodes/day) ☐ No concomitant therapy with Botox and an anticholinergic (no trials showing combination therapy is superior to monotherapy)	☐ Botox
Anal fissure ☐ Failure of two of the following convention treatments: topical nitrate preparations, topical CCB, sitz baths, stool softeners	☐ Botox
Initial Approval: 6 months, **Reauthorization:** 6 months if clinical improvement documented	

Botox will not be approved for the following uses:

1. Cosmetic purposes
2. Migraine HA
3. Tension HA

Notes:

Blepharospasm:

"There are no high quality, randomised, controlled efficacy data to support the use of Bt for blepharospasm. Despite this, other studies suggest that BtA is highly effective and safe for treating blepharospasm and support its use."[7] Before Bt, there were no effective medical or surgical treatments for blepharospasm. The results of Bt treatment for blepharospasm in open label observations were felt to be so dramatic that there have been few attempts at performing proper RCT.[2]

Strabismus:

- **botulinum toxin does not appear effective for 6th nerve palsy or adult horizontal strabismus and may not be more effective than surgery for esotropia or infantile esotropia (level 2 [mid-level] evidence)**
  - based on Cochrane review with limited evidence
  - systematic review of 4 randomized trials evaluating botulinum toxin for treatment of strabismus
  - all trials were small, 3 trials had inadequate allocation concealment
  - no significant differences comparing botulinum toxin vs. surgery for patients requiring retreatment for acquired esotropia or infantile esotropia in 2 trials
  - no evidence of prophylactic effect of botulinum toxin in treatment of acute onset 6th nerve palsy
  - botulinum toxin associated with poorer response than surgery in patients requiring treatment for horizontal strabismus in absence of binocular vision
  - complication rates ranged from 24% with Dysport to 52.2-55.5% with Botox and included ptosis and vertical deviation
  - Reference - Cochrane Database Syst Rev 2009 Apr 15;(2):CD006499
- EMG-guided injections of botulinum toxin may be an alternative to incisional surgery (Am Fam Physician 1997 Feb 1;55(2):544)
- successful reports of bilateral injections of botulinum toxin in 32 children with intermittent exotropia can be found in Ophthalmol 1997 Nov;104(11):1762 (Pediatric Notes 1997 Dec 11;21(50):199)
- **botulinum toxin injection effective for children with infantile esotropia and can produce binocular alignment of visual axes, based on case series**
  - 76 consecutive children 4-48 months with infantile esotropia treated with simultaneous bilateral injection of botulinum toxin type A 2.5 units into medial rectus muscles and followed up for 12-95 months after last injection, 36 children required multiple bilateral injections
  - injections were effective in reducing esotropia in 68 children (89%), boys required fewer injections than girls but overacting inferior oblique muscles were more prominent in boys
  - Reference - Arch Ophthalmol 1997 Nov;115(11):1411 in QuickScan Reviews in Fam Pract 1998 Jun;23(3):18
- review of botulinum toxin can be found in BMJ 2000 Jan 15;320(7228):161 full-text
- review suggests that treatment with toxin now favored over surgery for infantile esotropia; alternate patching for 2 weeks recommended before resorting to treatment with toxin, then bilateral injection of 2.5 units with repeat injection if no response (J Pediatr Ophthalmol Strabismus 2000 Mar/Apr;37(2):63 in Pediatric Notes 2000 May 4;24(18):70)

  -DynaMed

Cervical dystonia: involuntary activation of the muscles of the neck and shoulders; results in sustained abnormal posturing of the head, neck, and shoulders.
"Indirect comparisons between trials that used Dysport against placebo and trials that used Botox against placebo showed no significant differences between Dysport and Botox in terms of benefits or adverse events. A single injection cycle of BtA is effective and safe for treating cervical dystonia. Enriched trials (using patients previously treated with BtA), suggest that further injection cycles continue to work for most patients[9]." It appears that BtA is more beneficial than trihexyphenidyl in cervical dystonia, but comparisons with other anticholinergics are lacking[10].

Anal Fissure:

- dose used in studies has varied from 10-100 units
- often administered as two injections, one on each side of fissure
- Association of Coloproctology of Great Britain and Ireland recommends 20-25 units in divided dose on either side of fissure
- appears to have similar healing rate as nitroglycerin and calcium channel blockers, but may be less effective than surgery for chronic anal fissure
- –DynaMed

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Revision History:

Date	Changes	Pharmacist
2/9/2011	Document Created	CK

Targeted Immune Modulators Review

March 8, 2012 DERP Report Summary

6/25/12 DUEC Meeting, Jill Johnson, Pharm.D., BCPS

Generic	Brand	Indication	Safety data
Abatacept	Orencia	RA, JRA, JIA	
Adalimumab	Humira	RA, PsA, AS, JIA, CD, PlaqPs	
Alefacept	Amevive	PlaqPs	Missing
Anakinra	Kineret	RA	
Certolizumab	Cimzia	RA, CD	
Etanercept	Enbrel	RA, PsA, AS, JIA, PlaqPs	
Golimumab	Simponi	RA, PsA, AS	
Infliximab	Remicade	RA, CD, PsA, AS, UC, PlaqPs	
Natalizumab	Tysabri	CD	Missing
Rituximab	Rituxan	RA	Missing
Tocilizumab	Actemra	RA, JIA	
Ustekinumab	Stlara	PlaqPs	

RA=rheumatoid arthritis, JRA=juvenile rheumatoid arthritis, JIA=juvenile idiopathic arthritis, PsA=psoriatic arthritis, AS=ankylosing spondylitis, CD=Crohn's disease, PlaqPs=plaque psoriasis, UC=ulcerative colitis

- RA was the only indication in which there was enough comparative data to make any statement. Overall for RA, abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab, and tocilizumab were all better than placebo by a large margin. There is insufficient evidence
- For efficacy:
  - abatacept appeared to be similar to fixed dose infliximab at 6 months
  - adalimumab and etanercept were more efficacious than infliximab
  - etanercept was more efficacious than infliximab but failed to show a difference when one trial with heterogeneity was removed.
- **Summary for efficacy:**
  - **Adalimumab, etanercept ?> infliximab, abatacept**
  - Note: RCTs or metaanalyses results that examine this hierarchy will trump these observational indirect comparisons.
- For safety:
  - Abatacept better than infliximab
  - Short term: abatacept and adalimumab have lower side effects than other TIMs
  - Short term: infliximab has more discontinuations than abatacept, adalimumab, etanercept, golimumab
  - Serious infections: less common with abatacept vs cert, inflix, tociliz
  - Serious infections: more common with certo vs adal, anak, etan, goli, inflix, ritux
- **Summary for safety: (">" means better than)**
  - **Abatacept>infliximab; Abatacept, adalimumab>other TIMs**
  - **Abatacept, adalimumab, etan, goli > inflix**
  - **Abatacept >cert, inflix, tociliz**
  - **Adalimumab, anak, etan, goli, inflix, ritux >certolizumab**

JIA	No HTH trials. Support for abatacept, adalimumab, etanercept, infliximab, tocilizumab
AS	No HTH trials. Support for adalimumab, etanercept, golimumab, infliximab
PsA	No HTH trials. 2 systematic reviews provided indirect comparisons. No stat sig differences were seen among adalimumab, etanercept, infliximab. Support for abatacept, adalimumab, alefacept, etanercept, golimumab, infliximab, ustekinumab. No studies in children.
CD	No HTH trials. Support for adalmumab, certolizumab, infliximab, natalizumab. Only one dose-ranging study supported use in children (88% achieved remission.)
UC	No HTH trials. Support for infliximab. No studies in children.
PlaqPs	One HTH: ustekinumab >etanercept (low quality trial). One etanercept trial supports its use in children.

HTH=head to head

Conclusion: Adalimumab appears to have an advantage over other TIMs with efficacy for RA. It also appears to have a safety advantage over several other effective TIMs regarding adverse effects.

Reference: Targeted Immune Modulators. Drug effectiveness review project, Oregon Health & Sciences University, March 8, 2012.