State and Public School Life and Health Insurance Board Clinical and Fiscal Drug Utilization and Evaluation Committee
Minutes
November 5, 2012

The State and Public Life and Health Insurance Board, Drug Utilization and Evaluation Committee (DUEC) met on Monday, November 5, 2012 at 1:00 p.m., in the EBD Board Room, 501 Woodlane, Little Rock, AR.

Members present:
Matthew Hadley
Kat Neill
Mark McGrew
Larry Dickerson
Scott Pace
Dr. Hank Simmons

Members absent:
Kelly Chaney
Dr. William Golden
Dr. Joe Stallings

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

OTHERS PRESENT
Jill Johnson, UAMS College of Pharmacy/EBRx; Connie Bennett, Catamaran; John Kirtley, State Board of Pharmacy; David Keisner, EBD/UAMS; Jordan Brazeal, Pharm.D. Evidence-based Medicine Pharmacy Practice Resident; Doug Shackleford, Leslie Smith, Sherri Saxby, Sherry Bryant, Melida Vasquez, Makesha Thompson, Latryce Long, Cathy Harris, EBD; Lori Eden, Janna Keathley, AHH; Bridget Johnson, Pfizer, Rhonda Walthall, AR Highway & Transportation Dept; Barbara Melugin, Health Advantage; Frances Bauman, Novo Nordisk; Charlene Kaiser, Amgen; Mark Chambers, Compsych; Greg Dougherty, Department of Information System; Jim Chapman, Abbott Laboratories; Mark Declerk, Lilly Pharmaceuticals; David Williams, Forest Pharmaceuticals; Steve Singleton, AR Retired Teacher Association; Nicole Young, Jenny Ni, UAMS

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 June 25, 2012 minutes. Neil made the motion to approve. Dr. Simmons seconded. All were in favor. Minutes were approved.

EBD COVERAGE POLICY FOR HEPATITIS C VIRUS (HCV) *by Jill Johnson*

The committee reviewed the coverage policy for Hepatitis C Virus based on the current American Association for the study of Liver Disease (AASLD) guidelines.

No action taken by the committee.

SECOND GENERATION ANTIPSYCHOTIC (SGA) PA CRITERIA *by Jill Johnson*

Jordan Brazeal provided information regarding SGAs for use as an adjunctive therapy to antidepressant drugs in the treatment of Major Depressive Disorder (MDD) and irritability associated with Autistic Disorder.

A discussion ensued.

Recommendation: Implement PA criteria for SGAs for conditions other than Psychosis: Abilify for psychosis or Bipolar and risperidone for major depression or irritability for Autistic Disorder. Grandfather current user unless they have been off the drug for 6 months.

Pace made the motion to adopt. Dickerson seconded. All were in favor. Motion carried.

FIRST REVIEW MEDICATIONS *by Jill Johnson*

Drug Name	Tier Status

VIOKACE **T2**
Generic – Pancrelipase (pancrelipase 10440-39150-39150 and 20880-78300-78300
Dose/Indications - Tx of cystic fibrosis, pancreatectomy and pancreatic insufficiency

PERTZYE **T2**
Generic – Pancrelipase (pancrelipase 10440-39150-39150 and 20880-78300-78300
Dose/Indications - Treatment of pancreatic insufficiency due to cystic fibrosis or other conditions

KYPROLIS SOLN **T3 w/PA**
Generic - carfilzomib 60mg in a single use vial
Dose/Indications- Treatment of multiple myelomas who have received at least two prior therapies including bortezomib and an immunomodulator and have demonstrated disease progression on or within 60 days of completion of the last therapy

Drug Name	Tier Status

STRIBILD TABS **T3 w/PA, QL of 31/31**
Generic- Elvitegravir, Cobicistat, Emtricitabine tenofovir
Dose/Indications- Once daily, oral 4-in-1 combination antiretroviral for tx of HIV. Complete regimen and should not be administered with other antiretroviral for HIV

Note: If can be automated, preclude other highly active antiretroviral therapy (HAART) to be used simultaneously.

TUDORZA PRESSAIR INHALER **T2**
Generic- Aclidinium
Dose/Indications- Long-term maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema

XTANDI **T3w/PA, 31 day QL**
Generic- Enzalutamide capsule 160mg once daily
Dose/Indications- For treatment of prostate cancer

ISENTRESS CHEW 25 and 100mg
Generic- raltegravir
Dose/Indications- For treatment of HIV infection

- **All anti HIV drugs will have a 31 days supply limit. No 90 day fills.**

Reviewed & Excluded Drugs

BUTRANS
Generic – buprenorphine 5mcg/h, 10mcg/h, 20mcg/h transdermal patch
Dose/Indications - pain, mod-severe chronic

CODEINE SULF SOLN (30mg/5ml)
Generic- codeine sulfate
Dose/Indications- Mild to moderate pain solution

NEUPRO DIS
Generic- rotigotine TD patch
Dose/Indications- Transdermal system for tx of Parkinson's and restless leg syndrome

Note: Trial of rotigotine vs ropinirole in early PD showed rotigotine missed the non inferiority mark.

MYRBETRIQ
Generic – mirabegron 25 and 50mg
Dose/Indications- For treatment of overactive bladder

ZYTIGA
Generic- Abiraterone
Dose/Indications- prostate cancer

Note: Previously reviewed & excluded 10/4/11. Drug has limited medical benefit. As of 10/29/12 no new trials are out on Zytiga. Continue exclusion.

LYRICA SOLUTION
Generic- Pregabalin solution 20mg/ml
Dose/Indications- For diabetic neuropathy, fibromyalgia, neuropathic pain, partial seizures, post herpetic neuralgia, spinal cord injury

BINOSTO-
Generic- Alendronate effervescent tab 70mg
Dose/Indications- New formulation of alendronate (Fosamax) in effervescent tab for osteoporosis, osteoporosis prophylaxis, Paget's disease

Note: Exclude due to dosage form unnecessary.

RAYOS
Generic- delayed release prednisone 1mg - 5mg
Dose/Indications- Oral corticosteroid

Note: Exclude due to underappreciated need for delayed release prednisone

The committee decided by consensus to accept the recommendations for first review medications.

Chairman Hadley provided Johnson with a list of discussion topics for the next meeting.

DIRECTOR'S REPORT *by Jason Lee*

The committee agreed by consensus to meet the 1st month of each quarter in 2013.

Meeting adjourned.

ARBenefits

AGENDA

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

November 5, 2012 – 1:00 PM

1. **Call to Order** ..... *Dr. Matthew Hadley, Chairman*
2. **Approval of Minutes** ..... *Dr. Matthew Hadley, Chairman*
3. **Hepatitis C Fact Sheet discussion**.....*Jill Johnson, UAMS-EBRx*
4. **Butrans Review**.....*Jill Johnson*
5. **2nd Generation Antipsychotic PA criteria** .....*Jill Johnson*
6. **New Drugs** .....*Jill Johnson*
7. **Other discussion topics**..... .....*Dr. Matthew Hadley*
8. **Director's Report** .....*Jason Lee*

Fact Sheet

EBD Coverage Policy for Hepatitis C Virus (HCV)

EBD covers drugs for the treatment of HCV infection. Coverage of specific drugs and lengths of therapy is determined by the genotype of HCV. The current American Association for the Study of Liver Diseases (AASLD) Practice Guidelines 2011 recommend triple therapy with a protease inhibitor, peginterferon, and ribavirin as the standard treatment for HCV infection. All patients must have a liver biopsy prior to starting HCV RNA drug therapy. It is not covered for patients with decompensated liver cirrhosis.

Genotype 1:

The current AASLD guidelines recommend triple therapy with the regimen determined by whether the patient has had prior drug therapies for HCV. EBD covers triple therapy with peginterferon, ribavirin, and boceprevir.

The dosing is boceprevir 800mg (4 capsules) orally three times daily with food. Peginterferon alfa-2b 1.5 microg/kg SC once weekly + Ribavirin 400mg twice daily.

Treatment-naïve patients:

1. Week 1 through week 4, peginterferon with ribavirin alone is covered.
2. Week 5, boceprevir + P + R is covered.
3. Week 8, bloodwork must be measured for HCV RNA level. Regardless of what the week 8 measurement is, boceprevir + P + R is covered.
4. Week 12, HCV RNA is measured again.

- If HCV RNA is 100 IU/mL or more, all HCV treatment is stopped. EBD will cover no more HCV treatment.

5. Week 24, HCV RNA is measured again. If HCV RNA is detectable ($\geq$9.3 IU/mL), all 3 drugs will no longer be covered. If HCV RNA is undetectable, triple therapy with boceprevir + P + R will be covered through week 36.

- If HCV RNA was detectable at week 8 but not at week 12, boceprevir + PR is covered to week 36 (for a total of 32 weeks of boceprevir).

6. Week 36, no further boceprevir will be covered. P+R is covered through week 48. After completion of triple therapy, no further boceprevir, peginterferon, or ribavirin will be covered.

Prior-relapse and partial-responder patients:

Notes:

"Prior-relapse" means a patient with an undetectable HCV RNA level at the end of previous treatment with peginterferon + ribavirin, without subsequent attainment of a sustained virologic response (SVR). A SVR is undetectable HCV RNA 6 months after the end of the previous P + R therapy.

"Non-responder" was defined in the trial as a patient with previous treatment with an interferon + ribavirin with a decrease in the HCV RNA level of at least 2 $\log_{10}$ IU/mL by week 12 but with a detectable HCV RNA level during the therapy period. (This definition is actually a partial responder; nonresponders (null responders) were not studied in trials. Null responders had LESS THAN a 2$\log_{10}$ decrease in HCV RNA at treatment week 12 during previous treatment.)

1. Week 1 through week 4, peginterferon with ribavirin alone is covered.

2. Week 4 (end of week), HCV RNA is measured. Regardless of the result, boceprevir is added to P + R beginning with week 5.
3. Week 8, HCV RNA is measured. Regardless of the results, boceprevir will be covered to continue with P + R at least until the week 12 HCV RNA measurement.
4. Week 12, HCV RNA is measured again.
   - If HCV RNA is 100 IU/mL or more, all HCV treatment is stopped. EBD will cover no more HCV treatment.
   - If HCV RNA was detectable at week 8 and not detectable at week 12, boceprevir (with P + R) will be covered through week 36 (pending week 24 futility rule). P + R will be covered through week 48.
   - If HCV RNA was UNdetectable at week 8 and week 12, boceprevir (with P + R) will be covered through week 36 (pending week 24 futility rule). No further P + R will be covered.
5. Week 24, HCV RNA is measured again. If HCV RNA is detectable ($\geq$9.3 IU/mL), all 3 drugs will no longer be covered.

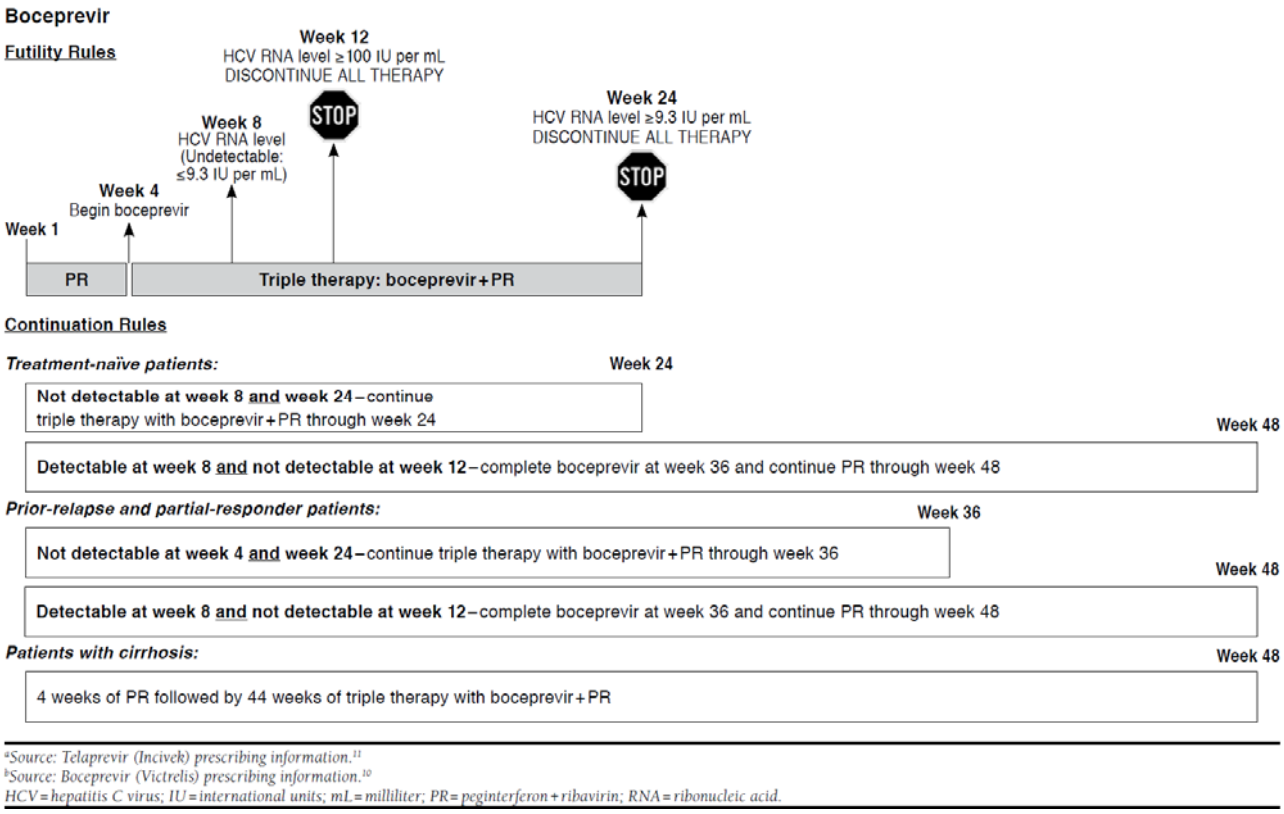
Previous Non-Responder patients (these patients were not studied in trials):

Note:

Non-responders (null responders) had **LESS THAN** a $2\log_{10}$ decrease in HCV RNA at treatment week 12 during previous treatment with an interferon + ribavirin.)

1. Week 1 through week 4 if P + R alone.
2. Week 5, boceprevir is added to P + R beginning with week 5.
3. Week 12, HCV RNA is measured again. If HCV RNA is 100 IU/mL or more, all HCV treatment is stopped. EBD will cover no more HCV treatment.
4. Week 24, HCV RNA is measured again. If HCV RNA is detectable ($\geq$9.3 IU/mL), all 3 drugs will no longer be covered. If not, treatment with triple therapy (B + P + R) will be covered through week 44, then no further boceprevir would be covered. P + R would be covered until week 48.

Following completion of treatment with triple therapy, no further therapy will be covered by EBD.



[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.

Genotypes 2 & 3:

Peginterferon alfa-2a plus low dose ribavirin 800mg will be covered for 24 weeks.

Genotype 4:

Combination peginterferon plus weight-based ribavirin will be covered for 48 weeks.

Genotype 6:

Peginterferon alfa plus ribavirin for 48 weeks will be covered.

References:

1. Bacon BR, Gordon SC, Lawitz E, Marcellin P, et al. Boceprevir for previously treated chronic HCV genotype 1 infection. N Engl J Med. 2011;364:1207-17.
2. Tungol A, Rademacher K, Schafer JA. Formulary management of the protease inhibitors boceprevir and telaprevir for chronic hepatitis C virus. J manag Care Pharm. 2011;17(9):685-94.
3. Poordad F, McCone J, Bacon BR, Bruno S, et al. Boceprevir for untreated chronic HCV genotype 1 infection. N Engl J Med. 2011;364:1195-206.
4. Ghany MG, Nelson DR, Strader DB, Thomas DL, Seeff LB. An update on treatment of genotype 1 chronic hepatitis C visus infection: 2011 practice guideline by the American association for the study of liver diseases. Hepatology. 2011;54(4):1433-1444.
5. Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update. AASLD Practice Guidelines. Hepatology. 2009; 49(4):1335-1374.

Use of Atypical Antipsychotics as Adjuncts in Depression and Autistic Disorder

Jordan Brazeal, Pharm.D.
Evidence-based Medicine Pharmacy Practice Resident

Adjunctive Treatment to Major Depressive Disorder (MDD)

Several second generation antipsychotics (SGAs) have been evaluated for use as adjunctive therapy to antidepressant drugs in the treatment of MDD. While the data support the efficacy of aripiprazole in treatment-resistant MDD (defined as unresponsive to standard therapy [i.e. antidepressants and/or psychotherapy] for 4-8 weeks[4]), the data also support the efficacy of a number of other SGAs, including quetiapine (both immediate- and extended-release formulations), olanzapine, and risperidone, for the same disorder. While reviewing, it became apparent that aripiprazole and risperidone have very similar efficacy findings in the primary endpoint, response to therapy, when evaluated on a number-needed-to-treat basis[1]. Aripiprazole does boast a greater reduction in the Montgomery-Åsberg Depression Scale (MADRS), lowering the score, on average, by 3.04 points. Risperidone, by comparison, lowers the score by 1.85 points[1]. (It should be duly noted that the MADRS is a max 60-points scale; thus, it can be argued that a difference of 1.19 points is not clinically significant.) Aripiprazole, in the trials, is associated with the troubling adverse effect of akathisia, increasing the rate by 18% over placebo, or a number-needed-to-harm of 6 patients; this side effect was not observed with risperidone[5]. Moreover, in other secondary endpoints, including remission, leaving the study early, suicide, suicide attempts, suicidal ideation, weight gain, and sedation, aripiprazole and risperidone are not clinically significantly different (although the data tend to slightly favor risperidone, rather than aripiprazole)[1]. Unfortunately, no head-to-head studies comparing the efficacy of risperidone and aripiprazole as adjunctive treatments in MDD have made their way to the mainstream of medical literature, to date.

References:

1. Chen J, et al. Second-generation antipsychotics in major depressive disorder: update and clinical perspective. *Current Opinions in Psychiatry.* 2011;24:10-17.
2. Komossa K, et al. Second-generation antipsychotics for major depressive disorder and dysthymia (Review). *Cochrane Database of Systematic Reviews.* 2010;12:1-222.
3. Lexicomp online. Aripiprazole. Accessed 7/3/12.
4. McDonagh M et al. Drug Effectiveness Review Project: Drug Class Review, Atypical Antipsychotic Drugs, Final Update 3 Report; Oregon Health & Science University: July 2010
5. Gelenberg A et al. Practice Guideline for the Treatment of Patients with Major Depressive Disorder. American Psychiatric Association Online (www.psychiatryonline.com). Accessed 7/3/12.

Irritability Associated with Autistic Disorder

The use of SGAs for alleviation of irritability in children with autistic disorders has been explored through various clinical trials, although only aripiprazole, risperidone, and olanzapine have been subject to more rigorous studies. Of those, risperidone and aripiprazole have been involved in trials with larger patient populations; olanzapine has been evaluated in one randomized, controlled trial with 12 subjects[3]. To date, there are no head-to-head comparisons involving SGAs in this usage, nor is there a published systematic review or meta-analysis. Thus, in order to establish preference for one SGA over another, indirect comparison involving careful evaluation of available literature has been utilized. Limiting search criteria to randomized, controlled trials evaluating the use of aripiprazole or risperidone in autistic disorder yielded 25 trials: 2 for aripiprazole and 23 for risperidone. Of these, both aripiprazole trials and 3 risperidone trials were selected for indirect analysis. Characteristics of the selected trials are summarized in the table below (page 4).

On a number-needed-to-treat basis, risperidone and aripiprazole appear to be equivocally efficacious in this population. Although response was not set forth in the trials as a primary efficacy outcome, it nevertheless assists in demonstrating the similitude between the two SGAs. The primary outcome, the change in baseline to endpoint of the ABC-I (not recorded in the table above), was also similar across the trials. The results, reported as change in score from baseline to week 8 (endpoint), are as follows (treatment, placebo): McCracken et al. (-14.9, -3.6); Pandina et al. (-13.4, -7.2); Shea et al. (-12.1, -6.5); Marcus et al. (5 mg/day, -12.4; 10 mg/day, -13.2; 15 mg/day, -14.4; placebo, -8.4); and Owen et al. (-12.9, -5.0). Thus, on average (weighted per subject size), risperidone differed from placebo in changes from baseline of ABC-I ratings by –8.1; aripiprazole by –5.59. The ABC-I is a caregiver-rated, 15-item scale, with each item rated 0-3; thus, the maximum (worst) rating is 45, and the lowest (best) is, of course, zero[2] (Table 2 below). It seems unlikely that a caregiver would notice an improvement of 2.5 points on this scale (the difference of the averages of risperidone and aripiprazole), and furthermore, it is not appropriate to conclude that risperidone is superior to aripiprazole based on the indirect comparisons presented here. What can be concluded, however, is that risperidone and aripiprazole are, at least in this population, therapeutically equivalent.

This leads to closer consideration of the drugs' side effect profiles. As recorded in the table above, both risperidone and aripiprazole have similar adverse effects, with somnolence, increased appetite, and weight gain being the most commonly reported. Based on weighted average, risperidone was associated with an increase of 2.63 kg over 8 weeks, and aripiprazole 1.5 kg over 8 weeks. Long-term data available for risperidone indicate an increase of 5.1 kg over 6 months[1]; long-term studies have not been performed on aripiprazole. Perhaps the most troubling adverse effects observed in the trials occurred with aripiprazole: extrapyramidal symptoms (including akathisia) and vomiting. These adverse events led to discontinuation of treatment in 12.7% of aripiprazole-treated patients in Marcus et al., and 10.6% of patients in Owen, et al. No patients withdrew from any of the risperidone trials due solely to adverse events. Thus, it appears that risperidone may be better tolerated than aripiprazole in this patient population.

It should also be noted that the population studied in either aripiprazole trial was substantially narrower than those studied in the risperidone trials. Although trials with either drug included patients with autistic disorder, the aripiprazole trials excluded patients with other autism spectrum disorders, including those represented in the risperidone trials: pervasive development disorder, child disintegrative disorder, etc. While it may be illogical to assume that aripiprazole is not effective in such populations, it is certainly illogical to discount the fact that risperidone <u>has</u> been shown to be effective in those populations. Moreover, aripiprazole, as mentioned above, has not been evaluated long-term (i.e. longer than 8 weeks) as has risperidone. Thus, it is not known whether the improvement in irritability seen with aripiprazole will be sustained. In a continuation trial evaluating the long-

term use (6 months) of risperidone, it was shown that patients on risperidone suffer significantly less relapse rates than those without treatment; again, these data are not available for aripiprazole.

Thus, if a SGA is elected for alleviation of irritability associated with autistic disorder, the recommendation is to use risperidone to the exclusion of aripiprazole, based on the evidence submitted above. Risperidone has less severe side effects, competitive efficacy, and more data available than aripiprazole.

Consider the odds: Why bet on a horse you've never seen race when the Triple Crown champion is racing, too?

Table 2. The Aberrant Behavior Checklist.

TABLE 3. Aberrant Behavior Checklist Community Scale Irritability Subscale Items[a]

Item Number	Item
2	Injures self . . .
4	Aggressive to other . . .
8	Screams . . .
10	Temper tantrums . . .
14	Irritable . . .
19	Yells . . .
25	Depressed . . .
29	Demands . . .
34	Cries over minor annoyances . . .
36	Mood changes . . .
41	Cries and screams . . .
47	Stamps feet or bangs . . .
50	Deliberately hurts himself/herself
52	Does physical violence . . .
57	Has temper outbursts . . .

[a]Each rated 0–3

References:

1. Aman M et al. Risperidone Treatment of Autistic Disorder: Longer-Term Benefits and Blinded Discontinuation After 6 Months. *Am J Psychiatry*. 2005;162(7):1361-69
2. Hellings J et al. The Overt Aggression Scale for Rating Aggression in Outpatient Youth With Autistic Disorder: Preliminary Findings. *The Journal of Neuropsychiatry and Clinical Neurosciences.* 2005;17:29-35
3. Malone, R and A Waheed. The Role of Antipsychotics in the Management of Behavioural Symptoms in Children and Adolescents with Autism. *Drugs.* 2009;69(5):535-48
4. Marcus R et al. A Placebo-Controlled, Fixed-Dose Study of Aripiprazole in Children and Adolescents With Irritability Associated with Autistic Disorder. *J Am Acad Child Adolesc Psychiatry.* 2009;48(11):1110-19
5. McCracken J et al. Risperidone in Children with Autism and Serious Behavioral Problems. *N Engl J Med*. 2002;347(5):314-321
6. Owen R et al. Aripiprazole in the Treatment of Irritability in Children and Adolescents With Autistic Disorder. *Pediatrics.* 2009;124(6):1533-40
7. Pandina G et al. Risperidone Improves Behavioral Symptoms in Children with Autism in a Randomized, Double-Blind, Placebo-Controlled Trial. *J Autism Dev Disord.* 2007;37:367-373
8. Shea S et al. Risperidone in the Treatment of Disruptive Behavioral Symptoms in Children With Autistic and Other Pervasive Development Disorders. *Pediatrics.* 2004;114(5):e634-41

Study (year)	Drug	Design	Duration	No. of pts	Age (yrs)	Inclusion criteria	Exclusion criteria	Dosing	Primary outcome measure	Definition of response	NNT	Common adverse effects
McCracken et al. (2002)	Risperidone	DB, PC	8 weeks	101	5-17 yrs mean: 8.8	ASD (DSM-IV-TR) with tantrums, aggression, self-injurious behavior, or combination of these	Serious medical disorders, "other psychiatric disorders requiring medication"	Initial: 0.25-0.5 mg/hs Titrate: 0.5 mg/day Max: 2.5-3.5 mg/day mg/hs	ABC-I mean change from BL to EP	≥25% ↓ in ABC-I @ week 8	1.8	Somnolence, ↑ appetite, weight gain, fatigue, drooling, dizziness
Pandina et al. (2006)	Risperidone	DB, PC	8 weeks	55	5-12 yrs P: 7.1 R: 7.4	ASD (DSM-IV-TR) + CARS score ≥30	SZX, other psychotic d/o, seizure d/o	Initial: 0.01 mg/kg/day Titrate: 0.02 mg/kg/day Max: 0.06 mg/kg/day	ABC-I mean change from BL to EP	≥25% ↓ in ABC-I + CGI-I ≤2 by week 8	2.7	Somnolence, URI, rhinitis, fever, ↑ saliva, ↑ appetite
Shea et al. (2004)	Risperidone	DB, PC	8 weeks	79	5-12 yrs P: 7.3 R: 7.6	PDD (DSM-IV-TR) + CARS score ≥30	SZX, other psychotic d/o, seizure d/o	Initial: 0.01 mg/kg/day Titrate: 0.02 mg/kg/day Max: 0.06 mg/kg/day	ABC-I mean change from BL to EP	≥50% ↓ in 2/5 ABC subscales w/out >10% ↑ in others @ week 8	3.4	Somnolence, ↑ appetite, weight gain
Marcus et al. (2009)	Aripiprazole	DB, PC	8 weeks	218	6-17 yrs P: 10.2 A_5: 9.0 A_{10}: 10.0 A_{15}: 9.5	Autistic disorder (DSM-IV-TR) with tantrums, aggression, self-injurious behavior, or combination of these	BPD, psychosis, SZX, MDD, other ASD (including PDD-NOS, Asperger, Rett or CDD)	Initial: 2 mg/day Target: 5, 10, 15 mg/day	ABC-I mean change from BL to EP	≥25% ↓ in ABC-I + CGI-I ≤2 by week 8	NNT_5=4.7 NNT_{10}=6.9 NNT_{15}=5.5	Sedation, tremor, drooling, EPS events, vomiting, fatigue, ↑ appetite
Owen et al. (2009)	Aripiprazole	DB, PC	8 weeks	98	6-17 yrs P: 8.8 A: 5.7	Autistic disorder (DSM-IV-TR) with tantrums, aggression, self-injurious behavior, or combination of these	BPD, psychosis, SZX, MDD, other ASD (including PDD-NOS, Asperger, Rett or CDD)	Initial: 2 mg/day Target: 5, 10, 15 mg/day	ABC-I mean change from BL to EP	≥25% ↓ in ABC-I + CGI-I ≤2 by week 8	2.6	Somnolence, vomiting, fatigue, ↑ appetite, any EPS event

DB = double blind; PC = placebo-controlled; ASD = autism spectrum disorder, DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision; ABC-I = Aberrant Behavior Checklist Irritability scale; CARS = Childhood Autism Rating Scale; CGI-I = Clinical Global Impressions Improvement rating; SZX = schizophrenia; BPD = bipolar disorder; MDD = major depressive disorder; PDD = pervasive development disorder; CDD = childhood disintegrative disorder; BL = baseline; EP = endpoint; NNT = number needed to treat

SOA DUEC JUNE 2012 - SEP 2012

Brand NAME	Generic Name	DOSE/INDICATION	SIMILAR THERAPIES ON FORMULARY/ TIER/AWP	Notes	DUEC Vote	IB Vote
Viokace	Pancrealipase (pancrelipase 10440-39150-39150 and 20880-78300-78300	Tx of cystic fibrosis, pancreatectomy and pancreatic insufficiency		Place where the others are. They are all about the same cost with small, varying degrees of ratios of lipase:amylase.		
Pertzye	Pancrealipase (pancrelipase 10440-39150-39150 and 20880-78300-78300	Treatment of pancreatic insufficiency due to cystic fibrosis or other conditions	Creon, Zenpep, Pancreaze, Viokace	Place where the others are. They are all about the same cost with small, varying degrees of ratios of lipase:amylase.		
Butrans	buprenorphine 5mcg/h, 10mcg/h, 20mcg/h transdermal patch	pain, mod-severe chronic	Set to reject in 2011. notes on review could not be found.	I never reviewed this before now. Buprenorphine is agonist/antagonist; can precipitate opiate w/d in opiate consumers. Labeled use: Management of moderate-to-severe chronic pain in patients requiring an around-the-clock opioid analgesic for an extended period of time. 1 patch q7d. $380/4 of 20mcg/h.(drugstore.com) Fentanyl is agonist. Fentanyl patch is generic 100mcg/h is $216/5, must be changed q72h.		
Codeine Sulf Soln 30mg/5ml	codeine sulfate solution	Mild to moderate pain	Codeine 30 mg tab	T1; or EXCLUDE. This is the only codeine sulfate solution in Facts & Comparisons. The tablets (15mg, 30mg, 50mg) can be crushed.		
Neupro Dis	rotigotine TD patch	Transdermal system for tx of Parkinson's and restless leg syndrome	Ropinirole extended release oral 4mg/day to 24mg/day	REC: exclude at this time. Trial of rotigotine vs ropinirole in early PD showed rotigotine missed the noninferiority mark. Giladi N, et al. Rotigotine TD patch in early PD: a R, DB, Controlled study vs placebo and ropinirole. Movement Disorders. 2007;22(16):2398-2404. Another trial showed rotigotine was ALSO NOT noninferior to pramipexole in advanced PD.		

Kyprolis Soln	carfilzomib 60mg in a single use vial.	Treatment of multiple myeloma who have received at least two prior therapies including bortezomid and an immunomodulator and have demonstrated disease progression on or within 60 days of completion of the last therapy		EXCLUDE. NCCN: Cat 1: based on high-level evidence; uniform NCCN consensus the intervention is appropriate. Cat 2A: based on lower-level evidence; uniform NCCN consensus the intervention is appropriate. Cat 2B: lower level evidence; consensus is not uniform. Cat 3: any level of evidence; major NCCN disagreement. Carfilzomib is 2A recommended by NCCN.org for MM that has been treated by 2 prior therapies including bortezomib and an immunomodulatory agent & have demonstrated dz progression on or w/in 60 d of completion of last tx. The peer-reviewed trial (Blood. 2012;119(24):5661-5670) was in bortezomib-naive patients. The ORR was 52.2% in pts who received the higher dose (20mg/m2 once, then 27mg/m2 subsequently). Weirdly, the NCCN.org placement of carfilzomib is in pts who are NOT bortezomib-naive per the PI. The PI cites a trial done in 266 refractory MM patients with the results: The primary endpoint was the overall response rate (ORR) as determined by Independent Review Committee assessment using International Myeloma Working Group criteria. The ORR (stringent complete response [sCR] + complete response [CR] + very good partial response [VGPR] + partial response [PR]) was **22.9%** (95% CI: 18.0, 28.5) (N = 266). Everyone received the drug (NO CONTROL GROUP). The median duration of response was 7.8 months (95% CI: 5.6, 9.2). Dose is max of 60mg per dose, 6 doses per month until dz progression.		

Myrbetriq	mirabegron 25 and 50mg	For treatment of overactive bladder	First in class with a different side effect profile than the other agents for treatment of overactive bladder such as oxybutynin, Detrol LA, Vesicare, etc	EXCLUDE. A beta-3 adrenergic agonist, in the bladder causing relaxation of detrusor smooth muscle during urine storage phase, thus increasing bladder capacity; onset w/in 8 weeks, t 1/2=50h. HTN in >10%. Not recommended in ESRD or severe hepatic impairment. PI states a clinical trial was done (Trial 1) for myrbetriq vs active control but shows results only vs placebo. Omission of any info on myrbetriq vs active control leads one to believe there was no difference?? Vs placebo, there was a statistically significant difference of -0.41 incontinence episodes in 24h, -0.6 episodes of urinations/24h, and an increase in urine volume of 11.9mL per urination.		
Stribild tabs	Elvitegravir Cobicistat Emtricitamine tenofovir	Once daily, oral 4-in-1 combination antiretrovial for tx of HIV. Complete regimen and should not be administered with other antiretroviral for HIV	NA	**T3 with PA**. If can be automated, we should preclude other HAART to be used simultaneously and place a QL of 31/31 days.Contraindications: other HAART tx, alfuzosin, ergot derivatives, lovastatin, midazolam, pimozide, rifampin, sildenafil for PAH, simvastatin, St. John's wort, triazolam.		
Tudorza Pressair Inhaler	aclidinium	Long-term maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema	Atrovent, Spiriva, ipratropium	400 mcg (1 inhalation) twice daily. One HTH trial with tiotropium. Not different. Cheaper than spiriva but Tudorza is BID; Spiriva is QD.		

Zytiga	Abiraterone	prostate cancer		10/4/2011: I recommended T3PA. Drug has limited medical benefit. QL of 120/30d. No 90 day fills. Criteria are: 1. Dx of metastatic prostate cancer, 2. has the pt received prior chemotherapy containing docetaxel. N Engl J Med 2011; 364:1995-2005. 1000mg (250mg tablets) daily. Extended overall survival by 3.9m (14.8 vs 10.9m). No difference in withdrawal due to AE's. Noteworthy: all authors were heavily invested and conflicted, many being employees of the manufacturer. Trial was (abir + pred) vs (plac + pred). The plac group took their meds a median of only 4 months while the abir group took abir a median of 8 months. **The DUEC alternatively chose to exclude the drug.** **To date 10/29/12: no new trials are out on Zytiga.**		
Xtandi	Enzalutamide capsule 160mg once daily	For treatment of prostate cancer	NA	The median overall survival was 18.4 months (95% confidence interval [CI], 17.3 to not yet reached) in the enzalutamide group versus 13.6 months (95% CI, 11.3 to 15.8) in the placebo group (hazard ratio for death in the enzalutamide group, 0.63; 95% CI, 0.53 to 0.75; P<0.001). The superiority of enzalutamide over placebo was shown with respect to all secondary end points: the proportion of patients with a reduction in the prostate-specific antigen (PSA) level by 50% or more (54% vs. 2%, P<0.001), the soft-tissue response rate (29% vs. 4%, P<0.001), the quality-of-life response rate (43% vs. 18%, P<0.001), the time to PSA progression (8.3 vs. 3.0 months; hazard ratio, 0.25; P<0.001), radiographic progression-free survival (8.3 vs. 2.9 months; hazard ratio, 0.40; P<0.001), and the time to the first skeletal-related event (16.7 vs. 13.3 months; hazard ratio, 0.69; P<0.001). Rates of fatigue, diarrhea, and hot flashes were higher in the enzalutamide group. Seizures were reported in five patients (0.6%) receiving enzalutamide. (NEJM 2012 Increased Survival with Enzalutamide in Prostate Cancer after CTX). **T3 PA: Criteria: 1. Dx of prostate CA, 2. Castrate levels of testosterone (<50ng/dL), 3. Previous tx with docetaxel, now with progressive disease. 4. ECOG performance level of 0-2 (although ECOG 2 pts did not meet statistical significance,the HR was 0.65 with a trend toward the upper 95% CI at 1.07).**		

Isentress chw 25 and 100mg	raltegravir	For treatment of HIV infection	Plan currently covers other oral form of Isentress with contigent therapy of another antiretroviral within past 30 days.	Line extension. Currently (10/2/12) EBD PAs Isentress with the lone criterion: . "Will Isentress be used in combination with other HAART medications that are recommended by the current HIV guidelines?". I rec the same for this one.		
Lyrica Solution	Pregabalin solution 20mg/ml	For diabetic neuropathy, fibromyalgia, neuropathic pain, partial seizures, post herpetic neuralgia, spinal cord injury	Lyrica 100mg cap	DUEC should exclude this or consider cost in making this decision. It is $0.81 (WAC) and $0.97 (AWP) per mL. May want to consider allowing only those without other tablets/capsules have it. Also, can open capsules.		
Binosto	Alendronate effervescent tab 70mg	New formulation of alendronate(Fosamax) in effervescent tab for osteoporosis, osteoporis prophylaxis, Paget's disease	Alendronate sodium oral tablet weekly	Exclude due to dosage form unnecessary.		
Rayos	delayed release prednisone 1mg - 5 mg	Oral corticosteroid	Prednisone 5mg tabs	Exclude due to underappreciated need for delayed release prednisone.		