

Preferred Drug List Advisory Committee Meeting  
Wednesday, October 15, 2008  
Cheyenne, Wyoming  
10 a.m. – 2 p.m.

Members present: Marion Smith, W. Joseph Horam, Whitney Buckley, Scott Johnston, Dean Winsch, Bill Harrison, Kevin Robinett

Members excused: Christie Graham, Renee Gamino

Ex-officio: Antoinette Brown, Donna Artery, Roxanne Homar

Guests: Laurie Roscoe (GHS), Brenda Stout (WDH), Steve Babineaux (Eli Lilly), Tim Hynek (Eli Lilly), Randy Hodgdon (GSK), Tim Haase (GSK), Carmen Pyper (Pfizer), Jay Liggett (Pfizer), Sandy Divks (OMJSA), Michael Dunn (Pfizer), Lyle Laird (BMS), Terri Craig (Pfizer), Barbara Boner (Novartis), Stan Rane (Novartis), John Stockton (Genentech), Joe Riedl (Boehringer Ingelheim), Janice Sprout (AstraZeneca), Todd Rodelever (Pfizer), Trish McDaid-O'Neil (AstraZeneca), Linda Craig (AstraZeneca), Tracy Brown (AstraZeneca), Randy Owens (BMS), David Block (Shire), Anthony DeBons (Shire).

Dr. Smith called the meeting to order at 10:05 a.m.

Review of Minutes

The minutes of the June 4, 2008 meeting were approved with amendments to spelling of aspirin.

The Committee discussed potential meeting dates for 2009. Wednesdays seem to have conflicts with other standing meetings, so will change to Tuesdays for 2009.

Atypical Antipsychotics

Marian McDonagh, Pharm.D., presented the Atypical Antipsychotic DERP report. Copies of the slides are available upon request.

*Public Comment:*

Jamie Street (Astra Zeneca) presented comments on Seroquel. Seroquel XR was recently approved for bipolar depression, mania and mixed episodes and bipolar maintenance. There is now a 50 mg strength. This is the only drug with the broad bipolar indications. Astra Zeneca has submitted applications for approval for major depressive disorder (MDD) and general anxiety disorder (GAD). Dr. Street urged the Committee to allow Seroquel and Seroquel XR on the preferred drug list.

Dr. Robinett asked about the dosing for MDD and GAD. The final dosing is dependent on FDA approval. He then asked what the logic is for these indications. Seroquel hits the neuroepinephrine transporter providing it with antidepressant and anti-anxiety effects. It is the only medication in this class with this mechanism of action. The move to the XR formulation is due to adherence issues with twice daily Seroquel. The XR formulation appears to have better adherence. The patent for Seroquel will expire in 2012 and the XR formulation in 2017.

Terri Craig (Pfizer) presented an article titled "Principles of Antipsychotic Prescribing for Policy Makers, Circa 2008. Translating Knowledge to Promote Individualized Treatment" published in the Schizophrenia Bulletin on April 2, 2008. This is a statement drafted by the National Association of State Mental Health Program Directors Medical Directors. Four recommendations are made to ensure appropriate access. Terri also presented the "Consensus Development Conference on Atypical Antipsychotics and obesity and diabetes" published in Diabetes Care in February 2004.

Steven Babineaux (Lilly) provided comments regarding Zyprexa. Retrospective observational research shows a measurable difference in effectiveness. There are better use patterns with Zyprexa and those on Zyprexa are more likely to be on monotherapy than patients on Seroquel or Risperdal. The time to discontinuation is longer with Zyprexa than others. Early data from the EUFAST study shows that there is less discontinuation with Zyprexa in first-episode schizophrenia, which was excluded from the CATIE trials.

The Committee questioned the difference between consensus statements which indicate that clozapine has the worst effects on weight and metabolic factors while DERP shows that olanzapine is actually worse. Marian McDonagh explained that it is a difference in the analysis that is done. DERP looks only at direct comparisons of the drugs. To say which is actually worse is a murky area.

Sandra Dirks (Ortho McNeil Janssen) provided comments. She often hears the terms lack of evidence, not enough evidence and conflicting evidence during reviews of this drug class. She is concerned about the weight given to the CATIE trial. Abilify was very new during the trials and Invega was not yet on the market. She encourages the Committee to consider the Schizophrenia Bulletin article provided by Pfizer. Invega has a unique delivery system and advantage of being a major metabolite. She reminded the Committee that 74% of patients changed drugs in the CATIE trial. Limiting access may result in adverse outcomes for patients. Risperdal Consta increases adherence. The data is all retrospective but shows decreased rates of hospitalization and relapse.

Lyle Laird (Bristol Myers Squibb) provided comments on Abilify. In the spirit of evidence based policy there are three key areas for Abilify. Abilify has 13 unique indications including schizophrenia, bipolar disorder, major depressive disorder, and acute agitation. There is extensive efficacy and safety data in pediatrics now. It is safe and well-tolerated across the full dosage range. There are no clinically significant changes to weight and metabolic factors compared to placebo. Abilify has a unique

mechanism of action related to the others as it has antagonist as well as partial agonist properties. It is not approved for use in elderly patients with dementia psychosis. All of the drugs in this class have the same black box warning for this condition. Abilify also carries the black box for increased risk of suicidality due to its indication for MDD. Lyle requested that the Committee allow open status on the formulary.

Anna Edwards (NAMI, WY) provided comments. She opposes the proposal to decrease access to mental health agents by including them on a PDL. She applauds and understands the need to decrease costs; however this could lead to serious unintended consequences. Open access to these drugs is critical to recovery. Without them, patients are at risk for suicide, hospitalization, unemployment, homelessness and incarceration. There is no one size fits all approach. Everyone has unique responses to psychiatric medications. We need more options, not fewer. Limiting access to these drugs will increase overall medical costs. Medical costs associated with limiting the number of drugs in one state was 17 times higher than the actual drug costs. Sometimes cost cannot be measured in money, but must be measured in contribution to society. Restricting low-income access to these drugs will decrease recovery. "Medication delayed is tantamount to medication denied."

Deb Hinkel (NAMI, Laramie) has a child with schizophrenia. He has had five hospitalizations and spent seven months in a New Jersey treatment facility. Studies don't consider anything but the medications. Patients must have open access and the ability to work with providers to see what really works. She fears that changing her son's medications will lead to additional hospitalizations. It is a "crap shoot" and it doesn't make sense to have a PDL for mental illness. She asked the Committee to grandfather all existing patients.

The Committee asked if she saw temporary success with her son over the course of changing medications or if it was constant failure. She indicated that he did very well on Haldol to start, but they were concerned about adverse effects. They tried Seroquel for quite some time. Her son has had lots of head injuries which complicates things.

Roxanne provided some clarification indicating that the Department is very early in the process of reviewing this class. This is, in fact, the very first step that is taken. The Department takes it very seriously. The primary concern is quality patient care. If a PDL were to be implemented for this class, all existing patients would absolutely be grandfathered. Those stabilized on current medications would not be required to change!

Becky Foster (NAMI, Casper) also has a son with schizophrenia. He has made several attempts on her life in the past, but now, due to his medications, the house is calm. They have found ways to manage his illness and she would hate to lose that for him and herself. He would most likely end up in jail and others would also be in danger. She is glad to hear about grandfathering.

Dr. Brent Sherard thanked the speakers. He hears what they are saying loud and clear. He spent many years as a primary care physician in Wheatland and still believes that first

and foremost is quality of patient care. He worries about Medicaid which comprises 12.5% of the Wyoming state budget. It is a very conservative program in terms of eligibility, however, medications are an optional service (it is not mandatory). We do need to make sure that we are as cost-effective in medication coverage as we can be. With the checks and balances that are in place, he does not believe that the Department has ever denied a medication when it is the only drug that will work for a patient. We need to educate recipients and providers in order to maintain the viability of Medicaid. It is not just about money, it is about quality of care.

Dr. Johnston mentioned that we see a lot of high dose usage in this class and asked if there was data on this. Extrapyramidal side effects increase as the dose increase so there is no advantage over the older typicals. Marian indicated that there may be some evidence, however, it would not have been included in the DERP report as the question was not asked. Dr. Johnston asked about use of multiple antipsychotics concurrently. This issue was not included in the DERP report. Marian does not believe there are a lot of studies in this area, but cannot comment on the data.

There was discussion of the QT prolongation seen with ziprasidone. The studies specifically looking at this effect usually do not meet inclusion criteria for the DERP report. However, in studies that were included, it was not significant. They all have the black box warning. Because this came from the FDA, it is not possible to review the data and determine how the analysis was done. The evidence is likely weighted towards the older typical drugs simply due to the amount of time on the market.

*Committee Discussion:*

Safety:

Evidence of increased mortality when used for controlling behavior in elderly patients with Alzheimers.

Weight gain liability is a concern. From a side effect standpoint, drugs with higher rates of weight gain are not as safe. Clozapine and olanzapine have highest rates of weight gain.

EPS side effects: Risperdal is biggest culprit, then Abilify and ziprasidone, Seroquel and olanzapine are least. Propensity of a drug to cause EPS may relate to eventual development of tardive dyskinesia.

QTc effects of ziprasidone are a risk. Black box warning includes indications that are contraindicated. Probably overstated. Bigger culprits were Mellaril and Haldol. Cardiac deaths were not recognized with use of these drugs.

Agranulocytosis is an obvious safety issue with Clozaril. Also cardiomyopathy and seizure risk.

Increased prolactin levels with risperidone and paliperidone (higher than with other drugs). Long-term outcomes are unknown.

Efficacy:

In dementia, there is no clear evidence of benefit in controlling behavior. Clearly is risk.

Evidence regarding differences in efficacy is inconsistent.

Number of FDA indications does not necessarily correlate well to efficacy.

Atypical drugs are easier to tolerate than older, typical agents. They are better than older, typical agents in cognitive and emotional aspects.

Clozapine appears to be more effective than others, however is only used in a specific subset of patients.

Risperidone and olanzapine have been studied the most in the pediatric (school-aged) population.

Clinical experience:

Support the use of atypical antipsychotics in pediatrics for management of autism, behavior disturbance, childhood mood disorder and bipolar.

The effectiveness of multiple antipsychotics vs. single agents is unknown.

There are various situations in which the range of atypical antipsychotic medications can be reasonable first or eventual options.

Unbiased provider education on these agents is an important aspect of this process.

Take in to consideration recommendations published in the Schizophrenia bulletin.

The discussion then turned to provider education. Laurie Roscoe (GHS) commented that in her experience with other Medicaid programs, provider education is key. This can be accomplished through academic detailing and other forms of provider communication. Other states have found a recommended drug list (as opposed to a black and white PDL) to be effective. The key is to identify drugs that are similar. Data analysis to identify outliers for high doses, multiple agents, etc can be done for further provider education. States that do manage the class with a PDL require a minimum of a 30 day trial.

The recommendations listed above were moved and seconded with all in favor.

ADHD Medications

Marian McDonagh presented the DERP report on the ADHD medications. Slides are available upon request.

*Public Comment:*

Anthony DeLeon (Shire) provided comments on Vyvanse. Vyvanse is an amino acid prodrug which uses natural biological mechanisms to break down. Adderall XR was not lasting long enough. Vyvanse provides more consistent duration and symptom improvement (12 hours). There is also less pharmacokinetic variability with Vyvanse.

Stan Rane (Novartis) provided comments for Focalin XR. This drug can be used for ADHD across the full spectrum (for all ages). It has a 50/50 release mechanism using an enteric coated bead system. The capsule can be opened and mixed with food. Onset of action occurs in about one hour.

Steven Babineaux (Lilly) presented comments on Strattera. Strattera is non-controlled. It is the only medication approved for ADHD maintenance treatment in children and adolescents. Not all ADHD patients are the same and this can impact treatment selection. Comorbid anxiety and tics are not contraindicated with Strattera as with the stimulants. Strattera is uniquely suited for patients with comorbid substance abuse and diversion problems. It does carry a black box warning for risk of suicide and sudden death in those with cardiac abnormalities. In addition, it has a black box warning regarding severe liver injury. The ACAP recommends Strattera first-line in patients with substance abuse, anxiety or tics.

Sandra Dirks (Ortho McNeil Janssen) provided comments on Concerta. Concerta has the adult indication with doses up to 72 mg. It was studied up to 108 mg, however, the study group was not large enough for FDA approval. Studies comparing Concerta to Focalin show a difference in onset of action. This is expected as they have different release mechanisms. There is more effect early on with Focalin, but Concerta is superior to Focalin later in the day. These are not equivalent doses. It is different exposure at different times of the day. Concerta provides better coverage for homework and after-school coverage.

*Committee Discussion:*

Grandfather those currently on therapy

Long-acting available

Give a minimum of two weeks trial

To DUR: Limit maximum dose

Choices from dextroamphetamine SR (Adderall XR), methylphenidate SR (several choices – Concerta has diversion benefit, Metedate CD rapid acting and dosing choices,

Patch is unique for high dosing patient, Focalin XR less appetite suppression), non-stimulant/non-controlled. Lisdexamfetamine has a longer duration of action and seems to have less substance abuse potential.

Paucity of safety and efficacy data that shows any significant difference between drugs. Substance abuse/diversion is most common with methylphenidate and dextroamphetamine (immediate release). Known cardiovascular risk factors and concomitant medications which prolong the QT interval, should have EKG/cardiac monitoring. Black box warning for Strattera regarding suicidal risk.

Short-acting option available.

Sprinkle form option available.

To DUR: Recommend education on acceptable diagnosis process for kids and adults

There was a motion for approval of the recommendation which was seconded with all in favor.

There being no further business, Dr. Smith adjourned the meeting at 2:45 p.m.

Respectfully submitted,

Aimee Lewis, PharmD  
DUR Manager