Preferred Drug List Advisory Committee Meeting
Wednesday, June 4, 2008
Cheyenne, Wyoming
10 a.m. – 2 p.m.

Members present: Marion Smith, W. Joseph Horam, Whitney Buckley, Christie Graham, Scott Johnston

Members excused: Bill Harrison, Dean Winsch, Kevin Robinett, Renee Gamino

Ex-officio: Antoinette Brown, James Bush, Donna Artery

Guests: Dr. Laureen Biczak (GHS Data Management), Bert Jones (GSK), Marty Daniels (Merck), Greta Hoetzer (AZ), Al Roach (AZ), Steve Sckhaerrer (DSI), Jon Beaty (BI), Joann Ginal (BMS), Tony Molchan (Abbott), Jennifer Swiecki (Daiichi Sankyo), Barbara Boner (Novartis), Michele Pryeur (Novartis), Stephanie Davis (BMS), Pierre Thoumosin (Amgen), Tim Hynek (Lilly), Lori Howarth (Bayer), Layne Stewart (UW SOP), Lafe Ellerbeck (UW SOP), Janette Collins (UW SOP).

Dr. Smith called the meeting to order at 10:13 a.m.

Review of Minutes

The minutes of the October 10, 2007 meeting were approved as submitted.

Angiotensin Receptor Blockers (ARBs)

A previously recorded overview of the Drug Effectiveness Review Project, Angiotensin II Receptor Antagonists was provided by Susan Carson. Copies of the slides are available upon request.

Public Comment:

Greta Hoetzer (Astra Zeneca) gave an overview of Atacand (candesartan). This medication is approved for treatment of heart failure NYHA class II – IV. It has shown to decrease cardiovascular death and hospitalization for heart failure. It is also approved for hypertension alone or in combination with other antihypertensives. In the CHARM trials, Atacand was shown to decrease relative risk of cardiovascular death or hospitalization with a number needed to treat of 14 in CHARM alternative and 23 in the CHARM added trial. This is not a class effect. It is unique to Atacand. Losartan and valsartan were not able to show this difference, giving Atacand a benefit over the other drugs in the class.

Joann Ginal (Bristol Myers Squibb) gave an overview of Avapro (irbesartan). It is approved for hypertension alone or in combination with other antihypertensives and diabetic nephropathy. Avapro is one of only two drugs with this indication. Avapro is a

truly once daily drug. In the IDNT trial Avapro was better than placebo and amlodipine in time to ESRD, doubling of serum creatinine and death. Head to head trials were completed with losartan and irbesartan, showing a benefit for Avapro in both. Maximum effects may be seen as early as two weeks after initiation of therapy. Avalide (irbesartan/HCTZ) is uniquely approved for initial hypertension treatment in patients who are likely to need combination therapy (JNC-7 defined stage 2 hypertension).

John Beatty (Boehringer Ingelheim) gave an overview of Micardis (telmisartan). Micardis has the longest half-life of all drugs in the class. In MICAT II, hypertension was fully controlled in 70% of those with automatic measurement and 79% with physician visit measurement.

Michelle Puyeur (Novartis) gave an overview of Diovan (valsartan). Diovan is approved for hypertension alone or in combination with other antihypertensives and heart failure. It is the only drug indicated post-myocardial infarction and one of two approved for use in pediatrics aged 6 – 16. It is once daily for hypertension and twice daily for heart failure.

Jennifer Swiecki (Daiichi Sankyo) provided an overview of Benicar (olmesartan). This is also a once daily medication. It can be used for hypertension first line alone or in combination with other antihypertensives. Twice daily dosing of this medication has no clinical advantage. It is not metabolized through the cytochrome P-450 system, so has few drug-drug interactions.

Committee Discussion:

Efficacy:

Each medication has its own niche, although, it seems to be related to the way the studies were designed, specifically for each indication. It is difficult to determine if this is a class effect. The lack of head to head trials further limits ability to draw conclusions.

Recommendation: There is a paucity of evidence. The available evidence does not show a clear benefit for one ARB over another in regards to efficacy.

Safety:

Recommendation: There is a paucity of evidence showing a difference in safety in the general population.

Subpopulation:

Losartan and valsartan are the only drugs indicated in pediatrics (age 6 – 16). There is an increased cardiovascular risk for blacks with losartan. All have their niche indications.

There is no evidence that the others do not work, however physicians recognize the approved indications.

Recommendation: FDA approved indications (Table on page 5 of DERP report) should be made available either through preferred choices or through SmartPA. Evidence shows an increased cardiovascular risk for losartan in the black population. Losartan and Valsartan should be available for pediatrics aged 6 – 16.

Antiplatelets

A previously recorded overview of the Drug Effectiveness Review Project report on antiplatelet drugs was provided by Kim Peterson. Slides are available upon request.

The committee discussed the fact that in the CURE study low dose aspirin and higher dose aspiring showed a significant difference while 100 – 199 mg did not. This seems questionable. Dr. Johnston noted that the number needed to treat is in the 50 – 100 range and the number needed to harm is in the same range. Because these are so close, a large number of study subjects are needed to show a benefit. It is likely that there wasn't a sufficient number of subjects in this subgroup to show a significant difference.

Public comment:

John Beatty (Boehringer Ingelheim) provided an overview of Aggrenox (dipyridamole ER/aspirin). He indicated there was an error in the DERP presentation regarding the ESPS II and ESPRIT trials. The presentation indicated that the formulation of Aggrenox used in these two studies were not exactly like the formulation available in the US. Mr. Beatty indicated that in ESPRIT, 1.3% of patients were taking the exact formulation and most were taking low dose aspiring and dipyridamole ER separately. Aggrenox is indicated for decreasing the risk of recurrent stroke or TIA. Aggrenox has a 50% higher bioavailability than the immediate release formulations. Therefore, they are not interchangeable. Aggrenox shows a 22% decrease in relative risk of stroke compared to aspirin alone. It has similar bleeding rates as low dose aspirin.

Joann Ginal (Bristol Myers Squibb) gave an overview of Plavix (clopidogrel). There is some new information since the DERP report was released. Ms. Ginal indicated that 50 mg of aspiring may be subtherapeutic as 75 – 150 mg is the recommended range. Plavix is approved for patients who have had a recent myocardial infarction, stroke or who have peripheral artery disease. It has shown to decrease the rate of new myocardial infarction, stroke and other vascular death. It is contraindicated in patients with pathologic bleeding (bleeding ulcer, etc). TTP is reported rarely with clopidogrel use (4 cases/million or 11 cases/million patient-years). This is much less than seen with ticlopidine. The new guidelines recommend treatment with clopidogrel for up to one year following stent placement.

Committee Discussion:

Safety:

Use of a loading dose of ticlopidine vs. Plavix presents a major difference however, without a loading dose they do not appear that different. A loading dose is generally given in the hospital by a cardiologist who is aware of the risk and is probably not a huge consideration for this committee.

Clopidogrel is generally considered safer than ticlopidine due to lower risks of TTP and neutropenia. The trade-off is a higher risk of bleeding with clopidogrel.

Unlike the previous class, these drugs are all so very different. More efficacy results in more side effects.

Recommendation: If all risks are considered together, there is no evidence of a difference in safety. However, each has a unique safety profile that must be considered.

Efficacy:

There is some overlap in these drugs, but each is unique. It is difficult to separate out where one is better than the others. It is very dependent on the individual patient and diagnosis. The treatment guidelines recommend clopidogrel exclusively.

Recommendation: The evidence supports effectiveness of each antiplatelet agent for the FDA labeled indication.

Subgroups:

Recommendation: There is a paucity of evidence in subgroups.

<u>Long-acting opioids</u>

The previous recommendation was presented: The data available shows no significant differences in safety. Although there is no evidence, due to their long half-life, methadone and levorphanol may not be as safe in the elderly. The evidence does not show a significant difference in effectiveness. The committee would like access to a non-oral dosage form to be considered.

Dr. Johnston mentioned that this group of drugs was reviewed in the Workers' Compensation population. When you look at a conglomerate of all drugs, it appears that there is no benefit in any but methadone. It is difficult to look at this retrospectively, however. This may not mean that methadone works better, but that only a few physicians (experts) use methadone. Because these physicians are experts in this area, they may use the drugs more effectively, resulting in better outcomes.

An overview of the Drug Effectiveness Review Project report on long-acting opioids was provided by Roger Chou. Slides are available upon request.

Public Comment:

No public comment was provided.

Committee Discussion:

There is no need to change previous recommendation with the exception of the information on the elderly (because this population has moved from Medicaid to Medicare Part D). Oxymorphone seems to have the same disadvantage as Pallidone with respect to alcohol consumption resulting in immediate release of the medication.

Recommendation: Data available shows no difference in safety or effectiveness. The committee requests availability of a non-oral dosage form.

Triptans

The previous recommendation was presented: No difference in safety. Nasal forms cause stinging and higher withdrawal date. Slight benefit for rizatriptan in efficacy. Requested at least two agents to be preferred. Note longevity of experience and multiple dosage forms with sumatriptan.

There was no presentation of the report as the information has not changed since the last review by the Committee. The Department of Health has not moved forward with preferred drug selection up to now and is asking the Committee to review their previous recommendation and consider the new product Treximet.

Public Comment:

Karen Tiesen (Glaxo Smith Kline) gave an overview of Treximet. This product contains 85 mg of sumatriptan and 500 mg of naproxen sodium. The pathophysiology of migraines matches the tablet. The pharmacokinetics of this product results in a time to maximum concentration that is 30 minutes faster than Imitrex 100 mg. Naproxen release is delayed four hours after the sumatriptan which provides better coverage. Treximet's pivotal trial included six primary endpoints (others only had one). The product proved to be superior to either product alone and placebo for 2 hour and 24 hour pain relief, consistency of response and requirement for rescue medications. In the long-term safety trial, patients were able to take two doses, however 70% of patients took only one dose. Ms. Tiesen did not know what the statistic was for Imitrex 100 mg. This medication is ideal for the patient who does not receive complete relief from a triptan, who requires redosing or use of a rescue medication.

Committee Discussion:

The committee asked the presenter about the kinetics information. There is an article that was published in the Journal of Neurology with this information. The kinetics of the two drugs together in one tablet is different than when the two drugs are taken separately.

Safety:

Treximet appears to be as safe as the other triptans.

Efficacy:

Evidence shows similar efficacy (not head to head trials). There is no evidence regarding comparative efficacy of taking the two agents separately. It is probably appropriate for a person who fails a triptan, but not first-line. There seems to be potential, but there is not enough data at this time.

Treximet appears to be as effective as the other triptans.

Subgroups:

There is no evidence in subgroups.

These medications are indicated for adults aged 18 and up. Clinically, they are used in children over the age of 12. There is no preference for a specific product or dosage form for pediatrics.

Recommendation: Maintain previous recommendation with no changes.

The next meeting will be held October 15, 2008 in Cheyenne.

There being no further business, Dr. Smith adjourned the meeting at 1:40 p.m.

Respectfully submitted,

Aimee Lewis, PharmD
DUR Manager