

**Preferred Drug List Committee Meeting  
Meeting Minutes, Open Session  
June 2, 2010**

<p><b>Preferred Drug List Committee</b> Meeting Minutes, Open Session HP Enterprise Services Capital / Cedar Crest Room Topeka, KS</p>	<p><b>Members Present:</b> Michael Burke, M.D, Ph.D., Chair Kristen Fink, Pharm.D. Robert Haneke, Pharm.D. Kenneth Mishler, R.Ph., Pharm.D. Donna Sweet, M.D. Dennis D. Tietze, M.D.</p> <p><b>KHPA Staff Present:</b> LeAnn Bell, Pharm.D. Aimee Grubb, Recorder Shelly Liby Margaret Smith, M.D.</p> <p><b>EDS Staff Present:</b> Karen Kluczykowski, R.Ph. Lisa Todd, R.Ph.</p>	<p><b>Representatives:</b> Mike LaFond - Abbott Jerry Clewell - Abbott Jeff Knappen - Allergan Kim Lonergan - AstraZeneca Carol Curtis - AstraZeneca Jim Graves - BMS Jim Graham – Centocor OBI Patti Minear - Eli Lilly Kelli Frank - Eurand Darcy Gill - Genetech M. Patty Laster - Genetech Mark Veerman - J &amp; J Susan Zalenski – J &amp; J Barbara Belcher - Merck Todd Paulsen - Novo Nordisk Mary Shefchyk - Novo Nordisk Russ Wilson – OMJPI Phil King - Pfizer</p>
<b>TOPIC</b>	<b>DISCUSSION</b>	<b>DECISION AND/OR ACTION</b>
<p>I. Welcome and Announcements</p>	<p>Dr. Burke called the meeting to order at 10:02 am. Dr. Bell provided general parking instructions for Committee members and those members of the audience.</p>	
<p>II. Review and Approval of December 16, 2009 Minutes</p>	<p>The draft minutes from the December 16, 2009 meeting were reviewed. Dr. Burke requested that the draft minutes be amended to add the following statement at the beginning of the Targeted Immune Modulators (TIM) section: "... (See attached reference table designating first line and second line monotherapies and combination therapies status.)..."</p>	<p>Dr. Sweet moved to approve the minutes, with the additional amendment as requested by Dr. Burke.</p> <p>Dr. Mishler seconded the motion; motion carried with unanimous vote.</p>
<p>III. Ophthalmic Antihistamines/Mast Cell Stabilizers – New Class Review</p> <p>a. Public Comment</p> <p>b. Committee Discussion</p>	<p><b>Background: Antihistamine and mast cell stabilizer dual-action eye drops are among several medications used to treat allergic conjunctivitis/vernal conjunctivitis. Agents in this class include ketotifen (Alaway®, Refresh®, and Zaditor®), bepotastine (Bepreve®), epinastine (Elestat®), azelastine (Optivar®), and olopatidine (Pataday®, and Patanol®). Other agents used to treat allergic conjunctivitis/vernal conjunctivitis have different mechanisms of action, or are either an antihistamine or a mast cell stabilizer only, but not both.</b></p>	

	<p>Dr. Bell explained that this is a new class for review and the eight agents are a combination of antihistamines and mast cell stabilizers.</p> <p>Public Comment: None.</p> <p>Discussion: Dr. Burke referred to the reference table available in the committee members' meeting packets, noting that there was nothing provided in the handout materials that suggests superiority of one product over another. Dr. Mishler asked if over-the-counter (OTC) medications were included; and Dr Bell responded that OTCs may be included if they are cost-effective.</p>	<p>Dr. Haneke made motion that all eight combination drugs described were clinically equivalent.</p> <p>Dr. Fink seconded; motion carried with unanimous vote.</p>
<p>IV. Intranasal Antihistamines – New Class Review</p> <p>a. Public Comment</p> <p>b. Committee Discussion</p>	<p><b>Background: There are three medications in this class – olopatadine 0.60% (Patanase®), azelastine 0.10% (Astelin®), and azelastine 0.15% (Astepro®).</b></p> <p>Public Comment: None.</p> <p>Discussion: Dr. Burke stated that the Vermont review was done well and noted that the conclusion in the review was that all medications demonstrated similar effectiveness.</p>	<p>Dr. Sweet made motion that the three agents in this class were clinically equivalent.</p> <p>Dr. Mishler seconded; motion carried with unanimous vote.</p>
<p>V. Pancreatic Enzyme Replacement Product – New Class Review</p> <p>a. Public Comment</p> <p>b. Committee Discussion</p>	<p><b>Background: Although pancreatic enzyme replacement products (PEP) have been used for decades, they have only recently been approved by the FDA. In 2004 the FDA announced that to continue marketing them, all PEPs would have to be FDA approved by April 2008. This deadline was subsequently extended to April 2010. There are currently three PEP products approved by the FDA – Creon®, Zenpep®, and Pancreaze®. Per CMS guidance, state Medicaid agencies are no longer allowed to reimburse for non-FDA approved products.</b></p> <p>Public Comment: Jerry Clewell, Solvay/Abbott Laboratories - Creon® was the first enzyme replacement product to be FDA approved. The FDA has issued guidance regarding these products, advising that products are not interchangeable. The manufacturing process has been standardized to help patients and clinicians get started on this medication or to switch to different medications, and the predominant population served by these products are the cystic fibrosis population. This is a very fragile population so making changes in medication is challenging.</p> <p>Dr. Burke pointed out that the guidelines are similar in terms of units to be</p>	

	<p>given, starting dosage, etc., and asked for clarification on the products being "...not interchangeable..." Mr. Clewell responded that, since these are all animal extract products with each patient responding differently to the medication, there is no guarantee with switching to one form to another that the patient response will be the same.</p> <p>Discussion: Dr. Burke confirmed that the release characteristics are different among the different compounds. Dr. Haneke added that he wasn't sure the enzymes products have ever been standardized across the board and that he felt these products would be therapeutically equivalent but not bioequivalent. Dr. Sweet stated that her hospital has selected one brand only because of shelf life and felt too that these products are therapeutically equivalent but not bioequivalent.</p>	<p>Dr. Haneke made a motion that these three enzyme replacement products – all of which have been approved by the FDA - are therapeutically equivalent and can be placed on the PDL, but noted that there are differences in their bioequivalence.</p> <p>Dr. Sweet seconded the motion; it carried with unanimous vote.</p>
<p>VI. GLP-1 Agonists (Gliptins) – New Class Review</p> <p>a. Public Comment</p> <p>b. Committee Discussion</p>	<p><b>Background: There are two agents in this class. Exanatide (Byetta®) has been available since 2005. Liraglutide (Victoza®) was approved in January 2010. Both are Glucagon-Like Peptide-1 (GLP-1) receptor agonists that work by increasing insulin release in the presence of elevated glucose concentrations, decreasing glucagon secretion and delaying gastric emptying. The manufacturer of liraglutide completed a head-to-head trial against exanatide as well as an extension study of that trial.</b></p> <p>Dr. Bell advised these products were being presented as a potential new PDL class, there are two agents in this class serving the diabetic population, and that both agents have the same mechanism of action.</p> <p>Public Comment: Todd Paulsen, Novo Nordisk advised that liraglutide (Victoza®) has a Type II diabetes indication. He reviewed the key characteristics of this drug – extended half life of 13 hours, controls post-prandial blood glucose and fasting blood glucose, provided in a disposable flex-pen, and dosage can be given anytime throughout the day regardless of meals. There are two safety concerns. Pancreatitis is associated with this class of medications, albeit a very low possibility; and in early animal models with this drug, there was stimulation of C-cells in rats and mice which can lead to cancer in rats and mice, and therefore the medication labeling includes a contraindication for patients with a related history. Novo Nordisk recommends using metformin as first line agent and that Victoza® is recommended as second line.</p> <p>Dr. Sweet expressed concern with the increase in C-cells in animals and</p>	

asked if the black box warning was the same for both products and if not, why liraglutide has the black box warning where exanatide does not. Mr. Paulsen responded that exanatide does not have that safety issue but liraglutide does, and the reason was contributed to the extensive data shown while studying this product i.e. the longer period of time the animals are stimulated with this drug, there will be an increase in C-cell carcinoma incidents. He added that this was not the case with humans who were given the product for an extended time.

Discussion: Dr. Sweet stated that, while she finds that Victoza® is much more patient friendly (once a day dosage and the use of a pen), it is problematic when one product has a black box warning and the other medication does not. Dr. Fink asked if Byetta® has been indicated as a first-line medication, and Dr. Bell responded that it had just received first-line indication. Dr. Sweet did not feel the committee would be able to state that the two products are clinically equivalent at this time, and she added that this could be reviewed again in the near future to see what happens in terms of black boxes and first-line therapy and stated again that she was not comfortable at this time stating that the two products are totally equivalent.

Dr. Tietze remarked that the committee in the past has called certain pharmaceuticals clinically equivalent that had differences in delivery systems which made one product more convenient or patient friendly – insulin pens, for example. He added that the small study provided to the committee – involving only 700 patients - does not show superiority of one product.

Dr. Haneke noted that the products have very similar mechanism of action. Dr. Burke added that there had been a small study for efficacy completed but is fairly slim. There is the C-cell tumor risk for the one product, and also both products are injectable but the difference would be a dosage of 2 times a day vs. 1 time a day. From a patient's standpoint, the once daily would be preferred and for those patients unable to tolerate injections 2 times a day, that may call for an override as those situations may fall under the tolerability or formulation category for an override.

Dr. Bell reminded the committee that if a patient has a severe needle phobia or dexterity issue, then PA approval could be obtained, but not just for a compliance issue. Dr. Haneke thought it would be helpful, when requesting a PA, rather than stating that it is a compliance issue, to point

	<p>out that there is a clinical difference between the products. Dr. Bell advised that both products are on clinical PA now, that the matter before the committee is to determine therapeutic equivalence and appropriateness of inclusion of this class on the PDL.</p> <p>Dr. Sweet suggested that a motion be made to leave the class as is and to readdress at a future PDL meeting. She also requested that additional usage data be provided to help the committee get a sense of the clinical utility of the products.</p> <p>After much discussion, the consensus of the committee was that the members need more time and information on the usage of these products and will plan to readdress at a future meeting when more usage data and FDA information is available.</p>	<p>Dr. Sweet made motion to leave the class as is – as there is currently a PA in place for each drug - and readdress at a future PDL meeting.</p> <p>Motion was seconded by Dr. Tietze; motion and passed by unanimous vote.</p>
<p>VII. PPIs – New Agent (Vimovo®)</p> <ul style="list-style-type: none"> <li>a. Public Comment</li> <li>b. Committee Discussion</li> </ul>	<p><b>Background: In April 2010, the FDA approved Vimovo, a combination product of esomeprazole and naproxen (20/375 and 20/500 strengths). After posting the agenda online with placement it in the PPI class, the manufacturer contacted KHPA staff and indicated they felt inclusion in the NSAID class may be more appropriate. Committee guidance on appropriate placement is appreciated, in addition to determination of equivalence.</b></p> <p>Public Comment: Kim Longergan, AstraZeneca, clarified that the esomeprazole components of Vimovo® and Nexium® are two different formulations. Vimovo® compound is immediate release and Nexium® is extended release. It is estimated that 40% to 60% of people who use NSAIDs develop GI problems. Vimovo® has black box warning consistent with NSAID products that patients may see an increase in cardiovascular and GI risk.</p> <p>Discussion: Dr. Burke advised that the two issues before the Committee on this product were: a) to determine appropriate placement (NSAID class or PPI class) and b) to decide if this combo product offers any advantage over the current PDL products used individually. He added that, according to minutes from past PDL meetings, when combo products have been presented, the Committee’s position has been that the combination formulations were clinically equivalent and not superior to co-prescribed individual components of that product.</p> <p>Dr. Mishler pointed out that the active ingredient is a non-steroidal, which is indicated for arthritis.</p>	

	<p>Dr. Fink agreed that this product is indicated for arthritis and that the appropriate placement would be the NSAID class.</p> <p>Dr. Fink questioned where Vimovo® would fit within the NSAID class in terms of equivalency, and whether the comparison is being within the NSAID class as a whole, comparing to other single agents within the class, or comparing to other combination products.</p> <p>There was an additional discussion regarding determining which of these drugs would be placed on the preferred or non-preferred list. Dr. Burke advised that would be determined by the state Medicaid officials and that the Committee today would need to determine its position on whether or not Vimovo® is superior to the co-prescription of esomeprazole and naproxen. He added that a 2009 PDL review of NSAIDs determined that these agents were clinically equivalent.</p>	<p>Two separate motions were made.</p> <p>Dr. Fink moved that Vimovo® be reviewed as a NSAID class.</p> <p>Dr. Haneke seconded the motion. Motion carried by unanimous vote.</p> <p>Dr. Haneke made motion that the combination formulation in Vimovo® is clinically equivalent and not superior to co-prescribed individual components.</p> <p>Dr. Tietze seconded the motion. Motion passed unanimously.</p>
<p>VIII. NSAIDs – New Agent (Pennsaid®)</p> <ul style="list-style-type: none"> <li>a. Public Comment</li> <li>b. Committee Discussion</li> </ul>	<p><b>Background: There is a new agent in this class – diclofenac sodium 1.5% topical solution (Pennsaid®). This class was previously reviewed in 2002, 2004, and 2009. In 2009, two other topical diclofenac preparations were reviewed and determined to be clinically equivalent to orally administered NSAIDs.</b></p> <p>Dr. Bell stated that the new agent, diclofenac sodium 1.5% topical solution would be a new addition to NSAIDS class.</p> <p>Public Comment: None.</p> <p>Discussion: Dr. Sweet commented there was no evidence that would indicate this product is better than anything else available, that it is a solution rather than a gel but that the clinical efficacy is the same. Dr. Mishler asked if there were any topical non-steroidal products that are on the preferred list yet or if all require a PA. Dr. Bell responded that all are currently listed as non-preferred, that a PA is not required currently (due to currently being in the rules and regulations approval process), and that all are available as prescribed right now.</p> <p>Dr. Burke stated that, according to the minutes from the June 2009 PDL meetings, the last time the NSAIDs class was reviewed it was found that topicals were clinically equivalent to orals, although topicals probably would have less systematic adverse effects than orals.</p>	

	<p>Dr. Mishler asked about the availability of data on topical non-steroidals. Dr. Bell responded that one of handouts in the meeting packets included a data analysis for osteoarthritis (report by AHRQ) which compared efficacy and safety using topicals vs. orals. Dr. Burke added that both would have same efficacy but there is a difference in adverse effects.</p> <p>A brief discussion was held regarding if the Committee should create separate categories for topical and oral non-steroidals. The field of topical formulations is growing – gels, solutions, patches – and currently those products are in same category as orals.</p> <p>Dr. Bell advised that the NSAID class has already been reviewed and approved by the DUR, so the products discussed today may be non-preferred and will have a PA required once the rules and regulations process is completed, if they are not determined to be sufficiently cost-effective. If added as new PDL class, the DUR Board will review and determine the PA criteria for non-preferred agents. There will be general PA criteria for these non-preferred products.</p>	<p>Two separate motions were made.</p> <p>Dr. Sweet moved to separate the NSAID category by delivery systems – Topical NSAIDS and Oral NSAIDS.</p> <p>Dr. Fink seconded the motion. Motion carried with unanimous vote.</p> <p>Dr. Sweet made the motion that the Committee has determined that all topical delivery NSAIDs currently available are clinically equivalent for analgesia.</p> <p>Dr. Haneke seconded the motion; motion passed with unanimous vote.</p>
<p>IX. Biologics (TIMs) – New Agent (Actemra®)</p> <p>a. Public Comment</p> <p>b. Committee Discussion</p>	<p><b>Background: Biologics (a.k.a. Targeted Immune Modulators) were approved for inclusion on the PDL in December 2009. Classes were created by FDA-labeled indication. Tocilizumab (Actemra®) has one indication – treatment of adult rheumatoid arthritis as a second-line (after treatment with methotrexate or DMARD) therapy, and therefore should be compared to the other agents approved for adult RA.</b></p> <p>Dr. Bell reported that this class had been reviewed by the PDL Committee in December 2009 and that a new agent Actemra® has become available since that meeting. Reference was made to a handout from the December 2009 meeting: “Targeted Immune Modulators (TIMs) Approved Uses”. Request was made to correct #2 to read “...Conventional Method, DMARD therapy, or TNF failure....”</p> <p>Public Comment: Darcy Gill, Genetech, advised that this product is the only IL-6 antagonist on the market, that its safety and efficacy had been evaluated in extensive clinical trials and that patients showed improvement when treated with Actemra®.</p> <p>Dr. Haneke asked if the product is specifically classified as an IL- 6 receptor blocker or an antagonist; Ms. Gill responded that it was an</p>	

	<p>antagonist, binding to the receptor. Dr. Mischler commented that the black box warning for this product was very similar to other products in the same class. Ms. Gill responded that the warnings include TB and serious infections but that all TNFs have similar warnings.</p> <p>Discussion: Dr. Burke referred to the DERP report/handouts and commented on the diverse modes of action among the agents. He also noted that this new drug would be the first IL-6 receptor/inhibitor. He referred to action taken at previous meetings, when the Committee determined that all agents for adult RA which are approved for first and second line monotherapy are clinically equivalent and that PA should not be limited to second line agents. The Committee action also included separating out the drugs in the class approved only for combo use with methotrexate and DMARDs, determining those were not clinically equivalent.</p> <p>Dr. Burke continued that this new agent would fall into the group that was deemed clinically equivalent as second line monotherapy for adult RA. Dr. Haneke dissented, stating there are different mechanisms of action according to the drug MOAs and that he does not think a comparison could be made between TNF vs. IL-1 vs. IL-6. Dr. Mishler asked if it wouldn't be more effective to require a PA on all and allow the physician to determine the clinical equivalence.</p> <p>Both Dr. Sweet and Dr. Fink advised that the Committee has looked at similar classes in the past, such as seizure medications to determine clinical equivalence by reviewing medical outcome.</p> <p>Dr. Burke reminded the Committee that there was only one IL-6 to be considered at today's meeting, that he appreciated hearing Dr. Haneke's concern and noted that action taken by the Committee at previous discussions was determined after looking at clinical outcomes.</p>	<p>Dr. Sweet moved that the new agent is clinically equivalent to other second line monotherapy agents in the TIM class treating adult RA.</p> <p>Dr. Tietze seconded the motion.</p> <p>There was one dissenting vote by Dr. Haneke.</p> <p>Motion carried.</p>
<p>X. Long-acting Opioids -New Agent (Exalgo®)</p> <p>a. Public Comment</p> <p>b. Committee Discussion</p>	<p><b>Background: Long-acting opioids were approved for addition to the PDL in June 2009. They had previously been reviewed in 2004 and were not added to the PDL at that time. Updated DERP reports were available in 2009 that showed a lack of clinical superiority for any agent. Extended release hydromorphone (Exalgo®) was approved by the FDA in early 2010.</b></p> <p>Dr. Bell reported that the PDL Committee had reviewed this class in June</p>	

	<p>2009. This class had been added to PDL based on updated DERP reports. Initial DERP reports (2004 and 2008) indicated that there had not been enough trials to show clinical equivalence but did not show inequivalence either. A new agent, hydromorphone, has now become available in this class.</p> <p>Public Comment: None.</p> <p>Discussion: Dr. Burke added that today the Committee was reviewing the addition of one new agent, and at the June 2009 PDL meeting the Committee felt long-acting opioids were clinically equivalent with the primary outcome being analgesia. Dr. Sweet agreed, stating that the new product has the same indication and that she sees no clinical difference between it and other long-acting opioids.</p> <p>Dr. Burke commented the DUR had also previously taken action on this class, determining that patients who are taking more than 200 milligrams of a morphine equivalents per day should have additional monitoring. The DUR Board had recently approved a new policy requiring additional monitoring.</p>	<p>Dr. Sweet moved that the Committee find this new agent clinically equivalent to existing long-acting opioids</p> <p>Dr. Haneke seconded the motion; motion carried by unanimous vote.</p>
<p>XI. Drugs for Insomnia – New Agent (Edluar®)</p> <p>a. Public Comment</p> <p>b. Committee Discussion</p>	<p><b>Background: There is a new agent in the class – Edluar®, which is a sublingual form of zolpidem. Newer drugs for insomnia were reviewed by the PDL Committee in June 2005 and February 2006. Eszopiclone (Lunesta®), zaleplon (Sonata®), and zolpidem (Ambien®, Ambien CR®) were reviewed in 2005 and determined to be equivalent. Ramelteon (Rozerem®) was evaluated in 2006 for possible equivalence with the other non-benzodiazepine sleep agents, however was determined, in a divided vote, to not be equivalent. DERP has reviewed this class three times: 2005, 2006, and 2008.</b></p> <p>Dr. Bell advised that discussion for this new agent had been on the previous PDL meeting agenda and that a member of the public requested during that meeting that the discussion be delayed until today’s meeting.</p> <p>Public Comments: None.</p> <p>Discussion: Dr. Burke reported that at the August 2006 PDL meeting, it had been determined these classes of sedative hypnotics – Lunesta®, Sonata®, Ambien® – were clinically equivalent. The new agent being discussed today is a sublingual product which, for patients with</p>	<p>Dr. Haneke moved that the Committee found this product to be clinically equivalent to other sedative hypnotics in</p>

	<p>swallowing issues, could be superior; however, for those patients, the standard PDL override would be utilized to indicate that patient is unable to swallow a tablet.</p>	<p>this class.  Dr. Mischler seconded the motion; motion carried by unanimous vote.</p>
<p>XII. Adjourn</p>	<p>Dr. Burke asked if there were any remaining items to be discussed.</p> <p>Dr. Tietze requested clarification on whether or not the current timeline process for the PDL Committee – which is a review of a new drug and determination for clinical equivalence before placement on PDL - should be switched to a new default position whereby the new drug would be considered clinically equivalent with other agents in the same class until proven otherwise. He asked if the PDL Committee is currently bound by statute or regulations to review a drug within a certain timeframe; he also asked if new drugs are automatically covered by Medicaid and for how long. Dr. Bell responded that drugs are automatically covered by Medicaid, and there are statutory and regulatory restrictions in Kansas on the ability of Medicaid to manage drugs in the manner suggested by Dr. Tietze. Dr. Burke remarked he thought it would require a legislative action to make this change in the process and felt that the PDL Committee’s expertise is critical to making an informed decision regarding a new product. Dr. Bell advised there was nothing in the state’s statutes about a specific timeframe requiring PDL Committee review/action. She added that any manufacturer who has a rebate agreement with CMS has their products covered under the Medicaid Program but that under CMS rules, additional PA restrictions can be placed on products.</p> <p>In reference to today’s Committee action with the NSAIDs topicals and orals as well as separating first and second line monotherapies for clinical equivalence for the Biologic class, Barbara Belcher with Merck, asked what the process would now be for those companies which had entered into a contract arrangement with the state for supplemental rebates for one of these classes, but where the class has now been separated, whether that company’s contract would need to be renegotiated. Dr. Bell responded that for the new class, the company would need to enter into a new contract. Dr. Burke commented the Committee members are all conscientious about their role in this review process, mentioned that these new classes would now be required to go through the rules and regulations process, and asked Dr. Bell to reflect on this process and advise if any additional Committee follow-up is needed.</p> <p>Dr. Bell asked the Committee if they would like to review classes on an</p>	

	<p>annual basis – these would not necessarily be new classes but could also be classes which had been reviewed by the Committee quite some time back. Dr. Sweet responded she didn't think this would be an effective use of the Committee's time, if there wasn't any change in the products' clinical equivalency. The consensus of the Committee was to not review the classes on an annual basis.</p> <p>Dr. Tietze questioned the status of the management of mental health drugs, especially psychotropics. Dr. Burke responded that a Mental Health Prescription Drug Advisory Committee had been established in 2009 to provide guidelines and safety criteria for the prescribing of mental health drugs. One of the initial charges for the committee was to consider the establishment of a preferred drug list and prior authorization criteria for mental health drugs. There currently is a state statute, however, which prohibits mental health drugs from being included in the pharmacy management process.</p>	<p>Dr. Haneke moved to adjourn.</p> <p>Motion was seconded by Dr. Mishler; motion carried with unanimous vote.</p>
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