JIM GIBBONS
Governor

STATE OF NEVADA
DEPARTMENT OF HUMAN RESOURCES
DIVISION OF HEALTH CARE FINANCING AND POLICY
NEVADA MEDICAID

MICHAEL J. WILLDEN
Director

CHARLES DUARTE
Administrator

PHARMACY & THERAPEUTICS COMMITTEE

Meadow Wood Courtyard
5851 S. Virginia St.
Reno, NV

Committee Approved
Meeting Minutes
September 25, 2008

Committee Members Present:
Linda Flynn, R.Ph.
David Chan, R.Ph.
Justin Holt, Pharm.D.
Michael Karagiozis, DO
John Lee, MD
Chad Luebke, Pharm.D.
Rudy Manthei, DO (called in)
Chris Shea, Pharm.D.

Absent:
R.D. Prabhu, MD

Others Present:
Coleen Lawrence-DHCFP, Mary Griffith-DHCFP, Darrell Faircloth, DAG, Jeff Monaghan-FHSC, Dave Wuest-FHSC, Shirley Hunting-FHSC, Candis Lee Englant-FHSC, John Ostezan-Sepracor, Jinah Lee-Glaxo Smith Kline, Rex Adams, MD-Reno Rheumatology, Laura Litzenberger-Ortho McNeil Janssen, Lisa Wilson-Ortho McNeil Janssen, Craig Boody-Lilly, Christian Belleza-Allergan, Jodi Hittell-Merck, Michael McGuire-Forest, Doug Powell-Forest, Jane Stephen-Allergan, Sandy Sierawski-Pfizer, Mike Steelman-Pfizer, Adam Shprecher-Schering, Kirk Huffaker-Schering Plough, Naresh Singh, MD, R. Blanfarb, Kevin Monaghan-ABD, Stuart Stoloff, MD, Dean Donato-Alcon, Louise Spinelli-Pfizer, Michelle Conner-Pfizer, Cory Beynon-Glaxo Smith Kline, Emil Milas-Glaxo Smith Kline, Shawn Prince-Elan, Jim Cirelli-Biogen, Randy Carpio-VCG & Associates, Sarah Day-VCG & Associates, Phil Banegas-Ista Pharma, Barbara Irish, MD, Dan Bay-Abbott Labs, Lisa Robertson-Pfizer, Dierdre Monroe-Allergan.

I. Call to Order and Roll Call

Vice-Chair, Linda Flynn, called the meeting to order at 1:00 p.m.

II. Review and Approval of June 26, 2008 Meeting Minutes

MOTION: **Michael Karagiozis motioned to accept the minutes as written.**
SECOND: **David Chan**
VOTES: **Unanimous**
MOTION CARRIED

Ms. Flynn reminded the public that public comment is limited to five minutes per individual, organization or agency.

III. Urinary Tract Antispasmodic Agents

A. Public Comment

Dr. Karen Abbott, gynecologist, stated that she treats many female urology patients and women with chronic pelvic pain. 80% of women with chronic pelvic pain have endometriosis and of that 80%, 80% have Interstitial Cystitis (IC), a chronic inflammatory condition of the bladder. Patients with IC experience flairs, bladder ulcerations and pain. She has used Sanctura®, an antispasmodic, in its regular form for years to start long-term therapy. She feels the extended release version, Sanctura® XR, is better due to the local anesthetic effect on the bladder as well as the antispasmodic effect. There are no drug-drug interactions that she is aware of in her patients. Compliance rate in her patients has been good because of the way the molecule is; it does not cross the blood brain barrier as some other drugs in the class do. She has not seen somnolence or problems with cognition that some of her older patients have experienced with other drugs. She recommended it be considered for inclusion to the PDL.

Dr. Karagiozis asked if there are any evidence based studies that the drug actually acts as an anti-inflammatory. Dr. Abbott replied that it is not an anti-inflammatory but it has an anesthetic effect because it's predominantly metabolized in the kidney as opposed to the liver. Instead of the drug being excreted in the feces, it ends up in the bladder. With IC there is tremendous pain and spasticity of the bladder. When the drug is in the bladder, it has a local anesthetic effect and she added that there have been studies that have shown this.

Ms. Flynn thanked Dr. Abbott for attending the meeting and for her input, and wanted to clarify for disclosure, if Dr. Abbott receives any funding from drug manufacturers. Dr. Abbott replied no.

Dierdre Monroe, Allergan, spoke in support of Sanctura® XR. She stated that Sanctura® is not metabolized by the liver via the CYP450 pathway; it's metabolized by ester hydrolysis with a high concentration of 60% which shows up in the bladder and provides the local effect on the urothelium. As a highly charged, hydrophilic molecule, it does not readily cross the blood brain barrier. This was demonstrated in the pivotal trails where the instances of CNS effects were similar between Sanctura® XR versus placebo.

Jeff Monaghan asked if Ms. Monroe is aware of any good head-to-head studies that would help to differentiate the drug. Ms. Monroe replied that there are some good European studies as Sanctura® has been available there for twenty years and there are also some combination animal/human studies. She offered to send copies of the studies to the Committee. Dr. Monaghan pointed out that from an evidence-based standpoint, he is not aware of any good head-to-head studies.

Chris Shea asked Dr. Abbott what the typical age group is of someone that would experience IC. Dr. Abbott replied that IC tends to occur in women in their early teens and it can extend to women in their 60s who have retrospectively had IC for years that was misdiagnosed. In patients with endometriosis, some have had total hysterectomies, been put on drugs to fight the endometriosis and their pain is still there. Through cystoscopy, signs of these lacerations are seen in the bladder. IC is a new disease state; there are doctors that believe it does not exist including urologists in Reno. In her experience, with dietary and medical management, these women are pain free within three to four months.

Ms. Flynn noted that Justin Holt joined the meeting at 1:12 p.m.

Sandy Sierawski, Pfizer, spoke in support of Detrol® LA. Detrol® LA has been extensively studied, evaluated and peer reviewed with published articles and confirmed in post-marketing clinical practice. It's the leading branded anti-muscarinic therapy for overactive bladder for the last seven years. It has demonstrated efficacy and safety in various patient populations including adults, the elderly, sexually active females, males

and also those with severe urge urinary incontinence. Detrol® LA has a proven safety profile where no other drug in this class has shown superiority in terms of safety. The most commonly reported side effect is dry mouth which has been reported to be less frequent and less severe than other drugs in this class. In a non-industry supported evidence-based review of all overactive bladder agents, the authors used clinical trial discontinuation rates as a measure of the clinical importance of side effects and adverse events. Six of the seven studies comparing Detrol® LA to oxybutynin in any formulation found a lower rate of withdrawal for Detrol®. In the adherence literature, six published claims analyses were reviewed that compared Detrol® LA to the different formulations of oxybutynin. The results showed that overall compliance rates tend to be low in this class of drugs, but it did demonstrate that consistently, Detrol® LA had higher persistence rates versus oxybutynin. She provided the Committee a handout of utilization data. This class of drugs was originally reviewed by the Committee in the spring of 2007. Prior to that, Detrol® LA was the number one prescribed agent (for Nevada Medicaid) in this class of drugs utilizing 39% of the prescriptions. The year following, Detrol® LA utilization has increased to 49% of prescription utilization. She asked that the Committee have Detrol® LA available as a preferred product on the PDL and to not make any change that would result in interrupted treatment for patients.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that this item is on the agenda based on a request for a review of a new dosage form of an older agent, Sanctura®. The new agent is Sanctura® XR in a once daily dosage form. The immediate release (IR) form has been reviewed in the past, and up to this point, has not been added to the PDL. There is currently a broad range of agents available on the PDL. Four of the five available agents are currently on the PDL (Detrol® LA, Enablex®, oxybutynin and VESIcare®). All of these agents have been shown to be up to 75% effective in reducing the symptoms of overactive bladder (OAB). These bothersome symptoms include urgent continence and frequency. As noted in the drug review, the primary limitation in the use of this class is some of the side effects that can occur (dry mouth, constipation, urinary retention, blurry vision). These agents generally are selected based on their tolerability as well as cost. One particular agent has not been shown to be more effective than any other for overactive bladder. He referred to page six of the drug review which provides a good overview of the adverse event profile which is taken directly from the product literature not head-to-head comparisons. The potential for CNS side effects is greater with oxybutynin due to its ability to cross the blood brain barrier. The other agents in this class have an advantage in that they do not readily cross the blood brain barrier resulting in a lower incidence of CNS adverse effects. Oxybutynin is the only agent that is currently approved for children down to age five. There are no good head-to-head studies comparing Sanctura® XR to other agents. There is a study comparing the immediate release to oxybutynin in which it was found to have comparable efficacy, however, oxybutynin did have a higher instance of CNS side effects. At the last meeting, it was mentioned that Sanctura® may possess anti-inflammatory effects, but there is nothing in the literature to support that. It is an anti-muscarinic, anti-spasmodic agent like the other drugs in the category. The XR like the IR version of Sanctura® provides another option for treating OAB. In studies, it has not distinguished itself clinically from the other agents currently available. It is the recommendation of DHCFP and First Health that the agents in this class continue to be considered therapeutic alternatives.

C. Committee Discussion and Action to Approve Clinical/Therapeutic Equivalency of Agents in Class and Identify Exclusions/Exceptions for Certain Patient Groups

MOTION: **Michael Karagiozis motioned that the agents in this class be considered therapeutic alternatives.**
SECOND: **David Chan**
VOTES: **Unanimous**
MOTION CARRIED

D. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by First Health Services and the Division of Health Care Financing and Policy

Jeff Monaghan stated that from the State's standpoint, there is no impact if Sanctura® XR is added or not to the PDL. At some time, this market basket will get competitive to the point where it will make sense to thin it out. Therefore, DHCFP and First Health have no formal recommendation at this time. The PDL status of Sanctura® XR will be at the discretion of the Committee.

Ms. Lawrence noted that there was a considerable amount of testimony regarding the anesthetic effect of Sanctura® XR. Documentation of the anesthetic effect was not found in the studies. To assist the Committee in their decision, she recommended opening public discussion again and asking if there is any written documentation regarding the anesthetic effect.

Dierdre Monroe, Allergan, stated that a combination animal/human study was conducted where healthy volunteers received therapeutic doses of oxybutynin (Ditropan®), tolterodine (Detrol®) and trospium (Sanctura®). Rat models were given carbacol to have the symptoms of OAB and injected human urine. At a concentration of 60% in the bladder, Sanctura® was the only one that relieved the OAB symptoms for the rats. Dr. Chancellor of Pittsburg also has a study looking at identifying the anesthetic effect. It's hard to do with human models.

Dr. Monaghan said that the Committee's approach is to rely on evidenced-based studies. There is nothing in the product literature stating that there is an anesthetic effect.

E. Committee Discussion and Approval of Drugs for Inclusion on the PDL

MOTION: Michael Karagiozis motioned to add Sanctura® XR to the PDL.
David Chan referred to the chart on page 6 of the drug review and stated that without head-to-head studies the numbers are impressive compared to the other drugs.
Dr. Monaghan agreed stating that some of the numbers particularly in terms of the CNS side effects are impressive.
Dr. Luebke said that one of the limitations to this class are the side effects and felt this drug has a good profile in that regard.
Ms. Lawrence asked for clarification that the motion only includes Sanctura® XR and Dr. Karagiozis replied yes.
SECOND: David Chan
Darrell Faircloth asked for clarification regarding no recommendation from First Health. Is the proposal a net balance of four products on the PDL or is the proposal an addition of a fifth agent.
Dr. Monaghan stated that, in our opinion, they are therapeutic alternatives and the Committee agreed. It is the recommendation of DHCFP and First Health that the decision for modification of this class be left to the Committee's discretion since there is no impact on the State.
VOTES: Unanimous
MOTION CARRIED

IV. Ophthalmics, Glaucoma Agents

A. Public Comment

Dr. Lara McKnight, eye care provider in Reno and Carson City, spoke in support of Lumigan®. She stated that she has no financial interest in Allergan and is not receiving remuneration for her statements today. She said that she has been using Lumigan® for a number of years very effectively in glaucoma care. Primary concerns are patient compliance and the effectiveness of the product. As the number of doses is increased over the course of a day, there is less and less compliance with time. Prostaglandins started as second-line therapy but have now become first-line therapy. The goal in glaucoma care is to get pressure down 30% from baseline. Prostaglandins, Lumigan® in

particular, are very effective in getting pressure down 30%. The most common reason patients are taken off of prostaglandins is ocular irritation; extreme red eye, pain and irritation that makes the medication intolerable. The main side effect is lengthening and darkening of eye lashes. The advantage of the prostaglandins is that there are no systemic side effects as with other glaucoma care. With beta-blockers, which for a long time were first-line therapy, there are a lot of potential systemic side effects. In her experience with Lumigan®, she has seen the least amount of ocular irritation and the best control of a single medication. She stated that from a clinical point of view, Lumigan® has been a good performer and requested it remain on the PDL.

Christian Belleza, Allergan, spoke in support of Lumigan®. He stated that during the June meeting, the Committee reviewed the clinical benefits of Combigan® and Lumigan® and voted to retain Lumigan® as a preferred prostaglandin analog on the PDL. Several physicians have voiced their support for Lumigan® to remain on the PDL. Letters of support have been submitted by Drs. Robert Wolff, Kevin Miller and Rene Zamora. The categoric review prepared by these providers illustrates a superior intraocular pressure (IOP) lowering effect of Lumigan® and the benefits of Combigan® when patients need combination therapy to achieve additional therapeutic benefits.

Dean Donato, Alcon Laboratories, spoke in support of Travatan®. At the last Committee meeting and with the recent addition of Xalatan® to the PDL, it was suggested that one of the three PGA products may be removed from the PDL. If the Committee decides to move forward on this issue, he pointed out why the product Travatan®, which includes the only available BAK preservative-free PGA, Travatan® Z, should remain on the PDL. The vast majority of prescriptions in this category are written for patients over the age of 65 and on Medicare Part D. As a point of reference, Travatan® Z and Lumigan®, not Xalatan®, are by far the most represented and preferred agents within the top 15 national Medicare Part D plans. Within these plans, Travatan® Z is covered at a preferred level for 98% of these lives; Lumigan® 84% and Xalatan® at 49%. Along with the Provider Synergies drug review, Medicare supports and reinforces that there has not been any significant efficacy or tolerability issue associated with Travatan® or Travatan® Z. Currently, Travatan® and Travatan® Z have 65% of the Nevada Medicaid market-share; Lumigan® 30% and Xalatan® 5%. Removing Travatan® from the PDL and forcing these patients, who are currently well controlled on the product to another PGA for no good financial or clinical reason, would be a waste of State resources, cause provider and patient disruption and cost Medicaid more in time and money.

Dr. Karagiozis asked if market research has been conducted showing that the removal of Travatan® will cost the Medicaid program money or is it a personal belief based on a general belief of the dynamics of the system. Mr. Donato replied that maybe First Health would probably give the best comments regarding the financial impact of switching patients from medications they are well controlled on.

Dr. Monaghan stated that if the Committee felt strongly about continuity, the Committee has the option to grandfather patients on existing therapy and only have the PDL impact new patients. Dr. Manthei recommended the grandfathering of patients.

Randy Carpio, VCG and Associates representing ISTA Pharmaceuticals, spoke in support of Istalol®. Istalol® is indicated in patients with elevated intraocular pressure, ocular hypertension or open-angle glaucoma. Istalol® was approved in 2004, is a once-daily dose, non-selective beta-blocker which provides a better interior chamber penetration with less systemic absorption. With the potassium sorbate that has been added to timolol maleate with Istalol®, the better absorption into the interior chamber through the cornea provides less systemic absorption (75% less). Istalol® reaches C_{max} within the first 30 minutes versus agents with twice daily dosing at 60 minutes. The additional potassium sorbate allows for once-a-day dosing, absorbs quickly, allows patients to take less medication by eliminating one less drop, not a gel therefore no blurring, low cost, less systemic absorption and minimal BAK. He requested Istalol® be considered for inclusion to the PDL.

Barbara Irish, MD, Nevada Eye Consultants, spoke to the prostaglandin analogs, Xalatan®, Travatan® and Lumigan®. Although they have similar mechanisms of action, they have different side effect profiles. In her experience, Xalatan® appears to be the most well tolerated agent followed by Travatan® and then Lumigan®. There's a significant amount of irritation and redness that causes discontinuation of eye drops therefore poor compliance.

Dr. Karagiozis asked Dr. Irish regarding these three medications, would she support grandfathering patients who are currently on one of these medications and allowing the other two on the PDL. Dr. Irish replied that including all three would be helpful as they are all first-line agents.

Dr. Monaghan clarified that if adverse effects occur with PDL drugs, there are criteria for obtaining a non-preferred drug.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that this item was placed on the agenda based on a motion from the last meeting. Dr. Manthei requested that Xalatan® be added to the PDL, which occurred, so there are three prostaglandin analogs currently on the PDL. There was discussion of going from three to two agents. Dr. Manthei agreed to reach out to some of his colleagues and report back to the Committee with a recommendation.

Dr. Monaghan gave a brief overview of the prostaglandin analogs stating that they all significantly lower IOP and have become first line agents in treating glaucoma. It is the recommendation of DHCFP and First Health that the agents in this class be considered therapeutic alternatives.

C. Committee Discussion and Action to Approve Clinical/Therapeutic Equivalency of Agents in Class and Identify Exclusions/Exceptions for Certain Patient Groups

Dr. Manthei stated that he reached out to five glaucoma specialists (four in southern Nevada; one in northern Nevada). They all agreed that Xalatan® be available on the PDL. All three agents are similar in pressure lowering effect with Xalatan® having less allergic reaction. The controversy was Lumigan® versus Travatan® Z and their opinions were split. Some preferred the Lumigan® saying there was better effect but agreed allergic reaction is a problem. The physicians that used Travatan® felt that there was decreased allergic reaction with Travatan® Z. He agreed that having two agents on the PDL is a reasonable approach especially if existing patients doing well on Lumigan® or Travatan® can remain on the drug. He recommended Xalatan® and Travatan® Z be available on the PDL. He felt that the general ophthalmologist would tend to go with the Travatan® Z which has less allergic reaction and is better tolerated and that Lumigan® be available if there is failure on the two PDL agents.

MOTION: **Michael Karagiozis motioned that the agents in this class be considered therapeutic alternatives**
SECOND: **David Chan**
VOTES: **Unanimous**
MOTION CARRIED

D. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by First Health Services and the Division of Health Care Financing and Policy

Jeff Monaghan said it is the recommendation of DHCFP and First Health that Xalatan®, Travatan® and Travatan® Z continue to be preferred agents and those recipients currently on Lumigan® will be grandfathered to continue their therapy.

E. Committee Discussion and Approval of Drugs for Inclusion on the PDL

MOTION: **Rudy Manthei motioned to accept First Health's recommendation that Xalatan®, Travatan® and Travatan® Z be on the Preferred Drug List; Lumigan® will be non-preferred and patients currently on Lumigan® will be grandfathered to continue therapy.**
SECOND: **Michael Karagiozis**
VOTES: **Unanimous**
MOTION CARRIED

V. Intranasal Rhinitis Agents

A. Public Comment

Stuart Stoloff, MD, family physician, stated that he is one of the contributors to the rhinitis practice parameters for the American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology and serves on the task force of the American Academy of Allergy, Asthma and Immunology for rhinitis and has also written the guidelines for the diagnosis and management of asthma for the United States Expert Report 3 for the National Heart, Lung and Blood Institute for which he works for. He spoke in support of adding Patanase® to the PDL. There is a population of patients who either have allergic rhinitis or non-allergic rhinitis who do not respond well to intranasal corticosteroids. There may be associated side effects or they don't work or discontinue working. In that population, doubling the dose of many of the intranasal corticosteroids is not appropriate. The use of oral antihistamines gives potentially systemic oral side effects for that population. Patanase® is an intranasal agent, used twice a day for ages 12 and above. It has a rapid onset of action compared to the other intranasal antihistamine agents, has a very beneficial profile and low rate of somnolence and that is one of the clearly defined side effects of Astelin®. He would like to have Pantanase® available for his Medicaid patients.

Dr. Karagiozis asked if the individual antihistamines are in the same class of drugs as nasal steroids. Dr. Stoloff replied that intranasal corticosteroids are their own class. If you look at intranasal agents and you lump them in a class, they're all in the class. An intranasal antihistamine is not the same as an intranasal corticosteroid. They work by different pharmaco-therapeutic effects and have different molecules that they interact on. They have, in many patients, the same outcome. Until Patanase® was available, in his practice there was a significant reluctance of introducing a patient to the only available intranasal antihistamine because of the side effects and taste, but more importantly, somnolence. Approximately 18%-20% of patients that were administered Astelin® had effects similar to Benadryl®.

Dave Wuest asked if a patient presents with symptoms of seasonal allergy, both would be in the same basket of things chosen to treat the patient and Dr. Stoloff replied that is correct. Mr. Wuest said that First Health is not suggesting that they are the same molecule but they are a possible agent for the treatment of the disease and Dr. Stoloff agreed that they are an option for the same disease process.

Ms. Flynn asked to clarify for disclosure if Dr. Stoloff receives funding from any drug manufacturers. He replied that he contributed to the guidelines for the diagnosis and management of asthma; contributed to the guidelines for pregnancy and asthma; consults for the speakers bureau for almost every pharmaceutical company in the world that deals with allergy and asthma.

Dr. Karagiozis asked if Dr. Stoloff is or has been a consultant for both of the antihistamine companies and he replied yes.

B. Drug Class Review Presentation – First Health Services

Dave Wuest stated that in the past, the nasal corticosteroids have been reviewed; today's review is of the non-steroid drugs in the class (Astelin®, Patanase® and Atrovent®). Like all the other agents in this class, they are used to treat the symptoms of seasonal allergic rhinitis. Both Astelin® and Patanase® are antihistamines and mast cell stabilizers. Patanase® is indicated for the treatment of seasonal allergic rhinitis. Astelin® has the same indication plus the additional indication of symptoms of vasomotor rhinitis. Atrovent® is an anticholinergic which decreases bronchospasm and secretions from the nasal glands. Astelin® and Atrovent® are proven safe and effective in children. Patanase® does not have an indication for children less than 12 years of age. It is the recommendation of DHCFP and First Health that these agents be considered therapeutic alternatives.

Dr. Karagiozis asked if anticholinergics are within the broader group or within the steroids. Mr. Wuest replied intranasal rhinitis agents adding that the recommendation is not that the agents have the same molecule but can be alternatives to one another.

Dr. Monaghan suggested to clarify this that the name of the category could be changed to Intranasal Rhinitis Agents.

C. Committee Discussion and Action to Approve Clinical/Therapeutic Equivalency of Agents in Class and Identify Exclusions/Exceptions for Certain Patient Groups

MOTION: Michael Karagiozis motioned that the name of the class for these agents be changed to Intranasal Rhinitis Agents and that the agents in this class be considered therapeutic alternatives
SECOND: Justin Holt
VOTES: Unanimous
MOTION CARRIED

D. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by First Health Services and the Division of Health Care Financing and Policy

Dave Wuest said that it is the recommendation of DHCFP and First Health that Astelin® and Atrovent® be added to the PDL and to not add Patanase® to the PDL.

E. Committee Discussion and Approval of Drugs for Inclusion on the PDL

Dr. Karagiozis felt that out of respect for comments presented by Dr. Stoloff, he could not turn down Dr. Stoloff's request to add Patanase® to the PDL. David Chan agreed and asked why Patanase® should not be included.

Mr. Wuest replied that it's not in the best interest of the State to add Patanase®. Additionally, there has not been a good head-to-head comparison between the two antihistamine agents. He noted that if there is an adverse effect with the preferred agents, there is the prior authorization (PA) process for obtaining the non-preferred agent.

Dr. Karagiozis asked why Astelin® was chosen over Patanase®. Dr. Monaghan said that based on therapeutic equivalency, it can be a financial decision. He stated that the antihistamines are not first-line agents versus the steroids. He asked Dr. Stoloff if he normally prescribes a steroid first and Dr. Stoloff replied yes that the first-line agents recommended in the treatment of allergic and non-allergic rhinitis are intransal corticosteroids.

Ms. Flynn noted that Dr. Lee joined the meeting at 2:01 p.m.

Michael Karagiozis recommended that Astelin®, Atrovent® and Patanase® be added to the PDL but that Patanase® be reserved in the failure of the other agents or at the recommendation of the physician using a diagnosis code bypassing the PA process.

Ms. Lawrence stated that a claims history look back for drugs can be done but she did not recommend a look back for diagnosis since the pharmacy system will not include the diagnosis unless one has been required to bypass a PA. The PA process can be bypassed by requiring a diagnosis code on the prescription. Dr. Monaghan added that if there is agreement that the steroids are first-line, the system can do a 90-day look back and if there is an intranasal steroid in history, the Patanase® would go through without a PA.

Dr. Karagiozis asked Dr. Stoloff for his input on the look back. Dr. Stoloff stated that the major use of Atrovent® nasal spray is for rhinorrhea; it is not an antihistamine and would not be an appropriate agent for allergic rhinitis. He said that there are currently only two antihistamines on the market, Astelin® and Patanase®.

Mr. Wuest said that it would be in the State's best interest to add Astelin® and Atrovent® to the PDL. Patanase® will be non-preferred with a 90-day look back in claims history which will bypass the PA process if Astelin® is in claims history.

Ms. Lawrence stated for clarification that if there is no claims history of Astelin®, the normal PA process will apply.

MOTION: **Michael Karagiozis motioned to accept First Health's recommendation to add Astelin® and Atrovent® to the PDL. Patanase® will be non-preferred with the amendment that there will be a 90-day look back which will bypass the PA requirement for Patanase® if Astelin® is in claims history, otherwise, a PA will be required.**
SECOND: **Chris Shea**
VOTES: **Unanimous**
MOTION CARRIED

VI. Antimigraine Agents, Triptans

A. Public Comment

Jinah Lee, Glaxo Smith Kline, spoke in support of Treximet®. Treximet® is a single tablet that contains sumatriptan 85mg and 500mg of naproxen sodium. The pharmacokinetic profile of Treximet® is distinct. The time to maximum concentration for the sumatriptan in Treximet® occurs 30 minutes earlier compared to Imitrex® 100mg tablet given alone which aligns with the early phase of the migraine. The naproxen component contained in Treximet® reaches maximum concentration 4 hours later compared to naproxen sodium 500mg given alone which aligns with the later phase of the migraine reversing ongoing inflammation and preventing further release of prostaglandin. In pivotal trials, patients receiving Treximet® had fewer headache recurrences (13%) and 77% of the patients did not require rescue medication. Treximet® provides sustained, pain-free results versus sumatriptan, naproxen sodium and placebo. It represents an opportunity to reduce non-specific migraine therapy such as narcotics and potentially keeps patients from developing medication overuse. Due the superior efficacy of Treximet®, the decreased need for a second dose or rescue medication and a distinct pharmacokinetic profile, it is recommended that Treximet® be added to the PDL.

Dr. Shea asked if sumatriptan and naproxen have been looked at separately as two different entities versus the combination Treximet®. Ms. Lee replied that in order for the combined product to be approved, it had to be proven that the combination was better than the individual components. There were four arms in the pivotal trial: placebo, sumatriptan 85mg, naproxen 500mg and Treximet®.

Dr. Shea asked why the combined product is better than taking the two separate components together. Ms. Lee replied that there are no head-to-head trials. Mr. Wuest added that First Health's search could not find any head-to-head studies that compared taking the two separate components together to taking Treximet®.

B. Drug Class Review Presentation – First Health Services

Dave Wuest stated that his class was last reviewed in June 2008. There are currently three agents on the PDL in the anti-migraine class (Imitrex®, Maxalt®, Relpax®). Sumatriptan is now commercially available as a generic tablet. The non-steroidal anti-inflammatory drugs (NSAID) are currently available with no restrictions. Treximet® is a combination agent. The two agents in this combination are available separately in various dosage forms. The sumatriptan contained in Treximet® is a 5-HT_1 receptor agonist and the naproxen is an NSAID. As with other NSAIDs, the mechanism is unknown but thought to be related to its prostaglandin inhibition. Treximet® provides two different mechanisms of action for relieving migraines. Results of claims data review indicates that 20% of Medicaid recipients that receive a triptan also have received an NSAID within 30 days of the triptan. It is the recommendation of DHCFP and First Health that the agents in this class continue to be considered therapeutic alternates.

C. Committee Discussion and Action to Approve Clinical/Therapeutic Equivalency of Agents in Class and Identify Exclusions/Exceptions for Certain Patient Groups

MOTION: **Michael Karagiozis motioned to accept First Health's recommendation that the agents in this class be considered therapeutic alternates.**
SECOND: **Chad Luebke**
VOTES: **Unanimous**
MOTION CARRIED

D. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by First Health Services and the Division of Health Care Financing and Policy

Dave Wuest stated that it is the recommendation of DHCFP and First Health that Treximet® not be added to the PDL. If a clinician determines that a patient needs a treatment with a triptan along with an NSAID, there are many choices available.

E. Committee Discussion and Approval of Drugs for Inclusion on the PDL

MOTION: **Chad Luebke motioned to accept First Health's recommendation to not add Treximet® to the PDL.**
SECOND: **Justin Holt**
VOTES: **Unanimous**
MOTION CARRIED

VII. Fluoroquinolones, Oral

A. Public Comment

Naresh Singh, MD, pulmonary intensive care specialist from Las Vegas and Director of Pulmonary and Intensive Care at the University Medical Center, disclosed that he is on the speaker's bureau for Ortho-McNeil, Pfizer, Boehringer Ingelheim, and Astra-Zeneca. He stated that it is his recommendation that Levaquin® (levofloxacin) be added to cover the individual deficiencies of Avelox® and Cipro® that are currently on the PDL. The top admitting diagnosis is respiratory in emergency rooms and hospital visits. The Infectious Disease Society of America and community infectious disease societies have algorithms and recommendations for acute exacerbation of acute bronchitis, sinusitis and community-acquired pneumonias. The recommendations for patients with co-morbidities are to cover gram-negatives along with gram-positives. Avelox® was originally selected for its narrow spectrum to reduce collateral damage. It is now also indicated for intra-abdominal infections. Hospitals, including University Medical Center, in their admitting pathways for COPD exacerbation have choices; either the Avelox® box or the Rocephin® zithro box. The Rocephin® zithro box is often selected by emergency room physicians because it has some gram-negative coverage but it's inadequate. Typically,

emergency room physicians do not order sputums because they anticipate a short stay admitting patients for 23 hour observations. At 48 hours, a number of patients have failed outpatient therapy or in the hospital are failing to improve so gram-negative coverage is added. Cefapine is added to Avelox® or cefapine is added to replace Rocephin® resulting in subsequent sputum being incorrectly negative. The result is an extended stay and the discharge antibiotics have deficiencies which contribute to a higher relapse rate which then has to be addressed as outpatients, recurring emergency room evaluations or as inpatients. In pneumococcus, the resistant gene for penicillin and zithromycin are close to each other so there is a 30% cross-resistance. By adding Levaquin®, outpatient failures and length of hospital stay can be reduced.

Dr. Karagiozis asked Dr. Singh to comment on Levaquin® use in HIV patients. Dr. Singh stated that HIV patients would be categorized as co-morbidities. The most common organism of infection in HIV patients is pneumococcus. Because they are on various agents to boost their immune system, having a deficiency to not cover gram-negatives in the same antibiotic puts them as risk. They do have a higher incidence of admission for respiratory infections.

Dr. Karagiozis disclosed that he has a potential conflict in that Dr. Singh is his pulmonologist. He stated that he will retain his right to vote in this matter because his opinion is based on his HIV experience.

Dr. Monaghan asked if Dr. Singh is referring to his hospital experience. Dr. Singh replied that these patients are “frequent flyers”. The “frequent flyers” seek care both at physician offices, emergency rooms or quick cares as well as in the hospital. These patients are not able to get levofloxacin as an outpatient. Typically what’s thrown in is doxycycline, cefapine or Avelox®. A certain number of these patients have gram-negative organisms and fail initial therapy. Patients discharged from the hospital on Levaquin® are not able to obtain it as an outpatient and are often given a substitute or the prescription goes unfilled. A certain percentage of these patients have co-morbidities. Some do not have a positive culture identifier because the culture was obtained late and have a relapse rate.

Dr. Monaghan stated that it’s his understanding that the American Thoracic Society and the Infectious Disease Society of America recommend moxifloxacin, gemifloxacin or levofloxacin 750mg for community-acquired pneumonia with co-morbidities and high risk. Dr. Singh stated that he agreed with that.

Dr. Karagiozis asked what percentage of patients may fall in the gram-negative category and Dr. Singh replied patients with a high-risk profile, approximately 15%.

Dr. Monaghan asked if Dr. Singh has had strep pneumonia failures that he’s had to go to Avelox® when Levaquin® was started. Dr. Singh replied yes that Avelox® is a good drug which he uses a significant amount of the time. There are Avelox® failures and he will then give the patient samples of levofloxacin and they improve.

Ms. Flynn disclosed for the record that her son is a patient of Dr. Singh’s but that will not influence her vote.

Laura Litzenberger, Ortho-McNeil Janssen, spoke in support of Levaquin®. She referred to her testimony from the June 2008 meeting minutes and offered to answer any questions. Dr. Lee stated that at the last meeting, an issue was raised about the safety comparisons between Avelox® and Levaquin® regarding excretion in the gut. Ms. Litzenberger replied that Levaquin® is almost 100% excreted renally unchanged; 4% of the drug is metabolized and excreted into the gut. Avelox® is 25% excreted into the gut. Theoretically, the higher the load of antibiotic could change the flora and potentially be a difference in the amount of C. difficile. Dr. Lee asked if that is a theoretical concern or is there any data. Ms. Litzenberger said that there are epidemiological studies that rank all antibiotics. Within the fluoroquinolone class, moxifloxicin (Avelox®) has a higher odds ratio than Cipro® and Levaquin®. Dr. Monaghan asked if the package literature

contain the same warnings regarding C. diff. and she stated it's a class effect in terms of the warnings.

Adam Shprecher, Schering-Plough, spoke in support of Avelox® (moxifloxacin). Moxifloxacin is a broad spectrum fluoroquinolone antibiotic that's especially known for its gram-positive activity. It's available as a 400mg dose for all indications including acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, community-acquired pneumonia including multi-drug resistant strep-pneumo, and uncomplicated and complicated skin structure infections. It's the only the only fluoroquinolone antibiotic that's indicated for the treatment of intra-abdominal infections caused by susceptible microorganisms. Moxifloxacin also covers the gram-negative organisms in the abdominal cavity and covers anaerobes. Other fluroquinolones have to be combined with other agents such as metronidazole to treat gut flora. The community-acquired pneumonia and elderly trial (CAPRI Trial) showed that Avelox® was efficacious and safe for hospitalized, elderly patients achieving a greater than 90% cure rate in all severity and age groups and was associated with a faster clinical recovery than Levaquin® therapy with a comparable safety profile. A second publication from the CAPRI Trial demonstrated that Avelox® had a comparable cardiac safety profile, and since this data was released, there have been updates to the package insert for both Avelox® and Levaquin®.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that the PDL is currently broken down by the second generation fluorquinolones (ciprofloxacin) and the third generation fluoroquinolones (moxifloxacin [Avelox®]). Ciprofloxacin is a valuable agent due to its superior gram-negative activity and proven effectiveness in UTIs. The third generation fluoroquinolones have a broad spectrum activity and have shown usefulness particularly in penicillin-resistant strep-pneumonia. The discussion today focuses on two agents, Avelox® versus Levaquin®. When used judiciously for an appropriate diagnosis with the correct dose and the correct duration of therapy, infectious disease specialists that he has spoken with agree that clinical outcomes and adverse effects are similar. In community-acquired pneumonia (CAP), the American Thoracic Society and the Infectious Disease Society of America recommends for high risk patients with co-morbidities, either Avelox®, Factive® (gemifloxacin) or Levaquin® 750mg. They specify Levaquin® 750mg. For patients with CAP, the 750mg is needed to obtain the dose needed for the gram-positive, strep-pneumonia coverage. Avelox® does not require dosage adjustment with renal insufficiency; Levaquin® does. Ciprofloxacin and Levaquin® are indicated for UTI; Avelox® is not. Avelox® produces reliable anaerobic activity hence it has an indication for abdominal infections. Avelox® is 48 times more active against strep-pneumonia invitro. Levaquin® has a five day short course of therapy indication for community-acquired pneumonia as well as acute sinusitis. The overriding issue for these drugs is appropriate use. For instance, if ciprofloxacin is being used for upper respiratory infections; it shouldn't be and Avelox® shouldn't be used for UTIs. Is Levaquin® being under-dosed for CAP? He reviewed the "Drug versus Diagnosis" chart which indicated that 2% of patients on Avelox® with a diagnosis of urinary infection were on no other antibiotic; 0% of patients on ciprofloxacin with a respiratory diagnosis were on no other antibiotic. He reviewed the utilization data and noted that duration of therapy for Levaquin® 750mg averaged 7.5 days indicating that the five day course is not being applied. It is the recommendation of DHCFP and First Health that the third generation fluroquinolones continue to be considered therapeutic alternatives when used for appropriate diagnosis, dosage and duration of therapy.

C. Committee Discussion and Action to Approve Clinical/Therapeutic Equivalency of Agents in Class and Identify Exclusions/Exceptions for Certain Patient Groups

MOTION: **Michael Karagiozis motioned to accept First Health's recommendation that the agents in this class be considered therapeutic alternatives.**
SECOND: **David Chan**

VOTES: Unanimous
MOTION CARRIED

D. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by First Health Services and the Division of Health Care Financing and Policy

Jeff Monaghan stated that it is the recommendation of DHCFP and First Health that there be no changes to the current PDL for the second and third generation fluroquinolone classes.

E. Committee Discussion and Approval of Drugs for Inclusion on the PDL

Dr. Karagiozis disagreed with the recommendation based on his patient population. He stated that in this drug category, getting a prior authorization (PA) through is not a good idea. If a patient is really ill, he uses the 750mg and not the 500mg of Levaquin®. Dr. Monaghan asked what his normal duration of therapy is. Dr. Karagiozis replied that it depends on the diagnosis. If the patient is HIV positive, his duration for therapy is a week because he doesn't trust the short-course. If the patient is not HIV positive, he chooses a five day course.

MOTION: Michael Karagiozis motioned to add Levaquin® 750mg to the PDL.

Darrell Faircloth asked for clarification if it's being added for a specific diagnosis or across the board coverage on the PDL.
Dr. Karagiozis said that he's recommending the 750mg and referred to First Health's data that the clinicians are using the drug appropriately. At 750mg, the average quantity of prescriptions is 7.5 which compared to the Avelox® is 9.4.
Dave Wuest clarified that 7.5 is not the number of prescriptions but the average number of pills.
Dr. Monaghan asked what the risks are if only the 750mg is available and someone wants to treat a UTI and knows that the 750mg is available without a PA, will there be over treatment.
Dr. Karagiozis replied that it would be inappropriate to use Levaquin® under those circumstances. His concern at lower doses is allowing the drug to possibly develop resistance. He asked Dr. Singh to comment.
Mr. Wuest stated that another fear of adding only the 750mg is Levaquin® has a lot of renal dosage requirements. If limited to the 750mg, overdosing is a concern in the elderly population.
Dr. Singh stated that dosing could be limited to either dose (500mg or 750mg) for five days and if an extended course is required, a PA could be obtained. That allows for a person who has a reduced creatinine clearance, whether on dialysis or not, will get 500mg for five days which should be more than sufficient to cover their respiratory and perhaps urinary tract. Allowing for a five day course without a PA will achieve all the objectives to appropriately treating immunocompromised patients, treating renally impaired patients and reduce resistance to levofloxacin.
Dr. Karagiozis agreed with Dr. Singh supporting limiting therapy to a five day course. This will allow time to obtain a PA for a patient requiring extended therapy and will limit people casually using Levaquin®.
Dr. Karagiozis offered an amendment to his original motion to limit Levaquin® to a five day course of therapy. A PA will be required for an extended course of therapy.
Dr. Shea stated that what he's seen in his practice with acute care and skilled rehab patients is a rejection for Levaquin® resulting in a prescripton for ciprofloxacin regardless of the type of infection. He continues to see prescriptions for ciprofloxacin for respiratory tract infections which has lead to treatment failure because there has been no improvement after fourteen days and IV antibiotics are then needed. He supported providing Levaquin® with a five day course. He recommended at some point having the Drug Use Review (DUR) Board review Levaquin® utilization.
Ms. Lawrence asked what the next step is if more than five days of therapy is needed.
Dr. Karagiozis replied a PA would be required. He stated that physicians who are basically "knee jerking" are going to be weeded out because it will be easier to do

Avelox® or ciprofloxacin and Levaquin® will be used appropriately. A seven or ten day prescription for Levaquin® will require a PA.
Ms. Lawrence stated that she is trying to determine whether the review of over-utilization in this case falls within the scope of P&T or DUR. What PDL exception criterion applies to the sixth day?
Dr. Monaghan stated that is has to be fairly general. When the Call Center receives that call, the prescriber would simply need to say that the patient requires continuation of therapy. He asked Dr. Karagiozis if the five day limitation applies to the 750mg only.
Dr. Karagiozis replied that the five day limit applies to all strengths of Levaquin®.
SECOND: Chris Shea
VOTES: Unanimous
MOTION CARRIED

VIII. Lipotropics, Other

Due to time constraints, this item was deferred to the next meeting.

IX. Report by FHSC on Brand Name Preferred Drugs Converted to Generic Status and Line Extensions

Jeff Monaghan referred to the report in the meeting packet and noted that a new drug, Alvesco®, has been released in the inhaled corticosteroid category that will remain non-preferred until the annual review unless there is a reason to look at it sooner.

X. Review of Next Meeting Location, Date, and Time

The next meeting is scheduled for December 11, 2008 in Las Vegas.

XI. Public Comment

No comment.

XII. Adjournment

MOTION: Michael Karagiozis motioned to adjourn the meeting.
SECOND: David Chan
VOTES: Unanimous
MOTION CARRIED

Meeting adjourned at 2:59 p.m.