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Governor

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

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PHARMACY & THERAPEUTICS COMMITTEE

Las Vegas Chamber of Commerce
6671 Las Vegas Blvd. S., Suite 300
Las Vegas, NV

Committee Approved
Meeting Minutes
June 26, 2008

Committee Members Present:
David Chan, R.Ph.
Linda Flynn, R.Ph.
Justin Holt, Pharm.D.
Michael Karagiozis, DO
John Lee, MD
Chad Luebke, Pharm.D.
Rudy Manthei, DO
R.D. Prabhu, MD

Absent:
Robert Horne, MD
Chris Shea, Pharm.D.

Others Present:
Coleen Lawrence-DHCFP, Mary Griffith-DHCFP, Darrell Faircloth, DAG, Gabriel Lither, DAG, Jeff Monaghan-FHSC, Dave Wuest-FHSC, Shirley Hunting-FHSC, Mike Steelman-Pfizer, Roland Baldwin-Wyeth, Laura Litzenberger-OMJSA, Elena Pizzi-AstraZeneca, Roianne Byrd-AstraZeneca, Mandy Hosford-AstraZeneca, Carlos Palasciano-Hawthorn, William Rowe-Forest Research, Doug Powell-Forest Pharmaceuticals, Leila Mosavi-Maulik-Roche, Scott Brown-TEVA, Bob Paeillo-Pfizer, John Stockton-Genentech, Felizia Fuller-Biogen Idec, Annie Ogoslalick-Abbott, Daniel Bay-Abbott, John Berry-Pfizer, Dean Donato-Alcon, Jay Jennings-Sanofi-Aventis, Jane Stephen-Allergan, Deirdre Monroe-Allergan, Mark Miller-Allergan, David Abrahamson-Merck, Teev Heinmanson-Schering Plough, Steve Hill-Schering Plough, Csilla Csoboth-Boehringer, Sedrick Spencer-Roche, Brian McManus-GSK, Cory Beynon-GSK, Betty Kuhn-Takeda, Maresh Singh-Physician, Jon Beaty-Boehringer Ingelheim, Chris Almeida-Purdue, Shaun Prince-Elan, Marietta Nelson-Physician, David Case-Astellas Pharma, D. Black-Shire, Richard The-Physician, Jennifer Choi-CVT, Gary Dawson-Takeda, Bert Jones-GSK, Sabrina Aery-BMS, Jennifer Lauper-BMS, E.J. Milas-GSK, Lori Horwarth-Bayer, Craig Boody-Lilly, Tom Nicosin-Takeda, Rebecca Harr-Takeda, Janine Flournier-Sanofi-Aventis, Patti Vassar-Merck, Blake Hennington-Merck, Carter McCree-Sanofi-Aventis, Sandy Sierawski-Pfizer, Barbara Felt-GSK,

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 March 27, 2008, Meeting Minutes

David Chan pointed out that he had offered an "aye" vote on Item VI.E. which is not documented in the minutes and requested the minutes be corrected.

MOTION: **Michael Karagiozis motioned to accept the minutes with correction as noted.**
SECOND: **John Lee**
VOTES: **Unanimous**
MOTION CARRIED

Coleen Lawrence stated that an annual review of the Preferred Drug List (PDL) is required by statute. The annual review process consists of two categories, drugs that will be considered for change and drug classes without proposed changes. Public comment is limited to three minutes and only new information will be permitted for comment per entity. Public offering comment is asked to disclose any affiliations with drug manufacturers.

Ms. Lawrence said that in the absence of Chairman Robert Horne, Vice-Chair, Linda Flynn will conduct the meeting.

III. Old Business – Nebivolol (Bystolic®)

Ms. Flynn stated that this item was included on the agenda at Dr. Horne's request. Because he is not in attendance to present further discussion, the item will be tabled.

ANNUAL REVIEW- DRUG CLASSES WITH PROPOSED CHANGES

IV. Antidepressants: Other

A. Public Comment

Roland Baldwin, Wyeth, spoke in support of Pristiq®, a new serotonin-norepinephrine reuptake inhibitor (SNRI). Starting dose is 50mg and ending dose is 50mg. There is a 100mg tablet available for psychiatry but for the general practitioner, 50mg is being promoted. It's an active metabolite of desvenlafaxine sulfonate with a predictable pharmacokinetic profile which consists of the following: mean terminal half-life of 11 hours; steady-state plasma concentration is 4-5 days; minimal inhibitor of the CYPP6 system; has bioavailablity of 80% after oral administration; plasma protein is low at 30%; adverse reactions are similar to the rate for placebo at 3.8%. The only dose adjustment is suggested for severe renal patients which is 50mg every other day. Studies indicate that there is no greater efficacy of doses greater than 50mg. Hypertension is a concern for patients on SNRIs but at 50mg, the supine systolic blood pressure only increased 1.2mg; the systolic and diastolic was 0.7. He requested Pristiq® be considered for addition to the PDL. If it's not added to the PDL, he requested it be available after a trial of one PDL agent.

Jeff Monaghan asked if there is not increased efficacy in greater than 50mg, why the 100mg is made. Mr. Baldwin replied that in the managed care setting, psychiatrists like to play with their antidepressants. To allow them to do that, the 100mg is available and the price is the same.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that this class was last reviewed in March, 2007. At that time, the Committee added Wellbutrin XL® 150mg and 300mg to the PDL and requested utilization data on generic buproprion immediate release. The issue was whether the immediate release version should be non-preferred. In the last year, there were 240 patients (830 claims) that received buproprion immediate release. In analyzing the doses received, there was no threat to the patient or that doses were being exceeded.

Dr. Monaghan said that desvenlafaxine sulfonate (Pristiq®) is a new agent in this drug class, but it is simply the major active metabolite of an existing drug, venlafaxine (Effexor®). It is given once daily for the treatment of major depressive disorder. The recommended dose is 50mg. Common side effects are similar to venlafaxine; dizziness, nausea, insomnia being the most common. In clinical trials, Pristiq® was dosed up to 200mg and 300mg per day; side effects increased but there was no increase in efficacy. 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

MOTION: R.D. Prabu motioned that the agents in this class be considered therapeutic alternatives.
SECOND: Michael Karagiozis
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

Dr. Monaghan stated that is it the recommendation of DHCFP and First Health that no changes be made to the PDL for this class. Pristiq® will be non-preferred and will be treated with same PDL exception criteria currently applied to the antidepressant class which is failure on one of the preferred agents before Pristiq® is authorized.

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

Dr. Karagiozis asked if a prior authorization (PA) will be required for Pristiq® versus looking at claims history. Dr. Monaghan replied that claims history will be looked at and if there is history, the claim will process without a PA. If there is no history, a PA will be required. Dr. Karagiozis stated that he can support that as long as the patient had been tried on other drugs and it avoided a PA.

MOTION: Michael Karagiozis motioned to accept First Health's recommendation that no changes be made to the PDL in this class. Prior authorization will not be required for Pristiq® if there is claims history of a trial of one other agent within this class in the past 90 days. Prior authorization will be required if there is no claims history.
SECOND: John Lee
VOTES: Unanimous
MOTION CARRIED

V. Antihistamines: 2nd Generation

A. Public Comment

Janine Flournier, Sanofi-Aventis, spoke in support of levocetirizine (Xyzal®). Levocetirizine was FDA approved in May, 2007, and is indicated for the relief of seasonal allergic rhinitis, perennial rhinitis and idiopathic urticaria in adults and children six years and older. It's available as a 5mg tablet and an oral solution. In studies comparing levocetirizine to fexofenadine and loratadine, fexofenadine demonstrated reduction and consistence in antihistimic property. A two week randomized controlled trial comparing levocetirizine with desloratadine in patients with allergic seasonal rhinitis, levocetirizine improved symptoms. She requested levocetirizine be considered for inclusion to the PDL.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that during the annual review in June, 2007, this class was reviewed and no changes were made. In July, 2004, the Committee placed edits allowing non-preferred agents to be approved if there was a past history of a trial of loratadine. Zyrtec® and Clarinex® pediatric formulations have been available on the PDL in the past for pediatric use. Since the last annual review, a new product, levocetirizine (Xyzal®), has been released. It is simply the R-enantiomer of an existing product, cetirizine (Zyrtec®); Zyrtec® being the racemic mixture. Cetirizine is a 5mg dose and only approved for children down to six years of age. The existing PDL agents are approved down to six months of age. The data on the drug is not impressive compared to existing

PDL agents. The clinical studies that have been submitted have been placebo controlled, but there is no good comparative data. Larger, longer term studies are needed to say this drug is better or superior clinically to existing antihistamines. Like Zyrtec®, levocetirizine is more sedating than other second generation antihistamines. Levocetirizine may have some theoretical advantages but there is no good clinical data indicating that it is better than the current PDL agents. 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

MOTION: John Lee motioned that the agents in this class be considered therapeutic alternates.
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

Jeff Monaghan stated that it is the recommendation of DHCFP and First Health that levocetirizine (Xyzal®) not be added to the PDL and recommended that this class be expanded to provide more choice and include cetirizine which is now available generically and over-the-counter. This would include cetirizine syrup, tablets and chewable tablets and apply the same edits as loratadine. If there is claims history of cetirizine or loratadine, a non-preferred agent will be available.

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

David Chan stated that in his practice, patients have complained that levocetirizine does give them more drowsiness and sedating affect.

MOTION: Michael Karagiozis motioned to accept First Health's recommendation to not add levocetirizine to the PDL and include generic and over-the-counter cetirizine syrup, tablets and chewable tablets applying the same edits as loratadine that if there is claims history of cetirizine or loratadine, a non-preferred agent will be available.
SECOND: Rudy Manthei
VOTES: Unanimous
MOTION CARRIED

VI. Cardiovascular: Antihyperlipidemics: Statins and Statin Combinations

A. Public Comment

Annie Ogoslalick, Abbott, spoke in support of Simcor® (niacin/simvastatin). Trials using statins to lower LDL cholesterol consistently show reductions in major cardiac events in various prospective long term trials. With the 25% to 35% relative reduction in cardiovascular events, there still is a residual risk of 65% - 75% of a cardiovascular event in patients appropriately treated with statin therapy. This residual cardiovascular risk is particularly high in diabetes patients treated aggressively with statins. Simcor® reduces LDL, non-HDL, total cholesterol, triglycerides, and increases HDL in patients with primary hypercholesterolemia, mixed dyslipidemia and hypertriglyceridemia. The safety and efficacy of the individual components of Simcor® are well established. Multiple studies were conducted to establish the safety and efficacy of Simcor®. She requested Simcor® be included as a preferred agent on the PDL.

Sandy Sierawski, Pfizer, spoke in support of Lipitor®. She provided utilization data from 2005 to 2007 and noted that over the last two years, 50% of statins use of adjunct therapies has increased by 6% and use of Vytorin® has increased by 18%. In 98% of the usage of simvastatin and Vytorin® in 2007, the doses were 20mg or greater per day which poses safety concerns. Fibric acid should not be used in patients receiving greater than 10mg of Zocor® and Vytorin® and simvastatin should not exceed 20mg per day when given comcomitantly with amiodarone or verapamil. Lipitor® was not on the PDL in 2007, however, it was the third prescribed branded statin after Vytorin® and Crestor®. She noted that the drug review provided by Provider Synergies identifies that there are only three agents Lipitor®, pravastatin and simvastatin with primary and secondary prevention data. The review contains studies on Lipitor® highlighting its efficacy and safety. There are a small number of studies for the other products without the same outcome. No cardiovascular outcome studies have been published for Crestor®, Vytorin®, Advicor®, Simcor® or Caduet®. She stated that Lipitor® has an excellent safety profile across the dose range and there are fewer drug interactions than with other statins with the exception of pravastatin.

Dr. Karagiozis asked the difference between a surrogate marker and an outcome marker. Ms. Sierawski replied that LDL is a clinical measurement that points in the direction but the actual outcome of preventing death or more cardiovascular disease is a primary outcome that is utilized for readily in clinical trials. Dr. Karagiozis asked if she's stating that Lipitor® has covered all those direct outcomes and that's better than surrogate markers and she replied yes.

David Abrahamson, Merck Schering-Plough, offered to answer any questions regarding the recent controversy surrounding Vytorin®. Dr. Lee asked for an update with respect to any expert bodies' recommendations on the use of Vytorin® and Zetia®. At the American College of Cardiology (ACC) meeting, the recommendation of the expert panel was to use Zetia® as the last resort after other drugs have been used. Recognizing that this controversy is not proven but there's some concern. Mr. Abrahamson responded that the consensus panel was a few individuals that didn't represent the ACC and it was a consensus panel's statement. The ACC and American Heart Association's (AHA) official position is that first line therapy in people who can tolerate statin is statins and you can titrate them to maximum tolerable dose. Beyond that, you can use cholestyramine, niacin, fibrate or Zetia®. Similarly, the statement from the National Lipid Association would parallel that.

Mandy Hosford, Astra Zeneca, spoke in support of rosuvastatin (Crestor®). In November, 2007, the FDA granted an indication for Crestor® to slow the progression of atherosclerosis at any stage of the disease. That is in addition to a normal treatment strategy in adults to lower total cholesterol and LDL. She referred to the CORONA study which was a prospective trial of statin in the treatment of heart failure. The mean age of the patient was 73. The primary endpoint was to see if Crestor® 10mg could reduce cardiovascular mortality, non-fatal heart attacks and non-fatal strokes. Crestor® did not reach its primary endpoint; however, looking at patients that suffered athrothrombotic events, there was a significant difference between Crestor® 10mg and placebo in this elderly population. The reduction of hospitalizations due to heart failure as well as any cardiovascular cause was significantly reduced in those patients on Crestor®. She cited the TNT Study which indicated that Lipitor® is the other statin with an indication for reducing heart failure hospitalizations. The same results were seen in symptomatic heart failure patients on Lipitor® 80mg as with Crestor® 10mg. She requested Crestor® remain on the PDL.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that this drug class was last reviewed in June of 2007. At that time, pravastatin was added and Altoprev® was removed from the PDL. There is one new combination drug in this class to review, Simcor®, which is a combination of time-release niacin and simvastatin. Statins have become the standard treatment for hyperlipidemia. As the table on page 12 of the drug review indicates, all agents in the

class produce a dose-dependent LDL lowering. The Adult Treatment Panel (ATP) III guidelines for the National Cholesterol Education Program (NCEP) released guidance in 2004 suggesting that more aggressive therapy should be considered as an option for high risk patients. New data indicates that high risk patients with normal LDL benefit from statin use. Numerous comparative trials have examined the impact of statins for cardiovascular outcomes. Per FDA-approved indications, only pravastatin and simvastatin are approved for actual reduction in mortality. Atorvasatin, lovastatin, pravastatin and simvastatin have all been shown and are approved for the prevention of coronary events.

During the past six months, new data has become available for rosuvastatin and simvastatin/ezetimibe. The JUPITER study was a long-term, randomized, double-blind placebo controlled study to assess rosuvastatin in the primary prevention of cardiovascular events in patients with moderate LDL levels and elevated inflammatory indicators (CRP >2). This study was stopped early based on the recommendation of the monitoring and steering committee because of the unequivocal evidence of a reduction in morbidity and mortality in patients receiving rosuvastatin versus placebo.

The other study that has received a lot of attention is the ENHANCE trial. It speaks to the issue of surrogate endpoints. This study demonstrated no significant difference between Vytorin® (ezetimibe/simvastatin) a combination product versus simvastatin alone in the primary outcome measurement of mean change in carotid artery intima media thickness (IMT), which is a surrogate endpoint. This contradicted the current mantra that lower is better. There's been criticism of the study design, but this study reinforces and exposes the shortcomings of surrogate endpoints. Lower may be better but how you get there may count as well. More studies need to be and are being done.

All statins are relatively well-tolerated. All have been associated with rhabdomyoslysis with the problem occurring in about 2 of every 100,000 patients. Liver function monitoring is recommended for all agents and all are Category X for pregnancy. All statins are extensively metabolized by the CYP450 system with the exception of pravastatin, fluvastatin and rosuvastatin. Pravastatin has the lowest potential for drug interactions but it's not as potent as some of the other agents.

Per the ATP-III guidelines, DHCFP and First Health are recommending that statins should be considered therapeutic alternatives in that they are first line drugs.

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

Dr. Karagiozis stated that the reason that the surrogate markers and the clinical outcomes are of importance is because a study released in March on HIV patients on protease inhibitors which showed patients are dying at six times the rate of their peer matched group due to myocardial events. These are in people whose surrogates would not have suggested that they were at that risk. He felt that these drugs cannot be considered clinically equivalent based on surrogates. Outcomes need to be considered to decide where these drugs play in their efficacy and their clinical benefit to the patients. He stated that he routinely puts patients on atorvastatin 160mg per day as well as omega-3 due to high elevations of cholesterol and triglycerides. He felt these agents cannot be considered equivalent based on the fact that they are all statins and surrogates are not the only criteria by which they are judged.

Dr. Monaghan stated that he is not suggesting that only surrogates be looked at. As he stated earlier, the ENHANCE study pointed out the weakness of surrogate endpoints. He asked if this study was a randomized, double-blind, controlled study comparing other drugs or placebo. If not, it may not be credible. Dr. Kargiozis replied that it was not a prospective study but a retrospective analysis. It was an accidental finding. The study was looking at mortality but not cardiac mortality; the cardiac mortality fell out. Multiple companies that manufacturer the drugs are looking at the data now with concern.

Dr. Lee requested clarification of the motion that the different statins should be considered therapeutic alternatives because of the mechanism of action and for their clinical outcomes data? Dr. Monaghan referenced the AMA's definition of therapeutic alternative included in the meeting binder which states: "Drug products with different chemical structures but which are of the same pharmacological and/or therapeutic class and usually can be expected to have similar therapeutic effects and adverse reaction profiles when administered to patients in therapeutically equivalent doses."

MOTION: John Lee motioned that the agents in this class be considered therapeutic alternatives.
SECOND: Justin Holt
AYES: Lee, Manthei, Flynn, Holt, Chan, Luebke, Prabu
NAYES: Karagiozis
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 based on the consensus guidelines that statins in general, not as specific agents, are considered first-line agents for treating hypercholesterolemia that the existing agents, simvastatin, pravastatin and lovastatin remain on the PDL as reasonable choices for most patients. The combination agents, Simcor® and Advicor®, should be on the PDL due to good outcomes data available. Atorvastatin (Lipitor®), rosuvastatin (Crestor®) or simvastatin/ezetimibe (Vytorin®) will be non-preferred but should be available for patients that have not reached goal with the statins. One approach to this would be implementing an edit which looks at claims history (90 day look back). If the patient has not reached their goal on one of the high-dose statins, the other agents will be available after a trial of an existing preferred agent.

Dr. Karagiozis asked if the patients have to be on a maximum dosage of simvastatin, pravastatin and lovastatin prior to switching. Dr. Monaghan replied yes that the dose has to be pushed to a high level prior to going to an alternative agent. The current PDL exception criteria will still be in place. If the patient doesn't tolerate one of these agents, if there are adverse outcomes, a prior authorization will be required, but that does meet the criteria for approval of an alternative drug.

Dr. Karagiozis felt a prior authorization should not be required if it's a situation where there's a clear indication. HIV patients on protease inhibitors should be started on Lipitor®.

Ms. Lawrence stated that it is the Committee's recommendations and experience of what they want to see on the PDL. There are edit options which can be considered such as requiring diagnosis codes if that will assist in certain patient populations to use certain lines of drugs.

Dr. Lee stated that using certain LDL reduction as your endpoint goes with the same discussion with using surrogate endpoints. He felt it would be reasonable to not require a PA if a cardiologist wanted to use Lipitor® as first-line therapy not just to achieve reduction but because of studies showing intensive lowering of LDL with proven outcomes data with Lipitor® for patients with coronary artery disease.

Dr. Monaghan asked Dr. Lee that with the clinical data on simvastatin, which is extremely impressive, what would make him want to go to Lipitor® before simvastatin. Dr. Lee said that there are a lot of secondary production studies with simvastatin. With Lipitor®, there are secondary production studies but it was taken one step further by using much lower targets, more intense treatment to achieve better outcomes. There are different outcomes with different statins.

Dr. Monaghan stated that as an advocate for the State, with a few minor exceptions, Zocor® (simvastatin), when it was under patent, had a tremendous amount of good work done in their outcome studies. There are a couple of studies with Lipitor® where an 80mg dose was compared to a 10mg dose showing that 80mg is better; but they didn't compare Lipitor® to Zocor® high dose. There is no data comparing Lipitor® to Zocor® high dose so to say because they did that study they are better is a leap.

Dr. Karagiozis stated that he did not disagree, but if a physician feels that Lipitor® is indicated, the physician shouldn't have to jump through hoops to get the drug to the patient. Due to the number of reasons a physician might switch to Lipitor®, he felt it should be added to the PDL.

Dr. Monaghan stated that DHCFP and First Health are recommending keeping the PDL the way it is, add Simcor®, and due to the recent data that's come out, make it easier to get to a higher potency drug, but also to follow the consensus guidelines of pushing statins to the maximum dose.

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

MOTION: Michael Karagiozis motioned that the existing agents for this class remain on the Preferred Drug List and to add Simcor® and Lipitor® to the Preferred Drug List.
SECOND: R.D. Prabu
VOTES: Unanimous
MOTION CARRIED

VII. Cardiovascular: Antihyperlipidemics: Other

A. Public Comment

E.J. Milas, Glaxo Smith Kline (GSK), spoke in support of Lovaza®, an omega-3-acid ethyl esters comprised of a minimum of 90% omega-3. Lovaza® makes up a newer class of drugs to treat hypertriglyceridemia. People commonly mistake it with fish oil and the difference is fish oil and supplements have 1,200mg of fish oil but very little to no EPA and DHA. It is only the EPA and DHA that have been proven to lower triglycerides and have a cardiovascular benefit. Lovaza® is an omega-3 acid ethyl esters dosed at four 1gm capsules per day with food. It is well studied making it a unique agent compared to supplements and has a low incidence of side effects and low drug interactions. It is efficacious in lowering triglycerides up to 45% and also lowers non-HDL and raises HDL cholesterol. It's comparable with a fibrate while providing the patient with essential fatty acids. The body does not make or synthesize omega-3 or omega-6 therefore it needs to be taken through diet. The western diet is deficient in omega-3 fatty acids as compared to omega-6 fatty acids. Loveza® had a label change in the last year to have it in combination with a statin, lowering triglycerides an additional 30%. However, the indication was not granted. He requested consideration be given to adding it to the PDL.

Dr. Karagiozis asked to explain the FDA's logic allowing a label change but not a change in indication. Mr. Milas replied that he did not know the FDA's rationale. The FDA did want further outcomes studies in combination with a statin which GSK is doing with atorvastatin and rousuvastatin.

Dr. Monaghan asked how robust the outcomes data is. Mr. Milas said there is no definitive outcomes studies with randomized, double-blind, placebo controlled trials. However, a study was conducted in Italy at 1gm per day of Loveza® or Omacor®, secondary prevention post-MI with 11,000 patients. It lowered mortality 20% in that study which is believed to be primarily driven by reduction in sudden death which was a reduction of 45%. It was submitted to the FDA; the indication was not granted because it was open label.

David Chan asked how significant this product is compared to omega-3 that can be obtained anywhere. Mr. Milas replied that supplements are not FDA-regulated so it's not known what the product contains. Loveza® is FDA-regulated, has proven claims and has indications with a minimum of 90% omega-3 fatty acids. It's been well studied with a consistent dose.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that this class was last reviewed in June, 2007, with no changes. Two new fibric agents have been released in the last year, Lipofen® and Fenoglide®. Fibric acid agents have been shown to reduce cardiac mortality and morbidity in both primary and secondary prevention trials. They lower triglyceride levels and raise HDL-C levels to a greater extent than statins. They should be considered to be an alternative to the statins for specific lipid disorders and can be used as add on therapy. The fenofibrates are less likely to interact with the statins as compared to gemfibrizol. In terms of Lipofen® and Fenoglide's® place in therapy, they offer no significant advantage over existing agents and have a disadvantage in that they both have to be taken with food versus at anytime with the existing preferred agent Tricor®. 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

MOTION: **Michael Karagiozis motioned that the agents in this class be considered therapeutic alternatives.**
SECOND: **John Lee**
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 DHCFP and First Health recommend that Lipofen® and Fenoglide® not be added to the PDL and no changes be made to the current PDL for this class.

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

MOTION: **Michael Karagiozis motioned to add omega-3s to the Preferred Drug List specifically, Lovaza® and Omacor®.**
SECOND: **No second offered.**
MOTION: **John Lee motioned to accept First Health's recommendation that no changes be made to the Preferred Drug List in this class.**
SECOND: **Rudy Manthei**
Dr. Prabu stated that some patients would benefit from omega-3 fatty acids and recommended Lovaza® be added to the PDL.
AYES: **Lee, Manthei, Flynn, Holt, Chan, Luebke**
NAYES: **Karagiozis, Prabu**
MOTION CARRIED

VIII. Ophthalmic Glaucoma Agents

A. Public Comment

Deirdre Monroe, Allergan, spoke in support of a new ophthalmic combination solution, Combigan®, which received FDA approval in October, 2007. Combigan® is a combination of 0.2% brimonidine, an alpha-agonist, and 0.5% timolol, a beta blocker. It's indicated for the reduction of elevated intraocular pressure (IOP) in patients with glaucoma or ocular hypertension. It's available in a 5ml and 10ml bottle, and dosed

twice per day approximately twelve hours apart. Combigan® has a dual mechanism of action. Timolol, as a beta blocker, reduces aqueous humor production and brimonidine, as an alpha-agonist, also reduces aqueous humor production and increases uveoscleral outflow. Benefits include convenient dosing in a single bottle which reduces the number of daily drops and is less confusing for the patient. There is no washout effect versus multiple drop regimens. There is also the potential for improved compliance since many patients receive two or more drugs to improve their IOP control. In the Phase 3 trial, Combigan® was dosed twice a day and achieved significant lower IOP versus brimonidine 0.2% at three times per day or timolol at twice per day. The allergy rate was also low. In another study to determine efficacy and tolerability of Combigan® versus Cosopt® in patients with glaucoma, Combigan® reduced mean IOP was 15.6ml of mercury versus 17.2ml for Cosopt®. Combigan® has a statistically significant lower incidence of ocular burning, stinging and the bad taste left in the month. She asked that Combigan® be included on the PDL.

Dr. Marietta Nelson, practicing ophthalmologist, spoke in support of Xalatan®. She stated that Xalatan®, Lumigan®, and Travatan® are the number one prescribed glaucoma agents all over the country. All three are good and effective drugs. In her experience, Xalatan® is more comfortable for patients therefore they are more likely to use it. Lumigan® and Travatan® both work well but cause a little more irritation and redness.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that this class was last reviewed in June, 2007. Since the last review, a new combination agent, Combigan®, has been released. Combigan® is a combination of brimonidine and timolol and is indicated for the reduction of IOP with glaucoma or ocular hypertension. 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: Rudy Manthei motioned that the agents in this class, including Combigan®, be considered therapeutic alternatives.
SECOND: John Lee
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 because patients often require combination therapy to adequately control IOP, from a compliance standpoint, it is the recommendation of DHCFP and First Health to add Combigan® to the PDL.

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

Dr. Manthei stated that based on history, in his opinion, Combigan® is not a primary medication. If the patient failed other agents, Combigan® would be considered. Having a combination on the PDL would be very reasonable.

MOTION: Justin Holt motioned to accept First Health's recommendation to added Combigan® to the PDL.
SECOND: John Lee
VOTES: Unanimous
MOTION CARRIED

MOTION: Rudy Manthei motioned to add Xalatan® to the PDL with Lumigan® and Travatan®.

Dr. Monaghan asked if Dr. Manthei would consider going with two of the three agents versus three of three agents (Xalatan®, Travatan®, and Lumigan®). It may be in the State's best interest that two of the three be made available versus three of three.
Dr. Manthei offered to reach out to the glaucoma specialists in the area to eliminate one agent and bring a recommendation to the Committee at the next meeting.
Dr. Monaghan stated that First Health can review the literature and provide a review when this drug class is agendized.
SECOND: Michael Kargiozis
VOTES: Unanimous
MOTION CARRIED

IX. Ophthalmic Quinolones

A. Public Comment

No comment.

B. Drug Class Review Presentation – First Health Services

Jeff Monaghan stated that this class was last reviewed in June, 2007, with no recommended changes. Since then, a new strength of an older product has been released, IQUIX®, which is levofloxacin 1.5% solution versus Quixin®, levofloxacin 0.5%. IQUIX® is indicated for corneal ulcers but not for blepharitis or conjunctivitis. There are a number of antimicrobial agents available for routine eye infections. More serious infections, those that threaten vision, require a broader spectrum of antibiotics such as the flouroquinolones.

Several studies have been published regarding corneal penetration of the flouroquinolones as measured in the aqueous humor during surgery. While this seems important, the study endpoints do not represent clinical outcomes nor do they provide insight in the concentrations achieved with the FDA-approved regimens.

In vitro studies indicate the two fourth generation agents, gatifloxacin (Zymar®) and moxifoxacin (Vigamox®) appear to provide better coverage for gram positive and resistant organisms than the third generation agents. Unfortunately, there are no good comparative clinical trials.

It is the recommendation of DHCFP and First Health that the agents in this class, including IQUIX, 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: Rudy Manthei motioned that the agents in this class be considered therapeutic alternatives.
SECOND: John Lee
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 IQUIX® not be added to the PDL at this time.

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

Dr. Manthei agreed that IQUIX® should not be used as a first-line agent. The existing drugs on the PDL are very adequate.

MOTION: **Rudy Manthei motioned to accept First Health's recommendation not to add IQUIX® to the PDL.**
SECOND: **Michael Karagiozis**
VOTES: **Unanimous**
MOTION CARRIED

X. Respiratory: Long Acting Beta Adrenergic

A. Public Comment

Barbara Felt, Glaxo Smith Kline, spoke in support of salmeterol (Serevent® Diskus). In addition to asthma, salmeterol is indicated for exercised-induced brochospasms in patients four years and older and monotherapy in patients with COPD. Both the ATS guidelines and the GOLD guidelines support the use as monotherapy of salmeterol in COPD patients. It's not appropriate for use as monotherapy in asthma but should be used in addition to control medications. Since potentially most of the patients on salmeterol monotherapy will be COPD patients, it is worthwhile to consider the device. The diskus device, which is the only device salmeterol is now available in, is an easy to use device. When the device is open, the patient clicks and the device punctures the foil and exposes the medication which is then inhaled through a low-resistance device. She requested salmeterol be placed on the PDL. Dr. Monaghan stated that it is currently on the PDL.

Teev Heinmanson, Schering Plough, spoke in support of formoterol (Foradil®). Formoterol is a long-acting beta-agonist acting as a selective beta-$_2$ andrenergically separate full agonist. The indication is for broncho-constriction in patients with COPD as well as maintenance treatment of asthma and prevention of bronchospasm. This product should not be used as a single entity to treat asthma. It's also indicated for prevention of exercise-induced bronchospasm in patients five years of age and older. Onset of action is five minutes similar to albuterol. There is sustained bronchodilation of over twelve hours and is dosed every twelve hours. It reduces the need for rescue medication as been proven in several clinical trials. Based on this information, he requested that formoterol be added to the PDL. Dr. Monaghan stated that it is currently on the PDL.

B. Drug Class Review Presentation – First Health Services

Dave Wuest stated that this class was last reviewed in December, 2007. A new product has become available since that time, Perforomist®. It's chemically formoterol which is the same product currently on the PDL in a nebulizing solution as opposed to an inhaler. Perforomist® is indicated for COPD. The current PDL agents are indicated for COPD with the additional indications for the treatment and prevention of bronchospasm associated with asthma as well as the prevention of exercised-induced bronchospasm. Perforomist® is not indicated for the treatment and prevention of bronchospasm associated with asthma as well as the prevention of exercised-induced bronchospasm. There is similar mechanism of action with smooth muscle tissue in the lungs and side effect profiles are similar throughout the class. The FDA requests that all products manufactured in this class contain labeling to alert healthcare professionals and patients that these medications may increase the chance of severe asthma episodes and death when these episodes occur. The American College of Chest Physicians and the American College of Allergy, Asthma and Immunology have concluded that devices for the use of delivery of bronchodilators and steroids can be considered equivalent. 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

MOTION: **Chad Luebke motioned that the agents in this class be considered therapeutic alternatives.**

SECOND: **Michael Karagiozis**
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 no changes be made to the PDL and Perforomist® not be added to the PDL.

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

MOTION: **David Chan motioned to accept First Health's recommendation that no changes be made in this class and not add Perforomist® to the PDL.**
SECOND: **Rudy Manthei**
VOTES: **Unanimous**
MOTION CARRIED

XI. Respiratory: Nasal Corticosteroids

A. Public Comment

Barbara Felt, Glaxo Smith Kline, spoke in support of Veramyst®. Veramyst® is the only intranasal steroid that has the FDA approval to talk about ocular symptoms proactively in seasonal allergic rhinitis in patients twelve years and older. Currently, there are five studies that have demonstrated statistically significant benefits; sometimes to the second generation antihistamines and sometimes to placebo. The placebo contained everything in Veramyst® minus the active drug. This was not seen with Flonase®. In two studies of Veramyst® versus Allegra®, there was a placebo tablet and placebo inhaler in both groups. Nasal symptoms, quality of life and ocular symptoms were studied. Veramyst®, down the board, was statistically significant versus placebo in everything. Allegra®, down the board, was not statistically significant versus placebo in anything. When comparing the two active treatments, Veramyst® versus Allegra®, the only thing not statistically significant was the ocular symptoms. The Veramyst® device is unique due to the size of the nozzle which is beneficial in the pediatric population. Veramyst® does not smell and it has a low volume mist which does not run down the back of the throat.

Dr. Lee asked about the ocular effects. Ms. Felt stated that Veramyst® reduces ocular symptoms not side effects more than placebo. Dr. Monaghan asked if there was comparison to another intranasal steroid and she replied no.

Teev Heinmanson, Schering Plough, had no presentation but entertained questions from the Committee regarding Nasonex®. No questions were offered.

B. Drug Class Review Presentation – First Health Services

Dave Wuest stated that since the last review of this class, a new product, Omnaris® (ciclesonide) has been released. Omnaris® is a nasal inhaler. All devices used with the agents in this class can be considered to be effective. The side effect profile is the same throughout the class. 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

MOTION: **Michael Karagiozis motioned 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 stated that it is the recommendation of DHCFP and First Health to remove flunisolide from the PDL and add generic fluticasone; Nasonex® to remain on the PDL.

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

MOTION: Michael Karagiozis motioned to accept First Health's recommendation that Nasonex® remain on the PDL and to remove flunisolide from the PDL and add generic fluticasone.
SECOND: Justin Holt
VOTES: Unanimous
MOTION CARRIED

Chairperson Linda Flynn called for a ten minute break.

Ms. Flynn called the meeting to order at 3:16 p.m.

XII. Annual Review - Drug Classes without Proposed Changes

A. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by First Health Services and the Division of Health Care Financing and Policy without Changes

1. Analgesics: Long Acting Narcotics
2. Antibiotics: Cephalosporins 2nd Generation
3. Antibiotics: Cephalosporins 3rd Generation
4. Antibiotics: Macrolides
5. Antibiotics: Quinolones 2nd Generation
6. Antibiotics: Quinolones 3rd Generation
7. Anticoagulants: Injectable
8. Antidepressants: SSRIs
9. Antiemetics: Oral, 5-T3s
10. Antifungals: Onychomycosis Agents
11. Anti-Migraine Agents: Triptans
12. Bone Ossification Agents: Bisphosphonates
13. Cardiovascular: ACE Inhibitors & Diuretic Combinations
14. Cardiovascular: Angiotensin II Receptor Blockers & Diuretic Combinations
15. Cardiovascular: Beta Blockers
16. Cardiovascular: Calcium Channel Blockers & Combinations
17. Central Nervous System: ADHD/Stimulants
18. Central Nervous System: Sedative Hypnotics
19. Electrolyte Depleters
20. Erythropoiesis Stimulating Proteins
21. Gastrointestinal Agents: H2RAs
22. Gastrointestinal Agents: PPIs
23. Growth Hormone Agents
24. Hepatitis C Agents
25. Herpetic Antiviral Agents
26. Immunomodulators: Injectable
27. Immunomodulators: Topical
28. Leukotriene Modifiers
29. Multiple Sclerosis Agents
30. Nasal Calcitonins
31. Ophthalmic Antihistamines
32. Otic Fluoroquinolones
33. Respiratory: Inhaled Anticholinergic Agents
34. Respiratory: Inhaled Corticosteroids/Nebs
35. Respiratory: Short Acting Beta Adrenergic-Inhalers/Nebs

36. Urinary Tract Antispasmodics

Dierdre Monroe, Allergan, spoke in support of Sanctura® XR, which currently is the only once daily antimuscarinic for the treatment of overactive bladder (OAB). Antimuscarinic agents constitute the only drug class with broad accepted efficacy in the treatment of OAB. It's well tolerated and has a low incidence of all the anticholinergic adverse events. Sanctura® XR is not extensively metabolized by the liver but is excreted by the kidney. It does not interact with other drugs which are metabolized through the CYP450 system. Many of these are elderly patients on chronic medications and the potential for drug interactions can be eliminated. She provided letters of support form Dr. Karen Abbott and Dr. Scott Verinof. She requested Sanctura® XR be considered for addition to the PDL.

Dr. Kargiozis stated that Dr. Abbott indicates that there is anti-inflammatory affect with Sanctura® and the class is antispasmodics. He felt that Dr. Abbott may think that this belongs in a different drug class. Ms. Monroe replied that since Sanctura® XR is metabolized 60% as the parent compound within the bladder, they feel there is a dual mechanism of action affecting the urgency symptoms that the patient is having which Dr. Abbott attributes as the feelings that the inflammatory as discussed in the ureter lining of the bladder.

Dr. Monaghan informed the Committee that Sanctura® immediate release has been reviewed in the past. If there are drug categories that the Committee feels that need further review, they can be reviewed at a future meeting. It is the recommendation of DHCFP and First Health based on the clinical evidence that First Health is aware of and based on discussions with the State, there is no compelling reason to suggest any changes in these categories. If Committee members feel otherwise or information presented today influence that decision, it can be scheduled for a future meeting.

Dr. Karagiozis felt that since two urologists are talking about it, he would like this to be presented at a future meeting addressing the inflammatory factor (Interstitial Cystitis). Otherwise, he agrees that if it's just another urinary tract antispasmodic to move on.

Dr. Monaghan stated that the State and First Health feel the PDL selection is more than adequate but if the Committee requests, it can be agendized for a future meeting.

Bert Jones, Glaxo Smith Kline, asked if the triptan category will be reviewed at the September meeting. Dr. Monaghan stated that a new triptan product has been released but did not fall within the timeline for this meeting. It will be reviewed at the September meeting.

Laura Litzenberger, Ortho McNeil Janssen, requested that the Committee consider a full review of the third generation flouroquinolones. Levaquin® has been approved by the FDA for the past eleven years and there has been no change in the resistance trends. One of the reasons could be due to the indication of high-dose short course therapy for community-acquired pneumonia and for bacterial sinusitis. The World Health Organization and the Infectious Disease Society of America suggest that there is less of a chance for resistance with high-dose short course of antibiotics and there is more possibility of patient compliance. The preferred quinolone currently on the market does not have a five day indication for community-acquired pneumonia or for sinusitis. She requested a re-review of this category.

Dr. Monaghan asked why the average course of therapy doesn't seem to line up with the short course recommendations. Those are studies seen in the commercial market place where these drugs are being given for six, eight or ten days. Ms. Litzenberger stated that she does not have an answer but the indication is for five days and that is the way the drug is promoted.

Richard Teh, internist in private practice, requested that the Committee consider adding Levaquin® to the PDL. He has prescribed this drug extensively. It's very common in

the hospital and on most formularies. The current agent on the PDL is Avelox® which is 25% excreted in the gut. Levaquin® is excreted less than 5% in the gut. Safety issue is a concern.

Drs. Karagiozis and Lee requested that Levaquin® be agendized for the next meeting.

Elena Pizzi, AstraZeneca, spoke in support of Symbicort®. She stated that in asthma, long-acting beta-agonists are to be used in combination with inhaled corticosteroids. Astra-Zeneca has a new product which was launched June, 2007, which is a combination of an inhaled corticosteroid, desymide, and a long-acting beta-agonist, formoterol. She respectfully requested that the Committee consider a review of the combination product for asthma and consider adding Symbicort® to the PDL.

Dr. Lee asked what the review policy is on new drugs released in the market.

Dr. Monaghan stated that new drugs that are released that fall within an existing PDL category are reviewed. New drugs that are released that do not fall with a PDL category are available without restriction.

Jeff Monaghan stated that it is the recommendation of DHCFP and First Health that no changes be made to drug categories 1 through 36. If the Committee would like to have any of these classes reviewed, they will be agendized for a future meeting.

B. Committee Discussion and Approval of Drug Classes without changes for the PDL

MOTION: Michael Karagiozis motioned to accept First Health's recommendation that no changes be made to the PDL in drug classes 1 through 36.
SECOND: Rudy Manthei
VOTES: Unanimous
MOTION CARRIED

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

Jeff Monaghan reviewed the report.

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

The next meeting is scheduled for Thursday, September 25, 2008, in Reno.

Ms. Lawrence stated that because the majority of members are in Las Vegas, she will poll the members via email regarding their preference to have the meeting in Las Vegas or Reno.

XV. Public Comment

No comment.

XVI. Adjournment

MOTION: R.D. Prabu motioned to adjourn the meeting.
SECOND: Justin Holt
VOTES: Unanimous
MOTION CARRIED

Meeting adjourned at 3:34 p.m.