ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

Location of Meeting
Frontier Building, 3601 C Street, Room 890/896

MINUTES OF MEETING
April 20, 2018
8:00 a.m.

Committee Members Present:
Jeffrey Demain, MD, Chair
Robert Carlson, MD, (telephonic)
Charles Ryan, MD
Claudia Phillips, MD (telephonic)
Diane Liljegren, MD (telephonic)
Erin Naris, PharmD
Jay Butler, MD
John Riley, PA (telephonic)
Robert Carlson, MD
Ryan Ruggles, PharmD
Trish White, R.Ph. (telephonic)

Committee Members Absent:
Denise Evey, PharmD (excused)
Vincent Greear, R.Ph. (excused)
Jenna Hiestand, MD (telephonic)

Others Present:
Umang Patel, PharmD, Magellan Medicaid Administration
Elaine Edwards, Magellan Medicaid Administration
Jacob Kelly, MD (telephonic)
Colette Grower, Kron Associates

1. Call to Order – Chair

Dr. Jeffrey Demain welcomed everyone and called the meeting to order at 8:08 a.m. *Industry comments would be taken on red and blue classes only and were limited to three minutes. John McCall has accepted another position and will be replaced by Elaine Edwards at the next meeting.*

2. Roll Call

The roll call was taken, and a quorum was present. New committee members were introduced and welcomed.

3. Public Comments - Local Public/Health Practitioners

Dr. Demain provided general instructions for providing comment. For public comment and for health professionals that are local, we can either have you speak up front in the beginning or you can speak with your section. For industry representatives, it's when we come to that section of our agenda and the discussion is limited to three minutes, and we appreciate you adhering to that time limit.

4. Class Review, Discussion & Vote

Dr. Demain introduced Dr. Umang Patel from Magellan Medicaid for his April Pharmacy and Therapeutic (P&T) drug list. Dr. Patel stated that he will go over the major disease states, as a description; then relevant guidelines and changes; discussing market basket--new agents, new indications or new major studies, if applicable; market basket agents and utilization reviews; and, the last will be discussion and decision for the committee.

Just to refresh, there are three major color categories -- red is for new drugs to the market, blue is for any significant changes or information and green is for no significant changes.

The three drug sub-classes we will discuss today are cardiovascular, anti-infective, and genitourinary.

4-A. Cardiovascular: ACE-Inhibitors & Renin Inhibitors (Green Class); Angiotensin Receptor Blockers (ARB) (Red Class); Angiotensin Modulator/CCB Combinations (Blue Class); Antianginal and Anti-ischemic agents (Green Class); Anticoagulants (Red Class); Beta-Blockers (Blue Class); Calcium Channel Blockers (Blue Class); Erythropoiesis Stimulating agents (Green Class); Lipotropics, other (Blue Class); PCSK-9 Inhibitors (Red Class); Platelet Aggregation Inhibitors (Green Class); Pulmonary Arterial Hypertension (Blue Class)

Cardiovascular - ACE Inhibitors & Renin Inhibitors (Green Class)

Public Comments

Dr. Patel gave the Magellan presentation on hypertension. Approximately 85 million or 34% of adults in the United States have high blood pressure, along with 1 of 3 American adults having prehypertension. The highest prevalence is among African-American men and women at 40.3% and 42.9%, respectively. It is an independent risk factor for cardiovascular disease and can lead to heart failure and stroke, if uncontrolled for a prolonged period. It is estimated that hypertension is controlled in only 54.4% of patients with this condition. Dr. Patel went on to discuss the treatment guidelines from JNC-8, 2014; the American College of Physicians (ACP) and Academy of Family Physicians (AAFP) 2017; and, the American College of Cardiology (ACC) and American heart Association (AHA), 2017.

Per the Agenda, we will now talk about the ACE Inhibitors and Renin Inhibitors, Angiotensin Receptor Blockers (ARB) and Angiotensin Modulator/CCB Combo. Please note that the utilization sheet provided in the presentation contains a year's worth of data, which will allow committee members to see all claims regardless of seasonal changes and will provide a better view over the year.

The data in the sheets in front of you only provide data from October to December, 2017. Then the utilization rates for ACE Inhibitors & Renin Inhibitors were reviewed.

Dr. Demain asked if anyone has any comments.

Dr. Jacob Kelly - responded via telephone and stated that he had some brief comments. He wanted to comment on the Angiotensin Receptor Inhibitor, Entresto. He has a handful of patients with Medicaid on this medication. This is the medication reduces heart failure, reduces the number of patients that need defibrillators and even DRT devices. So, any and all access by our Medicaid population to this medication is probably reducing downstream costs, because I know it's an expensive drug. So, I would like to express my favor for continued easy access to this medication. Thank you for that consideration and I'd be happy to answer any questions the Committee may have about that.

Dr. Demain thanked Dr. Kelly for his comments. He noted that his comments pertain to the ARB medications and they will actually talk about that in a moment and have noted his comment.

Concerning the ACE Inhibitors, Dr. Demain asked if there are any questions or discussion for Dr. Patel. Hearing none, Dr. Demain shared a comment from earlier that there has been an update to the Guideline that the hypertensive goal now is 120/80 and greater than that should be considered for therapy, as opposed to 130/90. He believes that the American College of Physicians came out with that guideline about a month ago.

This is a Green Category. So, please review last year's motion.

Dr Patel stated that last year's motions for all three sub-groups are in his presentation. He offered to continue with his presentation so the discussion and decision can be made as a group, or the discussion can be broken down individually.

Cardiovascular - Angiotensin Receptor Blockers (ARB) (Red Class)

Public Comments

Mary Kemhus, from Novartis - she discussed Entresto, which Dr. Kelly commented on earlier. Last year she shared that Entresto was added to the AAHA, ACCP Guidelines, with a Class I recommendation, which is their highest to further review target mortality and hypertensive heart failure and reduce ejection fraction.

Today she would like to highlight a couple other things about Entresto and why it should be available to Alaska Medicaid clients through unrestricted access. The mortality rates of heart failure remain quite high. About 25% of heart failure patients are re-admitted to the hospital within 30 days of being discharged. And over 50% of patients die within 5 years of their diagnosis.

Entresto is the first drug in over a decade to demonstrate clinical and statistical ability with ACE Inhibitor, which, normally was considered the standard of care for heart failure with ejection fraction patients. The Paradigm Heart Failure Trial was the largest heart failure trial to date, showing a 20% reduction in the primary composite and it also showed a 30-day heart failure re-admission rate reduction of 38%. Several more recent analyses actually have demonstrated an improvement in heart

failure symptoms, including fatigue and shortness of breath, as well as other health quality of life indicators including physical and social function.

Finally, Entresto has a tolerable safety profile compared to ACE Inhibitor. It's important to note the Entresto should not be administered concurrently with any ACE Inhibitor, it's meant as a replacement for ACE Inhibitor/ARB. So, if you pass Entresto today, I would like you to please remember MAL guideline Therapy for heart failure with ejection fraction, it demonstrates superiority in standard of care and emerging data supports and prevents marketing study. I would be happy to take any questions, if you have them.

Dr. Demain asked if anyone had any questions for Mary. Hearing none, Dr. Demain thanked Mary for her testimony. Dr. Demain asked Dr. Kelly if he had any additional comments. There was no response, as he had left the call.

Dr. Patel continued. The reason this is a Red Class is because there is a new delivery system. A new medication named Prexxartan. It's a Valsartan Oral Solution.

The main indications for this medication are Hypertension in adults and children ≥ 6 yo to lower blood pressure; Heart Failure with a NYHA Class II-IV for patients who are unable to swallow Valsartan tablets--it has been shown to reduce hospitalizations; lastly, stable in left ventricular failure or dysfunction following an MI. It has been shown to reduce mortality in patients who are unable to swallow valsartan tablets. Prexxartan is FDA approved as of January 2018, but it is not on the pharmacy shelves yet. Medicare Pharma has planned it for the first half of the 2018 launch.

Dr. Demain asked if there are any questions for Dr. Patel regarding the ARBs? Hearing none, we will move on to our next group, which is the combined agents and then we'll talk about the class completely.

Cardiovascular: Angiotensin Modulator/CCB Combo (Blue Class)

Next are the Angiotensin Modulators with Calcium Channel Blockers (CCB). The utilization information is presented in two different combos. The top shows the ARB with CCB that have 25% non-preferred claims and 75% non-reviewed. The bottom is showing ACE Inhibitors and CCB of which 97% claims are preferred and 3% are non-preferred.

Dr. Demain noted that this is one of the few classes that we have not had overwhelming majority in our preferred category and was curious as to why. He asked Dr. Erin Narus if she could address that or provide insight as to how we could do better.

Dr. Erin Narus with the State of Alaska commented that they do look at trends with regard to utilization. In particular we look at the on and off, there are some combination products that are being used over some of the single ingredient products. So, there may be potentially a cost benefit situation. But, it does give an opportunity to look at the utilization trends within this particular combination class. It's a fairly small utilization pool, so the largest utilization is the Amlodipine/Valsartan -- (indiscernible) combination, which is currently listed as off.

Dr. Demain commented that in the past, historically, that if two products are approved, for example Valsartan/Amlodipine, if those are both on the formulary, the combination agent comes on, provided it's not a cost inhibitor? Is that still true?

Dr. Narus responded that generally with this particular reference of the PDL, this is from the 2015 and doesn't necessarily reflect the current PDL that had public comment close on March 26, 2018, so, the PDL that is going through the regulatory process, may have looked at this particular trend to evaluate that.

Dr. Demain provided a brief reminder for those that are new to our process, we have medically necessary--meaning that if a medication is required, and not a preferred agent, medically necessary can be written on the prescription and it will be filled, unless it's involved in a drug utilization review. So, any other comments or questions?

Dr. Ryan Ruggles mentioned that he sees that the brand name product is preferred, but the pharmacies are using the generic, and that's what's leading to that as well. Dr. Demain responded that that was a good observation. Any other comments or questions?

Dr. Diane Liljegren asked about Entresto. Where is that going to fall or are we not looking at that.

Dr. Narus commented that she can't speak specifically, but she believes that the will of the Committee was taken into consideration when building the new PDL. Since that particular PDL is going through the regulatory process, it is currently on the public notice web site for prescribers to be able to review and take a look at. It's continuing through that process.

Dr. Liljegren commented that if we order it, we just put medically necessary then? Dr. Narus responded that she is not sure if it is on the interim suspend list or not. But it is available and we do have utilization on it. Someone noted that Entresto is listed as interim. Dr. Liljegren thanked Dr. Narus for the information.

Dr. Demain stated that if there were no other comments, he asked that the previous motion be read. Dr. Patel responded that at the last review on January 20, 2017, a motion was made that for all three subgroups, therapeutic alternatives to include at least: One ACE-inhibitor; One ARB; One ARN agent. It passed unanimously.

Dr. Demain opened the floor to further questions, comments or motions.

DR. RUGGLES MOVED THAT FOR ALL THREE SUBGROUPS, THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST: ONE ACE INHIBITOR; ONE ARB; AND ONE ARN AGENT. IT WAS SECONDED BY DR. RYAN.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: Antianginal and Anti-Ischemic (Green Class)

Public Comment

Per Dr. Demain, because this is a Green Class, there will not be any public testimony.

Dr. Patel proceeded with his presentation. Approximately 610,000 people die of heart disease every year (equating to about 1 ~ 4 deaths). Coronary heart disease is the most common type of heart disease killing approximately 370,000 people annually. This is the leading cause of death for both men and women. Every year about 735,000 Americans have a heart attack. Of these, 525,000 are a first heart attack and 210,000 happen in people who have already had a previous episode. It presents as chest discomfort, including burning, heaviness or a sensation of choking; or pain in the jaw, neck, ear and shoulder. Symptoms include nausea, short of breath or sweating. The utilization reports were reviewed. At the last review on January 20, 2017, the motion was a class effect. The motion passed unanimously.

Dr. Demain opened the floor to further questions, comments or motions.

DR. RUGGLES MOVED THAT ANTIANGINAL AND ANTI-ISCHEMIC BE MOVED A CLASS EFFECT AND IT WAS SECONDED BY DR. RYAN.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: Anticoagulants (Red Class)

Public Comment

Dr. Demain read the following comments received via email:

Dr. Craig Skinner: In regards to the anticoagulant class, I think it is necessary to have at least Rivaroxaban and Apixaban on formulary for our Medicaid patients. Thank you, Craig Skinner, PharmD, BCACP, Alaska Family Medicine Residency Faculty, Providence Family Medicine Center

Dr. Steven Compton: Just wanted to drop a note to encourage coverage for non-popular aFib, our preference is in order for clinical safety and utility, are Apixaban, Rivaroxaban, and Dopigatran. Unlikely we will use much edoxaban. Steven Compton, M.D., FACP, FACC, FAHS, Chief of the Alaska Heart and Valve Vascular Institute.

Dr. Demain recognized the industry speakers who also wanted to provide comment starting with Dr. Mae Kwong with Jannsen.

Dr. Mae Kwong, pharmacist, Jannsen Scientific Affairs - her comments concern Xarelto, a direct oral anticoagulant. First, she noted that the prescribing information has been updated to include a new indication--the reduction of risk of recurrent of deep vein thrombosis (dvt) and in patients that continued risk after completion of initial treatment last six months based on findings of the Einstein Choice Study in which Xarelto, 10 mg daily result in a 74% reduction VTE compared to aspirin--the

comparable rates of major bleeding. The label change now reflects the 10 mg dose for extended treatment. In December, Jannsen filed a supplemental new drug application (NDA) with the FDA for the reduction in risk of major cardiovascular events in patients with chronic coronary artery disease (CAD) and a peripheral artery disease (PAD) into a use of acute ischemia in patients with PAD based on the compass clinical trials. That involved more than 27,000 patients. And it was stopped a year early due to overwhelming efficacy in the group receiving the vascular dose of Rivaroxaban of 2.5 mg twice daily in combination with aspirin. Xarelto reduced the risk of major events by 24% vs. aspirin alone. This benefit was seen on top of patients being on standard of care, about 90% of patients were on statin, 70% on ACE and ARB, and another 70% on beta blockers. If approved, rivaroxaban will be the only direct oral anticoagulant indicated for patients with CAD or PAD.

A breadth of real world evidence has demonstrated the consistent safety and effectiveness to the clinical registration program and non-verifiable patients. A recent study is the FDA's mini-sentinel published this year in comparison to Warfarin that has a ratio for increased GI bleeding with similar to the hazard ratio up there in the rocket pivotal study. More importantly, Xarelto was associated with a significantly lower rate of ischemic stroke with a hazard ratio of .61. Xarelto is being studied in ongoing paid gray trials for BTE prophylactics in the medically ill population. BTE treatment, as well as prophylaxis in cancer patients, as well as in patients with chronic heart failure and CAD. Plus, there is potential for several additional indications for Xarelto over the next 1 to 3 years. Thank you for your time and consideration to keep Xarelto available to Alaska Medicaid patients. I'm happy to take any questions. Thank you so much.

Dr. Demain thanked Dr. Kwong and asked if anyone has any questions for Dr. Kwong. There were no questions from committee members. Dr. Demain offered for Dr. Kwong to stay on the line in case questions come up later in the discussion.

Steven Hall, pharmacist and Associate Director with Health Economics and Outcome Research, Boehringer Ingelheim Pharmaceutical - He is here to provide testimony regarding the dabigatran capsules or Pradaxa. Dabigatran is the first and only NOAC with a specific reversal agent. It has a unique methodized action. Dabigatran is a competitive direct thrombin inhibitor. As a side note, the American Hospital Formulary System, or AHFS, re-affirms this in their new coding system. Dabigatran is listed as a direct thrombin inhibitor while other direct factor Xa inhibitors. It's indicated to reduce the risk of stroke ischemic embolism in patients with NVAF, through the treatment of GPTPE in patients who have been treated with parental anticoagulant for 5-10 days. Also, to reduce the risk of recurrence of DVT and PE in patients who have been previously treated and for the prophylactics of DVT and PE in patients who have undergone hip replacement surgery. Quickly, from a safety standpoint, there was a black box forming regarding discontinuation, which increases the risk of thrombotic events. As with any anticoagulant, if any coagulation is discontinued for any reason, other than pathological bleeding or completion of a course of therapy, coverage with another anticoagulant should be considered.

Also, epidural or spinal hematoma re-occur in patients treated with dabigatran who are undergoing spinal puncture. So, also contraindicated in patients with active pathological bleeding. Known serious hypotensive reaction and mechanical prosthetic heart valve. It's the most studied NOAC from a real-world analysis perspective. And real-world analysis results are very consistent with the results seen in the real-life trial, which was the basis for FDA approval. Further, as mentioned previously, many of the reversal agents specific for dabigatran is available known as idarucizumab or the brand name

Praxbind. When reversal of the anticoagulant effect in dabigatran is needed for emergency surgery, urgent procedures or in life threatening or uncontrolled bleeding, idarucizumab long antibody fragment binding the dabigatran with thrombosis.

So, one dose is recommended for all patients and dabigatran can be reinitiated 24-hours after idarucizumab is administered. This is critical, since reversing the anticoagulant effect of dabigatran exposes patients to thrombotic risks of their underlying disease. Therefore, to reduce this risk, it is important to resume anticoagulation as soon as it is medically appropriate. Notably, earlier this week, the FDA provided full approval for idarucizumab. The FDA granted accelerated approval in October, 2015, but continued approval contingent upon results from the Phase III Re-Verse AD Trial, the large study to investigate a reversal agent for a NOAC. The final results of Re-Verse AD were published in the New England Journal of medicine in July, 2017, and show that idarucizumab immediately reversed the anticoagulant effect of dabigatran. Thank you for your time and interest. And I'm happy to address any questions that you may have. And I respectfully request that Pradaxa retain its preferred formulary status. Thank you.

Dave Gross, Medical Affairs, Pfizer - he wanted to give the committee a brief update on Eliquis or apixaban and ask that you continue to maintain it on the Medicaid PDL. Eliquis is FDA approved to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (AF). Additionally, it's approved for the treatment of DVT and PE and to prevent re-occurrence following initial therapy and lastly for the prophylaxis of DVT in patients who have undergone hip or knee replacement surgery. As stated by one of my colleagues, I'll state the same thing, because it's a category issue, is that apixaban has a black box warning regarding increase risk of thromboembolic events if it's prematurely discontinued. And risk of spinal hematoma in patients undergoing neuraxial anesthesia or spinal puncture. In addition, the most common adverse events are related to bleeding, so providers are advised to evaluate symptoms of blood loss promptly. And lastly, it's contraindicated in use in patients with prosthetic heart valves.

In a head to head study vs. Warfarin, the Aristotle Trial, in patients with non-valvular AFib, and at least one additional risk factor for stroke, apixaban demonstrated statistically significant superiority vs. warfarin in both reduction in risk of stroke and systemic embolism and risk of major bleeding. While there are no randomized controls head to head clinical trials comparing the efficacy of apixaban vs. the other direct oral anticoagulants, there are many real world observational studies and indirect comparisons that exist in the literature. And I'll, because of lack of time, I will review one of those in a moment.

One thing I'd like to point out is that it's important to note that these real world observational studies are designed to establish association and not causation. They also do not imply interchangeability or establish comparative clinical efficacy or safety. That said, real world observational studies may add context for policy makers such as yourselves, whose primary focus may include an evaluation of the risk benefit profile of medications as they are used in clinical practice populations. So, these real-world data observational studies, they take data from very large claims data bases and then compare groups, but it's not randomized, control pit-hit (ph) trial like you have for FDA approval.

So, in one recently published analysis, of which I will review here, researchers compared a match cohort of adult non-valvular AFib patients who were prescribed either apixaban, rivaroxaban, or dabigatran. Using the IMS PharMetrics Plus database of retrospective cohort analysis evaluated rates

of all cause and major bleeding related hospitalizations. All cause healthcare and inpatient costs and bleeding related medical costs among anti-coagulant naive NVAF patients, who were prescribed apixaban, rivaroxaban, dabigatran or warfarin. And this was a two-year time frame that they looked at. Using one-to-one propensity score matching method, three cohorts were created. Apixaban vs. rivaroxaban, which included 8,000 patients; apixaban vs. dabigatran, which included about 5,400 patients; and apixaban vs. Warfarin, which included nearly 10,000 patients.

When compared to apixaban, the adjusted risk all-cause hospitalization was statistically significantly greater for patients treated with rivaroxaban, dabigatran, and warfarin. And major bleeding related hospitalizations were significantly greater for patients treated with rivaroxaban, dabigatran, and warfarin. Adjusted total all-cause healthcare cost and total major bleeding related medical costs, were statistically significantly lower for patients treated with apixaban vs. rivaroxaban or warfarin, but there was not a significant difference between dabigatran. In closing, there are several of these real-world data observational studies out there. I suggest you reach out and look at them, since we didn't have time to talk today. And, I think that you would agree that it would be important to continue covering apixaban on the Medicaid PDL. Thank you very much. If you have questions, please holler.

Dr. Demain thanked Dr. Gross and asked committee members if they had any questions. He also commented that the committee will talk about some of the studies he mentioned in a few minutes. Since there were no questions from the committee members, Dr. Demain moved on and asked if anyone else wanted to speak on anticoagulants. No one responded, so they moved on to discuss real world studies.

Dr. Patel presented his information on Anticoagulants and started with a description of the disease. Venous thromboembolism (VTE) is a significant public health problem in the United States (U.S.). It manifests as deep vein thrombosis (DVT) and pulmonary embolism (PE) and is a major consequence of various surgical procedures and medical conditions. DVT occurs when a thrombus composed of cellular material bound together with fibrin strands forms in the deep venous portion of the extremities, most commonly the legs.

The exact number of patients impacted by DVT and PE is unknown; however, it is estimated these conditions affect between 300,000 and 600,000 people in the U.S. every year. If left untreated, approximately 30% of patients who develop PE will die within the first few hours of the event. Generally, the risk of VTE increases with the number of risk factors present, major trauma, and age. Due to the risk of morbidity and fatal PE associated with DVT, prophylaxis has become the standard of care for patients at high risk for thrombosis.

Dr. Patel presented the treatment guidelines form the 10th American College of Chest Physicians (ACCP), 2016. It is broken down by the following disease states: orthopedic surgery (total hip replacement or knee replacement); VTE; DVT of leg or PE and no cancer; cancer. One of the new agents now on the market is betrixaban, brand name Bevyxxa.

The indication for this is the prophylaxis of VTE in adult patients hospitalized for acute medical illness who are at risk for thromboembolic complications due to moderate or severely restricted mobility. There is a black box warning for the increased risk of spinal/epidural hematoma when neuraxial anesthesia or spinal puncture is performed. The limitations are: effects during labor and delivery are unknown; should be used with caution during pregnancy; safety and efficacy has not been studied in

patients with prosthetic heart valves or pediatric patients; and there are no reversal agents. The only current therapy right now for reversal is fresh frozen plasma and active red blood cells for bleeding. The dosage was then outlined. The utilizations were reviewed. At the last review on January 20, 2017, the motion was made that therapeutic alternatives to include: One oral agent; One injectable agent; warfarin. The motion passed unanimously.

Dr. Demain opened the floor to further questions, comments or motions.

Dr. Liljegren commented that, in her opinion, rivaroxaban and apixaban are superior to the other NOACs, especially apixaban. Because of its safety, and it's not as renally excreted, you can use it in older patients. So, she would like it considered specifically.

Dr. Demain noted that the utilization seems to be fairly split between that and the rivaroxaban (Xarelto). They're both pretty good drugs. The reversibility issues may have some importance as well. Any thought about the ability to reverse?

Dr. Ruggles commented that in Alaska there are some situations where reversibility could be really important. However, with the others, in his experience, depending how emergent the situation, not taking the drug for a fairly short period of time, ends up being okay for the patient. It is his understanding that the State looks at past utilization as a consideration to move forward as well.

Ms. Narus confirmed that the State does take into consideration the comments received from Committee Members, clinical studies that are out there, and input from local medical professionals when making their decision about the formulary.

Dr. Demain noted that in the past, these agents have had consideration for very specific situations. But over the years, they've really broadened and their indications are parallel. Is that true? Ms. Narus answered, yes. Dr. Liljegren asked if the committee could include at least one NOAC that can be used for PE. Dr. Demain thought that that was a good suggestion.

DR. LILJEGREN MOVED THAT THERAPEUTIC ALTERNATIVES TO INCLUDE ONE ORAL AGENT, ONE INJECTIBLE AGENT, ONE NOAC THAT CAN BE USED FOR PE, AND WARFARIN. IT WAS SECONDED BY DR. RUGGLES.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: Beta-Blockers (Blue Class)

Public Comment

There was no public comment for this item.

Dr. Patel continued his presentation on beta blockers. One of the prime reasons why there was a treatment guideline update specifically for safety management by the American College of Cardiology (ACC), 2017. Beta blockers are recommended as first-line for long-QT Syndrome (LQTS) and suspected arrhythmic syncope, if no contraindications. Beta-blockers that lack intrinsic

sympathomimetic activity are recommended with catecholaminergic polymorphic ventricular tachycardia (CPVT) and stress-induced syncope. Beta-blockers might be reasonable in patients with recurrent vasovagal syncope (VVS). If syncope continues, flecainide, verapamil, fludrocortisone, midodrine, droxidopa, pyridostigmine, octreotide, or selective serotonin reuptake inhibitors (SSRI) may be options in select patients. The utilization report was reviewed. The motion from the last review on January 20, 2017, was made that a class effect to include both carvedilol and metoprolol succinate. The motion passed unanimously

Dr. Demain recalled that pharmacists seemed to prefer nebivolol (Bystolic). Hearing no other comments or questions, Dr. Demain asked if there was a motion.

DR. RYAN MOVED THAT A CLASS EFFECT INCLUDE BOTH CARVEDILOL AND METOPROLOL SUCCINATE. IT WAS SECONDED BY DR. RUGGLES.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: Calcium Channel Blockers (Blue Class)

Public Comment

There was no public comment on this item.

Dr. Patel continued his presentation by going directly to the utilization chart. He stated that 99% of claims are preferred and 1% of claims are non-preferred. The reason for this to be a blue status is nimodipine did come out with a new formulation named Nymalize. It is 30 mg/10 mL unit-dose cup for the treatment of subarachnoid hemorrhage. It is designed specifically for patients who require a dosage that is lower than the standard 20 mL (60 mg) dose.

Dr. Demain confirmed that it is the same concentration, just in a smaller cup. The motion from the last review on January 20, 2017, was that therapeutic alternatives to include at least: one short acting agent; one extended release agent; one nondihydropyridine agent. The motion passed unanimously.

Dr. Demain asked if there were any questions, comments, or a motion.

DR. RYAN MOVED THAT THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST: ONE SHORT ACTING AGENT; ONE EXTENDED RELEASE AGENT; ONE NONDIHYDROPYRIDINE AGENT. IT WAS SECONDED BY DR. RUGGLES.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: Erythropoiesis Stimulating Agents (Green Class)

Public Comment

There were no public comments on this item.

Dr. Patel continued his presentation by discussing anemia, which is a frequent complication affecting over 3 million Americans. It is associated with serious diseases, such as chronic kidney disease (CKD), diabetes, heart disease, and cancer, as well as chronic inflammatory conditions like rheumatoid arthritis or inflammatory bowel disease. Erythropoietin is a glycoprotein produced in the kidneys that stimulates RBC production from bone marrow. Acts on the erythroid progenitor cells in the bone marrow to cause late differentiation and maturity of the RBCs. Endogenous production of erythropoietin by the kidney is normally regulated by the level of tissue oxygenation. Hypoxia and anemia generally increase the production of erythropoietin, which in turn stimulates erythropoiesis.

In normal subjects, plasma erythropoietin levels range from 0.01 to 0.03 units/mL and may increase 100- to 1000-fold during hypoxia or anemia. However, patients with CKD have impaired production of erythropoietin, which is the primary cause of their anemia. Dr. Patel went on to discuss the treatment guidelines using erythropoiesis stimulating agents, as per the National Comprehensive Cancer Network (NCCN), 2017, and the American Society of Clinical Oncology (ASCO) and American Society of Hematology (ASH), 2010. The utilization rates were reviewed. The motion from the last review on January 20, 2017, was made that the drugs in the class were therapeutic alternatives. The motion passed unanimously.

DR. PHILLIPS MOVED THAT THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. IT WAS SECONDED BY DR. RUGGLES.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: Lipotropics, Other (Blue Class)

Public Comment

No public comment on this item.

Dr. Patel continued his presentation about lipotropics, other. He commented that he will be transitioning into a discussion of PCSK-9 inhibitors, so there is some overlap for background information. In terms of disease state, the National Health and Nutrition Examination Survey (NHANES) reported that in 2015 to 2016 approximately 12.4% of adults had high total cholesterol (≥ 240 mg/dL) and 18.4% had low HDL-C (< 40 mg/dL). This was found to be higher in women (13%) compared to men (11%). Many clinical trials have demonstrated that a high serum concentration of low-density lipoprotein cholesterol (LDL-C) and low levels of high-density lipoprotein cholesterol (HDL-C) are major risk factors for coronary heart disease (CHD).

There were three major studies--the AIM-HIGH study, the ACCORD trial, and the IMPROVE-IT study--conducted. All were very detailed and Dr. Patel provided a high-level summary. The AIM-HIGH Study enrolled a high-risk group of patients with established atherosclerotic CV disease and atherogenic dyslipidemia. These patients received either simvastatin or simva+niacin. The primary end point for this was time to first occurrence for coronary heart disease death, non-fatal MI, ischemic stroke, hospitalization for acute coronary syndrome or symptom driven coronary or cerebral

revascularization. This study showed, essentially, that the reduction in non-HDL and levels of niacin therapy did not further reduce ASCV risk in individuals treated to LDL-C levels of 40 to 80 mg/dL. As a result, Advicor, which was the niacin er lovastatin combo, and Simcor, which was the niacin er simvastatin combo were taken on the market in 2015 by the manufacturer.

The second trial, the ACCORD Trial looked at adults with Type 2 diabetes on statin mono therapy and to determine if the addition of fenofibrate does or does not reduce CVD end points. The primary outcome was for first non-fatal MI, non-fatal stroke or non-CVD mortality. This study found that patients with and without CV disease, the additional of fenofibrate to simvastatin therapy did not reduce the risk for CV event compared to simvastatin alone.

Lastly, the IMPROVE-IT study looked at patients greater than 50 years of age, either gender, hospitalized in the previous 10 days for ACS, which is defined as acute MI with or without ST elevation, or high-risk angina, LDL > 50 or fasting triglycerides < 350. The primary outcome was CV mortality, major CV event or major non-fatal stroke. The average additional reduction of LDL in this study of 17 mg/dL with the addition of ezetimibe to simvastatin. This study found that a significant reduction in MI and ischemic stroke and a nonsignificant increase in risk of hemorrhagic stroke were also reported with this combination therapy.

Dr. Patel then discussed the treatment guidelines from the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE), 2017, and the American Diabetes Association (ADA), 2017. The utilization rates were reviewed.

Dr. Demain commented that it seems that the use of fenofibrate did not provide any additional benefit as reported. But it still makes up about 21% of prescriptions, right? Dr. Patel clarified that the ACCORD trial was in addition to statin for those high-risk individuals. But the American Association of Clinical Endocrinologists do recommend fenofibrate for high-triglyceride levels as well.

There were no other questions or comments. The motion from the last review was that therapeutic alternatives to include at least one drug from each subclass. The motion was passed unanimously.

DR. RUGGLES MOVED THAT THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE DRUG FROM EACH SUBCLASS. IT WAS SECONDED BY DR. RYAN.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: PCSK-9 Inhibitors (Red Class)

Public Comment

Dr. Sylvia Churchill, pharmacist, Health Outcomes and Pharmical Economics, Amgen - I am here to talk about the PCSK-9 class. We make evolocumab (Repatha). In the last year, we did complete our 27,500 patient outcomes trial, which did show that 50-60% decrease in LDLs does translate into a decrease in the incidents of heart attack and stroke. That's one of the big think that people want to see. Not just that it lowers LDL, but that it translates to a decrease of cardiovascular events. That's a big deal and the FDA did add that to the label in December, 2017. I do want to focus on the prior off criteria that our in PCSK-9s, because I know that they will be discussed this afternoon.

There are two things that I'd like to bring up. One is the requirement for patients to have to step through two high-intensity statins before they can be considered for a PCSK-9. Now for efficacy, if you have all high-intensity statins should get you an approximately 50% decrease in LDL. If one does not get you to goal, changing to another one is not going to make any difference. In fact, even doubling the dose of the statin will only decrease your LDLs by an additional 6% on average. It's called the rule of 6's. So, for efficacy, it's better to step through just one high-intensity statin. For tolerance, that's a different story. If the patient is having muscle aches, with one statin, it's reasonable to try another because they do have differences in the incident of muscle symptoms.

Then the second think I'd like to see considered removed from the criteria is to have ezetimibe (Zetia) before you would use a PCSK-9. Zetia and the PCSK-9s are very different types of medications. Zetia decreases the absorption of cholesterol in the gut, so it's more of a topical effect, and the increase in LDL is much less dramatic that what you see with the PCSK-9--about 15-20%. Whereas, with the PCSK-9, it's about 50-60%. So, what most physicians do, is they always want to start with the statin and get them on the maximally tolerated dose you can and then, if you're not at goal at that point, the physician either wants to choose they would add Zetia, if you're close to goal and you have maybe 15-20% decrease to go, but if you still have a long way to go, that's where a provider would prefer to start with a PCSK-9. Making them step through ezetimibe when it's only going to decrease it a little bit, just adds time, hassle and yet one more medication to the patient's therapy. So, being able to choose rather than having to step through.

Dr. Demain asked what was the dosing interval for Repatha. Per, Dr. Churchill, it's every two weeks. It can also be given once a month. They're equally effective. It's just patient preference. No further questions.

Dr. Patel continued his presentation by discussing the PCSK-9 Inhibitors. He mentioned the Fourier study, a double-blind, multi-center center, granulized double-blind trial that took place in 1200 sites in 49 countries. The study looked at patients who are 40-85 years of age, clinical evidence of atherosclerotic disease, major risk factors for CV events and minor risk factors for CV events. The primary outcomes measured were major CV events defined as CV death, MI, stroke, hospitalization for unstable angina or coronary revascularization. Repatha was added to moderate or high-intensity statin therapy in patients with established atherosclerotic disease results and was found modest reductions in CV events, including MI and stroke. As a result, there was a 59% reduction in LDL levels and a 15% reduction in CV risk based on composite of CV death, MI, stroke, hospitalization for unstable angina, or coronary revascularization. The utilization was reviewed.

Dr. Demain noted that it reduced LDL, but does it actually reverse atherosclerotic plaque formation? Do you see regression, or is that not the case? Dr. Patel didn't believe so.

Dr. Churchill, it's a monoclonal antibody. With evolocumab, there was a study done specifically to look at if being on evolocumab will the decrease the size of atherosclerotic plaques in the body. And that was doing ultrasounds. I don't know all of the study, it's called Glygol. They did show that with use of evolocumab, the size of those plaques actually decreased over time. So that confirms how the LDL decrease is translating into less plaques, then less heart attack and less strokes.

Dr. Demain asked Dr. Novus if there are some specific criteria for who would not so much qualify to get the drug through DUR, but is there a strict criterion for this is the patient to consider this therapy in? Or, how rigid is that criteria.

Per Dr. Novus, those criteria are being reviewed by the DUR committee this afternoon. There are some vacancies, especially with the additional studies such as the Fourier study. They are being reviewed and we do take all of the comments received here. So, there are some considerations for updating those criteria to make sure they are the most reflective of the gestation population.

Dr. Demain you must monoclonal antibodies. You meet this, this, and this criteria. And that's been really accepted as practice parameter throughout that specialty.

Any other questions or comments? Dr. Ruggles had a question about the data provided in the presentation. Was it for a year or for three months? Dr. Patel responded that he needed to verify the information. Dr. Ruggles stated, no need to do so.

There were no other questions. At last year's review on January 20, 2017, it was moved a class effect. It was passed unanimously.

DR. RUGGLES MOVED THAT A CLASS EFFECT. IT WAS SECONDED BY DR. RYAN.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: Platelet Aggregation Inhibitors (Green Class)

Public Comments

There were no public comments for this item.

Dr. Patel continued his presentation in terms of platelet aggregation inhibitors, just a little bit of background. CV disease causes approximately 30% of all deaths in the United States (U.S.) in 2014. Death rates attributable to CV disease have decreased by 25% in the 10-year period from 2004 to 2014. Stroke is the 5th leading cause of death in the U.S. Inhibitor effects on platelet aggregation have led to a significant decrease in the rate of vascular events for both primary and secondary CV prevention trials. Aspirin has been shown to reduce CV morbidity and mortality in both primary and secondary prevention trials. A small percentage of patients with CV disease have aspirin resistance and, therefore, may be at higher risk for CV events. The failure to prevent a thrombotic event, the inability to inhibit platelet thromboxane formation, or the inability to cause prolongation of bleeding time. Guidelines for the management of aspirin resistance have not been developed. It is unknown if aspirin resistance can be overcome by increasing the dose of aspirin or adding another agent.

Dr. Patel then discussed the treatment guidelines, per the U.S. Preventative Services Task Force (USPSTF), 2016, and American College of Chest Physicians (ACCP), 2012. The utilization was reviewed.

Dr. Demain commented that Dr. Patel didn't review in the one-year post myocardial infarction, there is a recommendation for two agents for one year. Then, aspirin after that. Is that a preferred agent in that case in addition to aspirin? Guidelines state you could use two platelet aggregation inhibitors for that one-year post-MI period. Is there a preferred--could it be clopidogrel or whether it be Brilinta?

Per, Dr. Patel, he doesn't believe there was preference placed on one or the other.

Per Dr. Demain, this shows Brilinta is not preferred, but on this sheet, it shows that it is. Unless I'm missing something. Per Dr. Novus, the utilization sheet shows the committee the direction that the PDL will look.

Elaine Edwards from Magellan stated that currently, Brilinta is on the formulary as non-preferred and clopidogrel is preferred.

Dr. Demain, does this reflect what our vote was last time? That it has not been enacted yet? Per Dr. Novus, it is in the review process. So, we're reviewing it before our last review was approved.

No other comments or questions. The motion made at the last review on January 20, 2017, was that therapeutic alternatives to include at least clopidogrel, which was passed unanimously.

DR. RYAN MOVED THAT THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST CLOPIDOGREL. IT WAS SECONDED BY DR. RUGGLES.

THE MOTION PASSED UNANIMOUSLY.

Cardiovascular: Pulmonary Arterial Hypertension (PAH) Agents (Blue Class)

Public Comment

Dr. John Hartney, medical science liaison, Actelion Pharmaceuticals - his comments are about macitentan (Opsumit) which is indicated to delay the disease progression and reduce hospitalization for pulmonary arterial hypertension or PAH. Opsumit is the only endothelial receptor antagonist proved to reduce disease progression and reduce PAH related hospitalization in both mono therapy and combination therapy with PDE-5 inhibitors or hail bob. In the SERAPHIN Study, 492 symptomatic PAH patients were ran by Opsumit treatment of once daily. The treatment duration was 118 weeks. Find 64% patients were of a PAH specific background therapy. Opsumit reduced the risk of disease progression by 45% compared to a placebo, which was consistent irrespective of what a patient was receiving, PAH specific background therapy or not. In a published post hock analysis from SERAPHIN, Opsumit reduced the rate of PAH patient hospitalization by 50% and the number of hospital days by 52. Opsumit significantly improved health and quality of life and reduced the risk of experiencing a clinically needed total reduction in health-related quality of life in PAH patients. With regard to the safety profile, Opsumit, like all FDA approved PRHs, has endothelial toxicity for which there is a program. ERAs have caused elevations of aminotransferases, hepatotoxicity, and liver failure and decrease in hemoglobin concentrations. Obtain liver Obtain liver enzyme tests prior to initiation of OPSUMIT and repeat during treatment as clinically indicated. Peripheral edema and fluid retention are known consequences of PAH and ERAs. Monitor for signs of fluid retention after Opsumit initiation. The Most common adverse reactions to Opsumit (more frequent than placebo by

≥3%) were anemia, nasopharyngitis/pharyngitis, bronchitis, headache, influenza, and urinary tract infection.

In summary Opsumit is indicated to delay disease progression and reduce hospitalization for PAH. Opsumit is dosed 10 mg once daily and can be used as monotherapy or combination therapy with PDE-5 inhibitors. For these reasons, please consider adding Opsumit to the preferred drug list. Thank you for your time and consideration today. And I'm happy to answer any questions. There were no questions.

Dr. Patel proceeded with his presentation. The prevalence of Pulmonary Arterial Hypertension varies substantially depending on the type, etiology, and underlying condition; estimated to be approximately 15 per million people. Pulmonary hypertension (PH) is characterized by an increase in pulmonary arterial pressure and secondary right ventricular failure. This is defined as a resting mean pulmonary arterial pressure (mPAP) ≥ 25 mm Hg. Symptoms include dyspnea, dizziness, syncope, fatigue, edema (peripheral), angina, palpitations, and other symptoms, all of which are exacerbated by exertion. PH does not have a cure and, if left untreated, PH is a life-threatening disease with poor prognosis. Management of PH should be limited to specialized centers where clinicians are experienced in the evaluation and treatment of patients with PH. Although the number of approved therapies for PAH has grown in the past years, the prognosis is still poor, with approximately 50% mortality within the first 5 years after diagnosis.

There are many causes of PAH, including idiopathic or underlying disease and hereditary causes--cellular changes in the walls of pulmonary arteries, and it appears that mutations in the bone morphogenetic protein receptor type 2 (BMPR2) gene plays a key role in the pathogenesis of heritable PAH; other etiologies in PAH include drugs and toxins, collagen vascular resistance, human immunodeficiency virus (HIV), portal hypertension, chronic thromboembolism, and congenital heart disease. The World Health Organization (WHO) classifies PH patients into 5 groups based on etiology:

- Group I now refers to pulmonary arterial hypertension (PAH)
- Group II refers to PH due to left heart disease
- Group III refers to PH due to lung disease
- Group IV refers to PH due to blood clots in the lungs
- Group V refers to PH due to blood and other rare disorders

In 2013, clinical classifications were updated to provide the same PH classifications for adult and pediatric patients. In addition, the individual categorization of the persistent PH of neonates (PPHN) was included. For treatment guidelines, refer to the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), February 2016.

Updated information - bosentan (Tracleer), which is not new medication, there is an added indication in treatment of idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR) in pediatric patients age 3 years and older which is expected to result in an improvement to exercise ability. Treatment of pulmonary arterial hypertension (WHO Group I) in patients with WHO Class II to IV symptoms, to improve exercise ability and decrease clinical worsening.

The utilization was reviewed. In the January 20, 2017, review, a motion was made that therapeutic alternatives to include at least: one PDE5 inhibitor; one oral non-PDE5 inhibitor; and one inhaled product. It passed unanimously.

Per Dr. Demain, it appears that one component of this class was not reviewed last time. Are there any other comments or a motion?

DR. RYAN MOVED THAT THERAPEUTIC ALTERNATIVES TO INCLUDE ONE FROM EACH CLASS PLUS ONE INHALED PRODUCT. IT WAS SECONDED BY DR. RUGGLES.

THE MOTION PASSED UNANIMOUSLY.

Committee was on break from 9:53 a.m. to 10:05 a.m.

4B. Anti-infective: Antifungals, Oral (Blue Class); Antifungals, topical (Red Class); Antivirals, influenza (Blue Class); Fluoroquinolones, oral (Green Class); Hepatitis B agents (Blue Class)

Anti-infective - Antifungals, Oral (Blue Class)

Public Comment

There were no public comments for this item.

Dr. Patel gave his presentation about disease state descriptions for invasive and mucosal infections. Invasive infection from *Candida* is a major cause of morbidity and mortality in healthcare. Significant infections due to these organisms are generally referred to as invasive candidiasis; can be associated with candidemia and metastatic organ involvement. Candidemia is one of the most common bloodstream infections in US hospitals, typically ranking as the 3rd or 4th most common cause of healthcare-associated bloodstream infection. Over 90% of invasive disease is caused by the five most common pathogens: C. albicans, C. glabrata, C. tropicalis, C. parapsilosis, and C. krusei. Mucosal *Candida* infections (e.g., oropharynx, esophagus, vaginal) are not considered invasive. (source: *Infectious Diseases Society of America, 2015)*

Onychomycosis is a fungal infection of the nails that causes thickening, discoloration, and separation from the nail bed. It occurs in 10% of the general population, 20% in persons > 60 years, and 50% in those > 70 years old. Most often caused by dermatophytes. The recurrence rate of onychomycosis is 10% to 50%.

New information - **Posaconazole** with vincristine has been associated with: neurotoxicity; seizures; syndrome of inappropriate antidiuretic hormone secretion; peripheral neuropathy; and paralytic ileus. **Itraconazole** now has a box warning and contraindication has been updated with additional information on drug interactions with CYP3A4 inhibitors. **Lamisil** - Novartis has made a business decision to permanently discontinue Lamisil 250 mg tablets. They will remain available until approximately April 2018.

Dr. Demain asked if terbinafine is still available, it's just not branded. Dr. Patel stated that is correct.

Refer to treatment guidelines are from the Infectious Diseases Society of America for the treatment of: Candidemia in Nonneutropenic and Neutropenic patients; oropharyngeal Candidiasis; and esophageal Candidiasis. For treatment of onychomycosis, refer to the American Family Physician treatment guidelines; and, for treatment of onychomycosis in adults, refer to the British Association of Dermatologists treatment guidelines. The utilization was reviewed.

Dr. Demain commented that we addressed two things, Candidiasis and onychomycosis. We've not addressed any of the systemic mycoses. So, all of those other conditions have other recommendations too. So, this is when we're approving this category, we have to think beyond Candidiasis. Although, Candidiasis and onychomycosis are clearly the most common category.

Any other comments or questions? So, griseofulvin is still the treatment of choice for tinea capitus? Dr. Patel commented that Dr. Demain's question is a great lead-in to the next topic. It will be covered.

At the last review on April 21, 2017, therapeutic alternatives to include: at least one fluconazole tablet; one oral terbinafine preparation; and one pediatric preparation. This motion passed unanimously.

DR. RYAN MOVED THAT THERAPEUTIC ALTERNATIVES TO INCLUDE: AT LEAST ONE FLUCONAZOLE TABLET; ONE ORAL TERBINAFINE PREPARATION; AND ONE PEDIATRIC PREPARATION. IT WAS SECONDED BY DR. RUGGLES.

Per Dr. Demain, the percentage of voriconazole and itraconazole is low--it's like a couple of percentage of our prescriptions. So, medically necessary is reasonable. There were no further questions or comments.

THE MOTION PASSED UNANIMOUSLY.

Anti-infective: Antifungals, Topicals (Red Category)

Public Comment

There were no public comments for this item.

Dr. Patel continued his discussion about the disease state descriptions for topical antifungals. Tinea infections are caused by dermatophytes and are classified by the sites involved: Tinea pedis (Athlete's foot); tinea cruris (jock itch); tinea capitis (ringworm of the scalp); tinea versicolor (pityriasis versicolor); tinea corporis (ringworm on skin); tinea unguium (onychomycosis).

Dermatophytes are usually limited to involvement of hair, nails, and stratum corneum; three genera: *trichophyton, microsporum, and Epidermophyton.* Prepubertal children most often have tinea corporis or tinea capitis; adolescents/adults most often have tinea cruris, tinea pedis, or tinea unguium. Tinea is

often misdiagnosed based on appearance. Lifetime risk of acquiring tinea infections is between 10% and 20%.

The new agents to address in this category is Sponix Antifungal (undecylenic acid), which is also available over the counter. It is indicated for the treatment of tinea pedis and tinea cruris. It is organic unsaturated fatty acids derived from castor oil. The exact mechanism of action is unknown; it is shown to inhibit morphogenesis of Candida albicans. It should not be used to treat or prevent diaper rash. The dosing is specific for the type: tinea cruris: twice daily for two weeks; tinea pedis: twice daily for four weeks. Its availability is a 22% solution.

Dr. Demain asked how effective it is. Was there a comment on its efficacy? Dr. Patel did not see a comment on its effectiveness in the packet.

An update for medication Luzu is now indicated for treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *trichophyton rubrum* and *Epidermophyton floccosum* in pediatric patients. Luzu was previously only approved in adults.

For treatment guidelines, please refer to American Family Physicians and the Centers for Disease Control and Prevention for treatment of tinea infections. The utilization was reviewed. A motion was made at the last review on April 21, 2017, for therapeutic alternatives to include: at least one solution; one shampoo; one topical cream or ointment. This motion was passed unanimously.

DR. RYAN MOVED THAT THERAPEUTIC ALTERNATIVES TO INCLUDE: AT LEAST ONE SOLUTION; ONE SHAMPOO; ONE TOPICAL CREAM OR OINTMENT. IT WAS SECONDED BY DR. RILEY.

THE MOTION PASSED UNANIMOUSLY.

Anti-infective: Antivirals, influenza

Public Comments

There were no public comments for this item.

Dr. Patel continued his presentation and discussed the disease state description for antiviral, influenza. Influenza is a common illness affecting most people at least once in their lifetime. Uncomplicated illness typically resolves after 3 to 7 days. It is often self-limiting. Persons at higher risk for influenza complications are: < 2 years old or > 65 years old; immunocompromised patients; pregnant/postpartum patients; < 19 years old + long-term ASA therapy; American Indians/Alaska Natives; extremely obese patients; nursing homes/other chronic care facility patients; and, patients with specific, chronic disease states. Influenza vaccination is the primary method for preventing influenza. Virus strains included in the 2017-2018 U.S. trivalent influenza vaccines: A/Michigan/45/2015 (H1N1) pdm09-like virus, A/Hong Kong/4801/2014 (H3N2)-like virus, B/Brisbane/60/2008-like virus (Victoria lineage). Quadrivalent vaccines include the additional influenza B virus strain, a B/Phuket/3073/2013-like virus (Yamagata lineage).

For treatment, clinical benefit greatest when antiviral treatment is administered within 48 hours of illness onset. Antiviral medications are approximately 70% to 90% effective in preventing influenza and can be considered for prophylaxis in certain situations and within 48 hours of exposure; widespread and routine use is not recommended.

The Centers for Disease control and Prevention provided Neuraminidase Inhibitor Resistance Testing Results as of October, 2017, were presented. The utilization was reviewed.

Per Dr. Demain, noted that Relenza is not on this list, which is not recommended for patients with respiratory disease.

A motion was made at the last review on April 21, 2017, that therapeutic alternatives to include oseltamivir. It passed unanimously.

DR. RUGGLES MOVED THAT THERAPEUTIC ALTERNATIVES TO INCLUDE OSELTAMIVIR. IT WAS SECONDED BY DR. RYAN.

THE MOTION PASSED UNANIMOUSLY.

Anti-infective: Fluoroquinolones, oral (Green Category)

Public Comments

There were no public comments for this item.

Dr. Patel continued his presentation. Oral fluoroquinolones vary in the spectrum of antimicrobial activity. Older fluoroquinolones have a gram-negative spectrum of activity; newer fluoroquinolones have broad spectrums of activity covering both gram-negative and gram-positive bacteria. Fluoroquinolones are indicated for disease states such as: acute exacerbation of chronic bronchitis; acute sinusitis; bone and joint infections; community acquired pneumonia; febrile neutropenia; gonorrhea; infectious diarrhea; inhalational anthrax; intra-abdominal infections; lower respiratory tract infections; nosocomial pneumonia; pelvic inflammatory disease; plague; prostatitis; skin; typhoid fever; urinary tract infection.

As an update, the FDA stated that FDA patient cases and published study findings currently do not support reports that the medications result in detachment of the eye retinas or bulges or tears in the aorta blood vessel (Aortic aneurysm and aortic dissection); the FDA will continue to assess. DCD issued alert regarding recommendations for treatment of Shigella related to increased quinolone resistance in some isolates; recommends avoiding fluoroquinolones if the ciprofloxacin MIC is ≥ 0.12 mcg/mL. Levofloxacin - package insert and medication guide updated to state risk of completed suicide (oral and injectable formulations). The FDA advised that the serious side effects associated with fluoroquinolones generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections who have other treatment options. Updated WHO guidelines for the treatment of chlamydia; gonorrhea, and syphilis no longer recommend fluoroquinolones use.

In terms of Community Acquired Pneumonia, Pediatrics: pneumonia is a leading cause of death in children worldwide. More than 2 million children under the age of 5 years of age dies of pneumonia annually representing approximately 20% of all deaths in this age group. Annual incidence of pneumonia is approximately 3-4 cases per 100 children less than 5 years old. Most cases of pneumonia in school age children are viral, not bacterial. *S. pneumoniae* is the most common bacterial pathogen, occurring at an incidence of 4% to 44%. The most common atypical pneumonia includes *M. pneumoniae* (older children) and *C. pneumoniae* (infants).

In adults, community acquired pneumonia, together with influenza, remains the 7th leading cause of death in the United States (U.S.). In the U.S., 915,900 episodes of community acquired pneumonia occur in adults ≥ 65 years of age annually. Initial treatment for most patients is empirical due to the need for more accurate and timely diagnostic methods. *S. pneumoniae* is the most frequently isolated pathogen followed by *Mycoplasma pneumoniae, Haemophilus influenzae, Chlamydophila pneumoniae*, and Respiratory viruses.

For treatment guidelines for both community acquired pneumonia-pediatrics and community acquired pneumonia-adults, refer to the Infectious Disease Society of America.

Another disease state for oral fluoroquinolone is acute uncomplicated cystitis. Acute uncomplicated cystitis remains one of the most common reasons for antimicrobial medications. Microbials often involved with uncomplicated cystitis and pyelonephritis consists mainly of *Escherichia coli* (75%-95%); other microbials include *Proteus mirabilis, Klebsiella pneumoniae*, and *Staphylococcus saprophyticus*.

Antimicrobial resistance among uropathogens causing uncomplicated cystitis has increased. Fluoroquinolone resistance rates were still < 10% in most parts of North America; compared to previous years, there is a clear trend for increasing resistance. Local antimicrobial susceptibility patterns should be considered in empirical drug therapy selection, especially when treating *E. coli.* For treatment of acute uncomplicated cystitis, refer to Infectious Disease Society of America.

In terms of Skin and Soft Tissue Infections (SSTIs), between 2000 and 2004, there was a 29% increase in the total hospitalizations. SSTIs account for 6.3 million physician visits annually. Increased frequency is due, in part, to emergency of MRSA. Clinical evaluation goal is to establish cause and severity; pathogen-specific and local antibiotic resistance patterns need to be taken into account.

There is a new fluoroquinolone, Baxdela (delafloxacin). Indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria. Available by IV infusion and oral. Should only be used to treat infections that are proven or strongly suspected to be caused by bacteria. Contraindicated in patients with known hypersensitivity to Baxdela or other fluoroquinolones. Treatment guidelines for Skin and Soft Tissue Infections are form the Infectious Disease Society of America. The utilization report was reviewed. At the last review on April 21, 2017, the motion was a class effect. It passed unanimously.

DR. PHILLIPS MOVED THAT A CLASS EFFECT. IT WAS SECONDED BY DR. RYAN.

THE MOTION PASSED UNANIMOUSLY.

Dr. Liljegren advised that this was her last vote, as she has to leave for an appointment.

Anti-infective: Hepatitis B Agents (Blue Class)

Dr. Colleen Fong, pharmacist and Associate Medical Director with Gilead Sciences. She is here to provide testimony on behalf of Vemlidy, which is a tenofovir alafenamide, 25 mg oral tablet that was approved a year ago for the treatment and management of adults with chronic Hepatitis B, who are compensated cirrhotics. So, this is updated information regarding our ongoing clinical trials, primarily Studies 108 and Studies 110, which enrolled, respectively, both e-antigen negative and e-antigen positive patients. And to 96 weeks in comparison to tenofovir disoproxil fumarate, the efficacy end point of viral suppression was comparable in each farm. Not only that, in terms of polled analysis from safety, we do see form both groups comparable efficacy with slight or statistically significant improvement, not only in stem creatinine, but also in both bone and spine mineral density tests. In conclusion, what we see with Vemlidy is continued duration of improvement and consistent benefit compared to tenofovir disoproxil fumarate. And with that, we ask for continuance of Vemlidy, the Alaska PDL for patients. There were no questions for Dr. Fong.

Dr. Patel continued his presentation with a discussion about the disease state description of Hepatitis B. In 2015, a total of 3,370 new cases of acute hepatitis B were reported to the CDC from 48 states. The overall incidence was 1.1 cases per 100,000 population. After adjusting for under-ascertainment and under-reporting, it's estimated that 21,900 acute hepatitis B cases occurred. From 1990-2014, the rate of new HBV infections has declined. Greatest decline has bene among children born since 1991 due to routine vaccination. Since 2014, there has been an increase in the rate of new HBV infections, which is likely due to increasing injection drug use. During 2011-2012, there were approximately 847,000 noninstitutionalized people in the U.S. with chronic HBV infection. In 2015, there were 1,715 deaths related to HBV. This is an underestimated, as the estimated annual deaths due to HBV are 14,000. Chronic infection develops in approximately 90% of infants; 25% to 50% of children aged 1-5 years; and 5% in adults.

New information for Tyzeka (telbifudine) has been discontinued. Product may still be available until stock is depleted. Patients undergoing treatment for Hepatitis C virus infection (HCV) who are receiving oral direct acting antivirals (DAAs) may be at greater risk for HBV reactivation. Black boxed warning added to DAAs. The FDA has approved the removal of information related to lactic acidosis/severe hepatomegaly with steatosis from the black box warning of Viread. Pegasys has expanded indication in non-cirrhotic pediatric patients ≥ 3 years of age with HBeAg-positive chronic HBV infection and evidence of viral replication and elevations in serum alanine aminotransferase. For treatment guidelines, refer to the American Association for the Study of Liver Diseases and the World Health Organization. The utilization rates were discussed and the previous motion was on April 21, 2017, that drugs were therapeutic alternatives. It passed unanimously.

Dr. Phillips commented that based on the reading, it looks like Epiver and Hepsera were not recommended as first line treatment, but it seems to be what is preferred on the PDL.

Per Dr. Novus, there was a guideline change from the last PDL to a different position than we're in right now. That's part of the discussion this morning.

Dr. Demain, that's automatically figured in when it comes to what products that are ultimately selected. The guidelines are going to play a role in that selection process for us. Right? Dr. Novus, yes, that would be correct.

At the last review on April 21, 2017, the motion was that drugs were therapeutic alternatives. The motion passed unanimously.

DR. PHILLIPS MADE A MOTION THAT DRUGS WERE THERAPEUTIC ALTERNATIVES. DR. RUGGLES SECONDED THE MOTION. THE MOTION PASSED UNANIMOUSLY.

4C. GENITOURINARY - Benign Prostatic Hyperplasia (BPH) (Green Class); Genitourinary - Bladder Relaxant Preparations (Green Class); Genitourinary - Vaginal Antibiotics (Green Class)

Genitourinary - Benign Prostatic Hyperplasia (BPH) (Green Class)

Public Comments

There were no public comments for this item.

Dr. Patel continued his presentation with the disease state description for BPH. Approximately 14 million men in the United States have symptoms related to BPH. Approximately 50% of men demonstrate histopathologic BPH by age 60 years and this number increases to 90% by 85 years of age. Symptoms are induced by hyperplastic changes in prostate tissue, leading to prostatic enlargement. The resulting obstruction increases urinary outflow resistance and results in an impaired detrusor muscle response. Patients with PBH may present with bothersome lower urinary tract symptoms (LUTS) resulting from irritation (urinary frequency, nocturia, urgency, urge incontinence) and/or obstruction (difficulty initiating urination or passing urine, weak stream, involuntary postvoid dripping of urine, and sensation of incomplete bladder emptying). Most men with BPH experience only mild or moderate symptoms of obstruction. Sever BPH is more likely to occur in men over 60 years of age, can lead to urinary retention, renal insufficiency, urinary tract infections, hematuria, and bladder stones. For treatment guidelines, refer to the American Urological Association. The utilization reports were reviewed. There were no further comments or questions. At the last review on January 20, 2017, the motion was made that therapeutic alternatives to include: one alpha blocker and one androgen hormone inhibitor. The motion passed unanimously.

DR. RUGGLES MADE A MOTION THAT THERAPEUTIC ALTERNATIVES INCLUDE ONE ALPHA BLOCKER AND ONE ANDROGEN HORMONE INHIBITOR. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIOUSLY.

Genitourinary - Bladder Relaxant Preparations (Green Class)

Public Comments

There were no public comments for this item.

Dr. Patel continued his presentation with a disease state description. Overactive bladder (OAB) is a chronic and debilitating syndrome that is characterized by urinary urgency with or without urge incontinence, usually in combination with urinary frequency (8 or more voiding episodes per 24 hours) and nocturia (awakening 1 or more times per night to void). It is prevalent in approximately 16% of men and 17% of women. Approximately 20% in those older than 60 years of age. For treatment guidelines, refer to the American Urological Association, 2014. The utilization rates were reviewed.

Dr. Demain commented that some of the generics were non-preferred and made up 40% of the prescriptions. Per Dr. Novus, she doesn't know if they were technically non-preferred or if nomenclature thing. She will need to check on that. There's quite a number on the preferred list that they can override at the pharmacy. Sometimes when things switch from brand name to generic, it may not completely reflect that the generic was preferred in our reporting site. So, I have to go back and validate that we to whether or not it really is non-preferred within the system. But, generally, the generics will roll to a preferred status.

There were no further comments or questions. So, last year's motion was read. At the last review on January 20, 2017, the motion was made that drugs in the class were therapeutic alternatives. The motion passed unanimously.

DR. RYAN MADE A MOTION THAT DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. PHILLIPS.

THE MOTION PASSED UNANIMOUSLY.

Genitourinary - Vaginal Antibiotics (Green Class)

Public Comments

There were no public comments for this item.

Dr. Patel continued his presentation by providing some background on bacterial vaginosis. It is a polymicrobial clinical syndrome resulting from replacement Lactobacillus sp. With anaerobic bacteria, *G. gavinalis*, Ureaplasma, Mycoplasma, and numerous fastidious or uncultivated anaerobes. Symptoms include vaginal discharge, pain, itching, or malodor; it can be asymptomatic. It is associated with STDs and other female genital tract infections. A diagnosis requires three or four Amsel's criteria: abnormal gray discharge, vaginal pH > 4.5, a positive amine test, and > 20% of the epithelial cells being clue cells. The Nugent score is considered the standard for diagnosing bacterial vaginosis. Culture and sensitivity testing of bacteria are not routinely performed. Bacterial vaginosis may recur in up to 30% of women within three months after treatment. For treatment guidelines, refer to the Centers for Disease Control and Prevention, 2015. The utilization reports were reviewed.

Dr. Ruggles noted that on the sheets the utilization looks the opposite. Dr. Novus responded that this class has always been a challenge because we have a large portion of our pharmacies are able to purchase medications through the federal supply schedule. As such, sometimes the branded products are less expenses and/or they may be easier to acquire through that contract. While we have traditionally preferred the branded products because of the negotiated rates that we get from the manufacturers, for some of our smaller facilities, smaller, independent pharmacies, we recognize that there might be an imbalance between preferred and non-preferred because their actual acquisition cost of generic products in the private sector is easier to acquire. So, in a situation such as this, can it be the work that the State does in setting up the PDL is to try and gain as much of the negotiated rates where available and that also allow our smaller, independent pharmacies to acquire the generics at a lower acquisition cost. This one has always been a little bit off in the rates for this category for those reasons that I stated. This one is a very interesting one where we can garner some advantage by selecting the preferred agent where available.

Dr. Demain--we're not addressing the guideline for oral therapy, we're only looking at topical therapies here.

Dr. White was glad the state tries to help the smaller pharmacies. In the motion should we include an oral product? Per Dr. Novus, this is targeted specifically for the topical products. The oral products are looked at in another category. It is specifically looking at vaginal products and which of these products are most appropriate within that based on the recommendations.

A motion was made at last year's review on January 20, 2017, for a class effect. This motion passed unanimously.

DR. CARLSON MOVED A CLASS EFFECT. SECOND BY DR. RYAN.

MOTION PASSED UNANIMOUSLY.

5. Review Minutes from January 2018 Meeting

This item was not addressed.

6. Comments from Committee Members or Chair

This item was not addressed.

7. Adjourn

The next meeting will be on Friday, September 21, 2018.

The meeting moved into executive session at 11:03 a.m.