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Draft Meeting Minutes – March 28, 2013 P&T Committee

Springs Preserve
Banquet Room
333 S. Valley View Blvd
Las Vegas, NV 89107

Committee Members Present:

Adam Zold, Pharm.D.; Evelyn Chu, Pharm.D.; Shamim Nagy, MD; Weldon Havins, MD; Constance Kalinowski, MD; Ronald Shockley, MD, Kevin Desmond, RPh; Michael Hautekeet, RPh; David Fluitt, Pharm.D.

Others Present:

DHCFP: Gabriel Lither, Deputy Attorney General; Coleen Lawrence, Chief Program Services; Mary Griffith, RN, Social Services Program Specialist; Laurie Squartsoff, Administrator

Catamaran: Carl Jeffery, Pharm.D.; Kevin Whittington, RPh

HPES: Donna Perkins

Others: Scott Larsen, BMS; Sandy Sierawski, Pfizer; Brooks Hubbard, BIPI; Bill O'Neil, BIPI; Charissa Anne, J&J; Andi Stratton, Vertex; Laura Litzenberger, Janssen Sci Affairs; Jason Han, WAG/Student; Julie Bertuluit, GSK; Gregg Peterson, GSK; Leana Ramirez, Avella; Tracey Ricks, Reckitt; Camille Kerr, Allergan; Paul Krisruluis, Pfizer; Soneyla Azizi, Eisai; Michael Foster, Celgene; Robert Green, Celgeen; Eric Biros, Alcon; Vinson Lee, Amgen; Bret Fergusen, Pfizer; Mike Spader, Pfizer; Ken Kusgid, BIPI; Mike Pinocci, Pfizer; Doug Powell, Forrest; Phi Walsh, Sunovion; Michael Sullivan, BIPI; Neil Robert, AM; Efrain Alton, Merck; Molly Meekin, Hyperion

AGENDA

I. Call to Order and Roll Call

Call to order 1:01 PM
Shamim Nagy, MD, Chair: Meeting called to order at 1:01 PM
Shamim Nagy, MD, Chair: starting with roll call, starting at that end
Evelyn Chu, Pharm.D.: Evelyn Chu

Ronald Shockley, MD: Ron Shockley
Adam Zold, Pharm.D.: Adam Zold
Constance Kalinowski, MD: Connie Kalinowski
Michael Hautekeet, RPh: Mike Hautekeet
Kevin Desmond, RPh: Kevin Desmond
David Fluitt, RPh: Dave Fluitt
Weldon Havins, MD: Weldon Havins
Shamim Nagy, MD, Chair: Shamin Nagy
Gabe Lither, Deputy Attorney General: Gabriel Lither with the Attorney General's office
Carl Jeffery, Pharm.D.: Carl Jeffery with Catamaran
Kevin Whittington, RPh: Kevin Whittington with Catamaran

II. Public Comment

Shamim Nagy, MD, Chair: We'll start with Public Comments

Carl Jeffery, Pharm.D.: We had a request for a doctor to talk about Eliquis that is on the agenda later

Chris Miranda, MD: My name is Dr. Chris Miranda, I am an interventional cardiologist here locally in Las Vegas Nevada. I am here as an advocate for my patients to have Eliquis placed on the Medicaid formulary without prior authorization or step edit through warfarin. Warfarin has been a highly effective drug for the treatment of non-valvular a-fib for the last 50 or 60 years, but is also the most number one prescribed medication that kills patients around the world. So I would prefer not have to write warfarin for my patients without a high risk of killing them. Eliquis I think the most important endpoint it shows you is the absolute reduction in mortality compared to standard of care warfarin for non-valvular a-fib, I think that is the strongest statement you can make for this medication. It not only reduces the risk of primary endpoint of stroke and systemic embolism but also reduces the risk of bleeding, so you can have your cake and eat it too. There is no downside with this medication whatsoever. The only downside is that it is not as cheap as warfarin. So if you have any questions of me, I would be happy to answer them.

Weldon Havins, MD: Have you tried Pradaxa or Xarelto and how do they compare?

Chris Miranda, MD: Yes sir. Pradaxa is superior in the primary endpoint according to the FDA compared to warfarin and it also has a 9% reduction in total bleeding, so it is also superior to warfarin in terms of non-valvular a-fib, so before Eliquis came out, Pradaxa has been my number one choice of medication. Xarelto is non-inferior to warfarin. But it is easier to give, it is once a day. It doesn't have the robustness of data backing it as Eliquis and Pradaxa does, but it is still a very good option compared to warfarin.

Weldon Havins, MD: Why are you preferring Eliquis over Pradaxa?

Chris Miranda, MD: I prefer Pradaxa over Eliquis because Eliquis was just approved. So Pradaxa has been out for about 2 or 3 years now. I believe both options are excellent because there are some patients that would be better served with one drug than another drug, so they are both very good options. They are the two superior drugs as far as I'm concerned, they are very close in efficacy and safety.

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Gabe Lither, Deputy Attorney General: This is Gabe Lither for the record. When we have the public comment it is important that we don't have cost of the drug or medication involved, that is not something that this committee factors into its decision.

Ronald Shockley, MD: Is there a way to somehow reduce toxicity, is there something you can give a patient to reduce the risk of bleed?

Chris Miranda, MD: Okay, fair enough. So the best way to prevent a bleed, to treat a bleed, is to prevent it in the first place. The most devastating complication from oral anticoagulation is intracranial hemorrhage. So Pradaxa reduces that end-point by 75%, and Eliquis reduces that end-point by 49%, both statistically significant. Now, what if you say, they don't have antidotes, so I can't give you data on Eliquis yet because there hasn't been enough post-marketing experience yet. But I can give you data on Pradaxa which is probably similar to what you are going to get with Eliquis. If an individual comes into the emergency room bleeding on warfarin or bleeding on Pradaxa, the data says that the risk of death, despite having, quote, the theoretical antidote for warfarin, vitamin K, fresh frozen plasma and proton thrombin concentrates, the risk of death with a major bleed with warfarin is twice that of Pradaxa, and Pradaxa theoretically has no antidote. So you say, why is that? That's because these drugs have a much shorter half-life than warfarin. So Eliquis and Pradaxa are both twice-a-day drugs, their half-life is only 12 hours. So if you wait 12 to 18 hours, the majority of the drug is out of the patient's system and they will stop bleeding, even without the quote, antidote. These theoretical antidotes we have with warfarin really do not work. If you take an individual that has intracranial hemorrhage from warfarin and one from Pradaxa, the death rate is exactly the same at 49%, those patients die, or are completely disabled. But, you have ¾ less bleeds with Pradaxa. So even though warfarin has these theoretical antidotes, they still die of intracranial hemorrhage at the same rate as they do with Pradaxa with the antidote, so the way to treat a bleed is to prevent it in the first place.

Shamim Nagy, MD, Chair: No more questions? Thank you.

Chris Miranda, MD: You're welcome.

Shamim Nagy, MD, Chair: Any other public comments? No?

III. Review and Approval of the December 20, 2012 Meeting Minutes

Shamim Nagy, MD, Chair: So we move to discussion of minutes of the last meeting. I need a motion to approve.

David Fluitt, RPh: I make a motion to approve the minutes

Adam Zold, Pharm.D.: I second

Voting: Unanimous, "Aye".

Shamim Nagy, MD, Chair: Motion approved.

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IV. Status Update by DHCFP

Shamim Nagy, MD, Chair: Status update from DHCFP?

Coleen Lawrence: Good afternoon. Thank you everyone to coming to our new venue, I hope everyone likes this new venue that we have instead of being stuffed into a State building. It's a little packed, I think the Easter Bunny is here on the premises, so bear with us. If you find any Easter Eggs, put them down, they're not for you. First of all, we would like to welcome, in our audience today, our new administrator, Laurie Squartsoff. [Applause] Some of you may recognize her, she was actually previously with our division before in the pharmacy program, and she was also over with MediCal. So, we appreciate her coming back to our division. We are also in the Legislative session right now. Nothing that is affecting or impacting the P&T committee. Last year we had the Sunset Committee Bill that impacted the P&T Committee, however, the last session the Sunset Committee reviewed the P&T Committee and gave the recommendation to continue forward with the P&T Committee. So, that bill is still going forward with the Sunset Committee, but it doesn't directly impact us this session. So we are not monitoring any bills that would impact this committee this year. There are no bills that are impacting the preferred drug list or any of the pharmacy program. That's our update for today. Do you have any questions?

Shamim Nagy, MD, Chair: Thank you Coleen. Any program updates? Dr. Jeffery?

Carl Jeffery, Pharm.D.: Nothing from me.

V. Established Drug Classes

A. Bone Ossification Agents: Bisphosphonates

Shamim Nagy, MD, Chair: So we will start the first drug class review. The first class, bone ossification agents: bisphosphonates. Dr. Jeffery?

Carl Jeffery, Pharm.D.: Any public comment for the bisphosphonates?

Shamim Nagy, MD, Chair: Any public comments? No? Dr. Jeffery.

Displayed on screen:

Current PDL	Current NON PDL
ALENDRONATE	ACTONEL®
FOSAMAX PLUS D®	ATELVIA®
	BONIVA®
	DIDRONEL®
	ETIDRONATE

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	IBANDRONATE
	SKELID®

New Product: Binosto®

Carl Jeffery, Pharm.D.: We have a new agent in this class, Binosto, is the agent in this class that prompted us to review this class today. Osteoporosis is the most common bone disease in humans. Fractures are the most clinically significant manifestation. In the elderly, this is often a death sentence. It is important to increase the bone mineral density where we have the opportunity to decrease the risk of fracture, especially in the elderly and the post-menopausal women. They are approved for the treatment and prevention of osteoporosis in post-menopausal women and in patients taking a prolonged course of corticosteroids. The bisphosphonates also work by inhibiting the osteoclast activity and binding to the bone surface and facilitate bone resorption. All the agents in this class have been shown to be very effective, equally effective, there's not one agent that has been shown to be more effective than another agent. They are available once daily, once weekly, once monthly and there are some injectable products that are dosed even less frequently, but we are just talking about the oral agents today. Overall the most common side effect with these is the gastrointestinal issues. The patients have to be able to remain upright for at least 30 minutes after administration, and in case of one other one, that I can't remember the name right now, requires 60 minutes to remain upright. The new agent, Binosto, is the same as Fosamax, alendronate 70mg dosed once a week. The difference is this is an effervescent tablet. You dissolve it in water and drink it. It is a little bit easier to take for someone with swallowing difficulties. But it does not exclude them from having to not lay down for 30 minutes after taking. The swallowing is some benefit, but that's about it. So our recommendation is to consider all the agents in this class as clinically and therapeutically equivalent.

Shamim Nagy, MD, Chair: Do I have a motion?

Weldon Havins, MD: I move we consider all these agents therapeutically and clinically equivalent.

Michael Hautekeet, RPh: I second.

Shamim Nagy, MD, Chair: All in favor?

Board votes unanimous, "Aye".

Shamim Nagy, MD, Chair: Motion carries.

Displayed on Screen:

Proposed PDL	Proposed NON PDL
ALENDRONATE	**ACTONEL®**
FOSAMAX PLUS D®	**ATELVIA®**
	BINOSTO®
	BONIVA®

DRAFT

	DIDRONEL®
	ETIDRONATE
	IBANDRONATE
	SKELID®

Carl Jeffery, Pharm.D.: Because there have not been any head-to-head trials showing that one agent is more effective at reducing fracture, the trials are also hard to look at, because they do not actually measure the endpoint of reducing fracture, their endpoint is increasing bone mineral density. When you look at that endpoint, they are all equally effective, there is not one that outshines the others. With that information in mind, our recommendation is to keep the preferred list the same as it was before, and include the new Binosto agent as non-preferred.

Michael Hautekeet, RPh: I make a motion to keep the PDL list the way it is.

Weldon Havins, MD: Second.

Shamim Nagy, MD, Chair: Any questions before moving to voting? We already have a motion and second, start voting with Dr. Chu.

Board votes unanimous, "Aye".

Shamim Nagy, MD, Chair: Motion approved.

B. Hepatitis C Agents: Antivirals - Ribavirins

Shamim Nagy, MD, Chair: The next class, the hepatitis C agents, ribavirins.

Leana Ramirez: Hello, good afternoon, my name is Leann Ramirez. I am a pharmacist with Avella specialty pharmacy. The reason I am here today is that I would like to talk to you about RibaPak. It is a medication used for Hepatitis C therapy. I am doing this on my own time, I am not being paid or reimbursed to be here today, I simply want to make sure you are aware of the options available. For Hepatitis C therapy, patients are generally given an injection, they are given tablets, and it can be very overwhelming. It is a very hard treatment and the disease itself is one of the most common reasons for liver transplantations in the United States. When you are talking to a patient, we already have to talk them into taking therapy because it's hard, they have to take an injection and they have to take a tablet. Now, there are new medications that are out there and available that carry even more side effects. So I always tell my patients it is kind of akin to chemotherapy. Now if you have ever talked to a patient about taking chemotherapy, you have talk them into getting treatment. You have to talk them through the side effects and you have to talk them into actually taking the medication. So I'm telling them that they have to take this medication, it is going to make them feel terrible, they have to take it as scheduled. You have to change their diet, you have to change their routine. It is going to interrupt their sleep, they are going to feel like they have the flu all the time, and just when they are feeling better, it is time for their next dose. So what I want to show you today, I actually brought some visuals. This would be a daily dose, this would be up to 28 days on the capsules, for the ribavirin capsules. Patients consistently have 1200mg, these are 200mg capsules. Three capsules in the morning, three capsules at

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night. That's a lot to take on, especially if they have to do the injection once a week. They will also have other daily medications, their blood pressure pills, daily diabetic medications. Verses the Ribapak. Ribapak comes specifically formulated so they only have to take one tablet in the morning, and one at night. There are several studies out there that show adherence is increased with the decreased number of pills that we have patients take. And again, it is a very tough therapy, so my job is to get them through therapy. So if I have to talk to my patient and tell them this is what you are going to take, it makes it so much easier instead of saying this is what you are going to take. I appreciate your time.

Shamim Nagy, MD, Chair: Any questions? I have a question, are the side effects different?

Leana Ramirez: Well the side effects are the same because it is the same medication. What I am focusing on is mainly adherence. Because it is such a hard treatment, once they start, I need them to finish, and that is the best way they will be successful in treating.

Shamim Nagy, MD, Chair: Thank you.

Michael Hautekeet, RPh: So what is the strength of the Ribapak?

Leana Ramirez: So these Ribavirin are generally 1000 mg per day up to 1200 mg per day, based on body weight. The good thing about the Ribasphere is that is comes preformulated, it comes in 600mg tablets, and we can adjust the dose accordingly to whatever. So if they experience too many side effects, such as anemia, we can get them a lower strength of the Ribapak as well.

David Fluitt, RPh: So it isn't sustained release, it is just a higher dosage.

Leana Ramirez: Correct.

Kevin Desmond, RPh: Can you substantiate your claim with the amount of refills you have for the products? Do you have less refills for the lower strength for the higher strength.

Leana Ramirez: The lower strength Ribapak?

Kevin Desmond, RPh: Obviously the easier medication to take is the Ribapak, the one with the multiple tablets. Do have less issues with compliance based on refills?

Leana Ramirez: I do, yes. On this, they don't want to take it. It is hard for me to talk them into taking this. One of the biggest hurdles, when they forget it, you know, they forget it. But trying to talk them into taking three tablets, because a lot of times with triple therapy, they are taking Incivik for example. Incivik is an additional two tablets three times a day. Those have to be scheduled every 8 hours, it has to be with a high fat meal, and I know every 8 hours, two of those are generally within a normal day, there is going to be one dose that is just not in their schedule. So I am going to have them waking up super early to take it or staying up super late to take it. So it is easier to throw in one pill with the Incivik, versus throwing in three more pills with the Incivik.

Shamim Nagy, MD, Chair: Thank you

Leana Ramirez: Thank you.

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Displayed on screen:

Current PDL	Current NON PDL
RIBAVIRIN	COPEGUS®
	REBETOL®
	RIBASPHERE®
	RIBASPHERE® RIBAPAK

Carl Jeffery, Pharm.D.: Right now, we have on the preferred drug list, the generic ribavirin, the big brown bottle we saw with all the capsules. Over on the non-preferred side, we have to Copegus, Rebetol, Ribasphere and Ribapak, which is the prepacked pack she showed. The ribavirin products included in this review are only oral agents used to treat Hep C. There is an inhalation product used in the hospital for RSV in infants, which is not included in this review. The guidelines that are currently available do not give preference for one form over another, so they don't call out specifically the 600mg or the 300mg tablet or capsules. Since there is no new clinical information since the last time they were reviewed, I'm not going to go into the clinical side. At this point, we recommend that these agents be considered clinically and therapeutically equivalent.

Shamim Nagy, MD, Chair: I need a motion for therapeutic equivalency.

Adam Zold, Pharm.D.: I move that we accept the recommendation that the products in this class are therapeutically equivalent.

Evelyn Chu, Pharm.D.: Second

Shamim Nagy, MD, Chair: All in favor?

Board votes unanimous, "Aye".

Shamim Nagy, MD, Chair: Motion approved.

Carl Jeffery, Pharm.D.: Just a quick overview to refresh everyone's memory. The ribavirin should not be used as mono therapy, it is always paired with at least an interferon agent and sometimes with triple therapy with a protease inhibitor, telepravir or boceprevir. The ribavirin is available generically as capsules as we have seen, and as a tablet. There is a solution available, but it is only available as a branded product, the Rebetol. Ribavirin is available in the Ribapak as you saw, and is only available as a branded product in that form. Our recommendation is to keep the preferred list just as it is, with the generic ribavirin as preferred and Ribapak, Ribasphere, Rebetol and Copegus as non-preferred. And this is simply because there is no reason that people shouldn't at least try the generic ribavirin before the move to another agent.

Shamim Nagy, MD, Chair: Any questions?

Adam Zold, Pharm.D.: Are you saying the Ribapak would be available on failed therapy.

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Proposed PDL	Proposed NON PDL
RIBAVIRIN	Copegus®
	Rebetol®
	Ribasphere®
	Ribasphere® RibaPak

Carl Jeffery, Pharm.D.: Right, so they can get a non-preferred agent if they have tried and failed a preferred agent, or if they have a contraindication or some compelling indication for why they need a non-preferred agent.

Ronald Shockley, MD: Would that be based on intolerance?

Carl Jeffery, Pharm.D.: It could be based on intolerance, if someone has shown repeated attempts to keep them compliant, and they are still not compliant, I think that would be justification for moving to a non-preferred agent.

Robert Maul: Are these available at the local pharmacy like Walgreens or CVS?

Carl Jeffery, Pharm.D.: To my knowledge they are only available from specialty pharmacies.

Adam Zold, Pharm.D.: We actual get them in retail.

Carl Jeffery, Pharm.D.: Oh, ok, I stand corrected.

Shamim Nagy, MD, Chair: No more questions? We need a motion.

Weldon Havins, MD: I move we keep ribavirin as preferred on the preferred drug list.

Adam Zold, Pharm.D.: Second.

Board votes unanimous, "Aye".

Shamim Nagy, MD, Chair: Motion carries.

C. Respiratory: Inhaled Corticosteroid Agents – Single Entity

Shamim Nagy, MD, Chair: Next class, inhaled corticosteroid agents, single entity. Public comment? No public comment, then Dr. Jeffery.

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Current PDL	Current NON PDL
ASMANEX®	

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AZMACORT®	
BUDESONIDE NEBS*	
FLOVENT DISKUS®	
FLOVENT HFA®	
PULMICORT RESPULES®*	
QVAR®	

- New Agent – Alvesco®
- Azmacort has been discontinued

Carl Jeffery, Pharm.D.: The inhaled corticosteroid agents, single entity, the way it is currently is all the agents that are currently available are considered preferred, Asmanex, Azmacort, budesonide nebulizer, Flovent Discus, Flovent HFA, Pulmicort Respules, and QVAR. There is a new agent that is available, called Alvesco, and we'll talk about that in a minute. Azmacort has been discontinued and I think it has been off the market for years. They didn't want to reformulate their product to get rid of the CFC's to meet the requirement of the Montreal Protocol. The inhaled corticosteroids are used to treat asthma and if you look at the guidelines they are considered second line therapy after fast-acting beta adrenergics. They work by stabilizing the mast cells and intemediators that cause the asthmatic response. It is not really known exactly how they work, but they do differ in their potency and dosing schedules and dosing forms. I have outlined here the different forms. The QVAR is an HFA inhaler, whereas the budesonide is a dry powder inhaler, or the suspension for nebulizer, which we do have an age restriction on. The new one that is out is Alvesco, is a metered dose HFA inhaler. Fluticasone is a discus and the Asmanex is a twist inhaler. And as stated before, Azmacort is no longer available. Our recommendation is to consider all these agents therapeutically and clinically equivalent.

Shamim Nagy, MD, Chair: Any questions? Discussion? Need a motion?

Adam Zold, Pharm.D.: I move that we consider all these agents therapeutically equivalent.

Evelyn Chu, Pharm.D.: Second

Board votes unanimous: "Aye"

Shamim Nagy, MD, Chair: Motion approved.

Displayed on screen:

Proposed PDL	Proposed NON PDL
ASMANEX®	ALVESCO®

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BUDESONIDE NEBS*	
FLOVENT DISKUS®	
FLOVENT HFA®	
PULMICORT FLEXHALER®	
PULMICORT RESPULES®*	
QVAR®	

Carl Jeffery, Pharm.D.: There are several placebo controlled trials and several head-to-head trials showing that these products are effective. None of the head-to-head trials can really state that one product is better than the other. You will have one study supported by one drug company saying their product is better, but then another study with the opposing drug company to show their product is better. It all depends on the design. They are all approved for the maintenance therapy of treatment of an asthmatic with prophylactic therapy. The QVAR and Flovent are a little bit different because they are also approved for asthmatic patients who require systemic treatment. With that in mind, we make the recommendation to keep the preferred drug list as it was before and include the Alvesco as non-preferred.

Shamim Nagy, MD, Chair: Any questions?

David Fluitt, RPh: Were there any advantages to the Alvesco? Were there any studies to show it was better?

Carl Jeffery, Pharm.D.: To be honest, I don't know why it was introduced, I could find no advantage, it is only indicated down to age 12, so you can't get the younger pediatric patients. It is dosed twice a day, so it really has not advantage.

Michael Hautekeet, RPh: I make the motion to accept the recommendation to the preferred drug list.

Adam Zold, Pharm.D.: Second

Board votes unanimous: "Aye"

Shamim Nagy, MD, Chair: Motion approved

D. Anticoagulants: Oral

Shamim Nagy, MD, Chair: Next class, oral anticoagulants. Any public comment?

Robert Maul: My name is Robert Maul, I work at University Medical Center. I appeared before the board last year speaking on behalf of my patients at University Medical Center. In particular for the

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medication Xarelto. The reason I am here today is, I always hear from another pharmacist or a couple pharmacists at UMC that Xarelto will be taken off the preferred list. I always think, "Geez, No, Please." But I can see that you guys have such good insight and so far-sighted that my fears have no ground. My population at the University Medical Center are undocumented, homeless, people that have no real hope of going to Coumadin clinics much less being able to follow up in these clinics and Xarelto, which I thought was going to be taken off the preferred list today, but I assume it is not since you have another anticoagulant to discuss, has been a boon to my patients. Their medication is readily available, it is on the preferred list, it has cut since last year when I met with this board, I have had 22 patients which I have been able to take off Coumadin for various reasons who come in sub-therapeutic with clots who require a filter or various things. I have been able to transition them to Xarelto. In that period of time, we have probably saved 188 days of hospitalization for these individuals total. And who knows how much cost to the community. It is such a convenient product, I hope you will continue it forever, until a better product is available, as on the preferred list. I don't speak about other things that I don't know much about, but I know this medication and the group of medications has been a tremendous benefit to our clients, especially my patients who may not have access, I have to applaud the board for making it available and not putting patients through hoops and different things for getting this medication. I thank you so much.

Weldon Havins, MD: Have you tried Pradaxa or Eliquis?

Robert Maul: Yes I have. Once a day and a twice a day medication, I'm on a twice a day medication, I take my medication, and an hour later I'm at the hospital and I go, "Gee, did I take that medication?" A twice a day medication certainly if the patient can remember, but once a day, you know you have taken it or you haven't taken it with the biggest meal of the day. Some of my patients, that is breakfast, or maybe it is lunch or maybe it is at the mission. But once a day dosing is the way to go. Twice a day dosing, ok, I have had one adverse effect with twice a day medication, the patient did receive ten units of packed red blood cells and went into the ICU and passed out. I have had no untoward problems in the months with using Xarelto. There is an antidote available at University Medical Center and it is available at any hospital, and it is a wonderful product until something better comes along. Twice a day dosing? It may not happen. A lot of my folks don't have a place to stay, they are at the mission, they may not remember.

Shamim Nagy, MD, Chair: Any other Comments?

Sandy Sierawski : Good afternoon, my name is Sandy Sierawski, and I am a pharmacist here in Nevada and I work for Pfizer in their medical division. I am here to talk to you today about Eliquis and potentially adding it to the Nevada Medicaid PDL. As you know, Eliquis is an oral anticoagulant indicated to reduce the risk of stroke with system embolism in patient with non-valvular a-fib. It is a Xa inhibitor. I know that Catamaran has provided an extensive review document for all the oral anticoagulants, so I would just like to highlight a couple key pieces of information. There were two double-blind multi-national studies that evaluated efficacy and safety of Eliquis. One was the Aristotle trial and that was Eliquis vs. warfarin. There were over 18,000 patients in that study, and Eliquis was found to be superior to warfarin and reduce the risk of stroke and embolism by 21%. Superiority to warfarin was attributable

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to the reduction in hemorrhagic stroke and ischemic stroke with hemorrhagic conversion. So the purely ischemic strokes occurred with similar rates with both drugs. Eliquis also resulted in a significantly lower rate of all-cause death. Primarily because of the reduction of cardiovascular deaths, in particular stroke deaths and the non-vascular death rates were similar. Eliquis was superior to warfarin in the primary safety endpoint of major bleeding with a 31% relative risk reduction. Major GI bleeds were lower with Eliquis, numerically compared to warfarin. Eliquis also demonstrated a significant reduction in intracranial hemorrhage, as the physician noted with a 59% relative risk reduction. Eliquis demonstrated a significant reduction in fatal bleeds in warfarin with a 73% relative risk reduction. I do want you to know however that major intraocular bleeds were numerically in Eliquis vs. warfarin. The second study was AVAROSE, and that is where they compared Eliquis vs Aspirin. They took patients that were not candidates for warfarin and randomized them between Eliquis and Aspirin. And that study was stopped early based upon a pre-specified interim analysis that identified that Eliquis was demonstrated as superior efficacy to aspirin with a 55% relative risk reduction for the primary endpoint of stroke or systemic embolism. Eliquis did have a numeric increase in a major bleed compared to aspirin but it was not statistically significant. So the recommended dose of Eliquis is 5mg taken twice a day. Dose adjustment guidelines are listed in the PI along specific conversions to and from this oral anticoagulant, and other anticoagulant therapies. So rather than take too much for that, I do have copies of the package insert if anyone would like one, or I can answer any questions. I do want to make a couple other notations, and one is about the boxed warning of Eliquis, there is boxed warning, and that is to warn people if they discontinue therapy without, um, that could potentially increase the risk other thrombotic events or stroke. So it is recommended that patients if they are not discontinued from therapy because of a pathological bleed, then it is highly recommended that another oral anticoagulant be utilized. It is an oral anticoagulant, so the risk of bleeding can cause serious and potentially fatal conditions. So I am happy to answer any questions you might have.

David Fluitt, RPh: Is the only indication you have currently for this medication A-fib?

Sandy Sierawski : Yes it is.

David Fluitt, RPh: Is there any advantage to having a shorter half-life as compared to Xarelto, in terms of, I guess there is now an antidote, is there an advantage to a shorter half-life compared to Xarelto?

Sandy Sierawski : I am not aware of an antidote, but I will say with discussions I have had with people, that yes, it does have a shorter half-life, so it would be eliminated faster, if an adverse event or something were to occur.

Kevin Desmond, RPh: The Aristotle data was publicized in 2011, in the New England Journal of Medicine, the drug wasn't released until January of this year. Can you comment as to why?

Sandy Sierawski : Sure, the FDA requested some additional data. They didn't request additional data, they requested some information on how the data was collected, so they…I have a specific statement with me about this, um, I lost my train of thought, I'm sorry. The FDA requested information on how the data was collected, so no additional studies were required, the companies provided the data requested

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and it got approved then at a later date of December of 2012. So I don't have specifics on that, there is information on the letter that were sent out by the FDA on the FDA government website. And if you have more specific questions, I can submit one through our medical information.

Shamim Nagy, MD, Chair: Thank you.

Bill O'Neil: Hi, it's nice to see you all again. My name is Bill O'Neil. I am the associate director of health economics and outcomes with BI. I have had a chance to speak with you before, so I am going to try to limit my discussion on Pradaxa to information that is either new or different, and perhaps try to answer some of the questions that have already been raised. So as you know, Pradaxa is the only oral direct thrombin inhibitor in this class indicated for the reduction of stroke and systemic embolism in non-valvular a-fib patients. What is significant about that is that your non-valvular a-fib patients or Medicaid patients have five times the risk of developing a stroke vs. patients without non-valvular a-fib. And what we also know is that 9 out of 10 strokes are going to be an ischemic stroke, so it is a clot that is formed in the heart during a-fib and then it moves to the brain after they get back to rhythm. And so Pradaxa is the only new oral anticoagulant that has a statistically significant reduction in ischemic strokes. And that is important because that's why, physicians and healthcare practitioners, we are putting these patients on these medications. It also reduces hemorrhagic strokes by a great deal, and you heard the physician earlier speak about that. Intracranial bleeds also very good in terms of reduction of bleeding. I think what is also important, I appreciate your question on bleeding and I appreciate your question on dosing. One of the things that is helpful for Pradaxa is it now has been on the market for two years, there are 750,000 patients who have tried it, there are 5,000,000 prescriptions, and there are 20,000 physicians who are comfortable writing for it. When it was released, the FDA decided with other medications to monitor this class of drugs very closely and in November of this year, of 2012, they published the mini sentinel data, which was their looking at, they were basically looking at patients who were naive to warfarin and patients naïve to Pradaxa and looking at GI bleeding rates and intracranial bleeding rates. One thing discovered was that it was very consistent with what was in the RELY, 18,000 member study was and it was very consistent with each other, so there was really no concern about the bleeding rates in comparison to warfarin. They just published in the New England Journal of Medicine this last month a re-update on that to make sure people were looking at the data accurately. So I think that the real work data and experience is very helpful. I am not aware of any studies that look at once a day dosing and twice a day dosing and whether there is a difference in there. I can tell you there was a study to look at Department of Defense data. They were looking at patients who were new on warfarin and new on Pradaxa, and what they discovered after full year of following these patients was that patients on Pradaxa had maintained a 50% persistency rate while patients on warfarin maintained only a 24% persistency rate. Now there are no head to head trials with these new agents, but this is a study looking at a once a day medication with obviously Pradaxa which is dosed twice a day. So, we have some real world data that speaks loudly for the safety and efficacy and our recommendation for you today would be that you maintain Pradaxa on the preferred drug list. Patients can get a superior reduction in the risk of ischemic strokes. I would be happy to share some of that real world data if you would like or entertain any questions that you may have.

Shamim Nagy, MD, Chair: Have any studies been done comparing these new agents?

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Bill O'Neil: Unfortunately there have been no head to head trials. All the trails to date have been with the current gold-standard warfarin. So there are no studies that can compare however in May of last year, the FDA of last year, that is when they allowed us to change our package insert around superiority probably around the time they were relooking at the information for some of the new agents we were talking about today, so once they looked at that data, they felt compelled to allow us to give the superiority, particularly around ischemic stroke and hemorrhagic stroke which is also a critical thing to prevent. But unfortunately, there are no studies head to head.

Shamim Nagy, MD, Chair: any other comments

Ronald Shockley, MD: Did the FDA also give the superiority approval for bleeding and mortality.

Bill O'Neil: I'm glad you asked that. When you look at the RELY trial, if you recall this was a couple years ago, the RELY trial looked at warfarin, but there were two arms for Pradaxa, there was the 150mg dose and the 110mg dose. When you looked at the 150mg dose from a pure numbers, the mortality was actually better. But because we didn't have the statistical power because we broke it into three arms we were not able get the statistical superiority for the mortality. Depending on what bleeding you are looking at, the bleeding rates were lower or the same for Pradaxa with the exception of GI bleeds, and that is what the FDA was looking at through the mini-sentinel. And through the mini-sentinel they discovered in the real world, there were no differences in bleeds compared to warfarin.

Shamim Nagy, MD, Chair: Thank you. Any other comments?

Laura Litzenberger: My name is Laura Litzenberger and I am a pharmacist with Janssen Pharmaceutical and I am here to speak on Xarelto. Xarelto is currently approved by the FDA for six indications, the treatment of DVT, the treatment of pulmonary embolism, it is approved to reduce the risk of recurrence of DVT and pulmonary embolism, it is also approved for DVT leading to PE after hip or knee surgery and then like the other two anticoagulants, it is also approved for the reduction in risk of stroke associated with non-valvular atrial fibrillation. Catamaran did a great job of providing information on all these products. So I don't want to go over that, but I did want to clarify the information. On the DVT treatment and PE treatment and then the recurrence, bBecause of the way the publication was produced, there were two trials contained in the same publication so it looks like the extension trial. The EINSTEIN extension trial was an extension of the DVT trial, where it was a totally separate trial. Patients didn't have to be in the other trial to enter in to this trial, so it was a separate trial leading to a totally separate indication. So although it looks like in the material you were sent it was an extension of that trial, it was really a different trial with a different end-point, that end-point being once a person has completed treatment for DVT or pulmonary embolism, if you continue anticoagulation, would you see a benefit? And if you see a benefit, what risk would you get from those added months from the anticoagulant. And what they found, if you continue giving Xarelto then you save about I think it is 24 events, and what that costs you, which is a relative risk reduction of 82% and what it costs you is 4 major bleeds. So if you look at that in terms of intent to treat, no sorry, the number needed to treat to prevent one event is 17, and the number needed to harm or the number needed to have a bleed over

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placebo was 139. So the risk vs. benefit was there and that is why there was the separate indication for recurrence of DVT. Any questions on that? So then the other thing I just want to bring up, we've heard a lot about atrial fibrillation and Xarelto is approved for a once daily dose for the prevention of stroke associated with atrial fibrillation. But also in the Catamaran report that atrial fibrillation is a disease where the prevalence increases with age and in fact only about 5% of the people under age 65 get atrial fibrillation. So if you're looking at the population that Medicaid serves, it is mainly patients under the age of 65. So if you are making a decision of an anticoagulant based on the breadth of indications, not just one indication where the majority of the people that have indication may be receiving their pharmacy benefits somewhere else. Do you have any questions?

Shamim Nagy, MD, Chair: Thank you.

Robert Maul: Sorry, just for your information, I have an 82 year old lady who was visiting Las Vegas for three days and developed shortness of breath. She had a DVT and a pulmonary embolism, she was from mainland China, the first time she ever came out of the country. She was with her son and she had some problems with Coumadin anticoagulation for the time she has been in the hospital for three days. Her INR is therapeutic on Coumadin, however there is no way she is going to follow up with a Coumadin clinic in Yang Chang China. So she is on Xarelto today, tomorrow I will be discharging her home to China via a mercer airline. And that is a big boon to the family and patient and to the council of San Francisco, Master Bin is very appreciative of our assistance. And Xarelto has helped her get out of the hospital.

Coleen Lawrence: So while Carl is coming up here. I will put it back in perspective for the committee members. Remember this preferred drug list is for the fee for service population. So our population primarily down here in Las Vegas, and what you're looking at and in the rural, and we're talking about urban for Clarke and Washoe County is going to be aging, blind and disabled population. And in the rural population, it is going to be your aging, blind and disabled on the fee for service. And the rural population will be what we call the mommies and the babies. Because in the urban areas, Washoe and Clark County, they are the managed care population. This preferred drug list does not impact the managed care population. So a lot of you physicians who are in practices involved with us, and you know about the managed care population and this preferred drug list, this preferred drug list does not impact the managed care population, so remember this is for the fee for service population. So we throw out a lot of age demographics that we are talking about, just so we know what population we're talking about.

Shamim Nagy, MD, Chair: What is the age then?

Coleen Lawrence: Well fee for service could be of all ages, but we primarily have a large population of age, blind and disabled, so if you're 81 and disabled and come on to the program you qualify through age, blind and disabled categories. If you're over age 65, or you if you are under if you come on the Medicaid rolls through the age, blind and disabled category. Unless you're in the rural counties, you are not urban Washoe or Clark County, if you're outside of that area, then you are fee for service and what we call the mommies and babies program.

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Carl Jeffery, Pharm.D.: They will also have Medicare D as the primary drug coverage if they are over 65 or disabled.

Coleen Lawrence: Just to kind of keep it in perspective, because we're throwing a lot of ages out there.

Displayed on screen:

Current PDL	Current NON PDL
COUMADIN®	
JANTOVEN®	
PRADAXA®	
WARFARIN	
XARELTO ®	

New Product: ELIQUIS®

Carl Jeffery, Pharm.D.: What brought us here today is the addition of the Eliquis to the market. Right now on the PDL shown, we discussed this in November, were we added Pradaxa and Xarelto as preferred drugs. So today we're going to focus on Eliquis. There hasn't been a lot of new information, I think you heard about some of the new indications for Xarelto and Pradaxa has some new information. All of these oral anticoagulants are used for cardiovascular indications. Wafarin is a vitamin K antagonist, apixaban, which is Eliquis and rivaroxaban which is Xarelto are selective Xa inhibitors, where dabigatran or Pradaxa is anti-thrombin. For the approved indications, I will point out that Eliquis and Pradaxa are indicated for the same indications, to reduce the risk of stroke and systemic embolism with patients with non-valvular a-fib. Xarelto has recently added some new indications, and I'm not going to read all those. Then warfarin is the gold-standard and has been available for a long time and has many indications as well. Having that information which has been presented already, it is our recommendation that these products be considered therapeutically and clinically equivalent.

Shamim Nagy, MD, Chair: Any questions? I need a motion.

Adam Zold, Pharm.D.: I motion that all these agents are therapeutically equivalent.

Michael Hautekeet, RPh: I second

Board votes unanimous, "Aye"

Shamim Nagy, MD, Chair: The motion is approved.

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Displayed on Screen:

Proposed PDL	Proposed NON PDL
COUMADIN®	ELIQUIS®
JANTOVEN®	
PRADAXA®	
WARFARIN	
XARELTO ®	

Carl Jeffery, Pharm.D.: So just to briefly talk about Eliquis, I think you have heard all this before. It is a new Xa inhibitor, to reduce the risk of stroke and systemic embolism in patients with non-valvular a-fib. The recommended dose is 5mg twice a day, with a dose reduction based on age or body weight or creatnine, then it decreased to 2.5mg twice a day. No known dietary restrictions with Eliquis, it can be taken with or without food. It doesn't require routine anticoagulation monitors. The efficacy and the safety, we heard about the ARISTLE trial, very a large study, 18,000 patients enrolled, compared to warfarin which is the gold standard. The primary endpoint here was the rate of stroke or systemic embolism and all-cause mortality and major bleeding were also evaluated as secondary endpoints. Results showed that Eliquis significantly reduced the risk of stroke and systemic embolism by 21%, all-cause mortality by 11% and major bleeding by 31%. Eliquis is pregnancy category B, but should still be assessed for risk vs benefit. It should not be given to mothers who are breast feeding, because it is passed in breast milk. The safety and efficacy of Eliquis has not been established in pediatric patients. It is not recommend in severe hepatic impairment. Eliquis, as well as the other, this is across the board with Xarelto and Pradaxa, increases the risk of bleeding and can cause serious or fatal bleeding. Patients should be made aware of the signs and symptoms of bleeding. There is no specific antidote to Eliquis, such as vitamin K for warfarin, but we heard Dr. Miranda say the vitamin K doesn't seem to be that much of a miracle. So our recommendation for the preferred drug list is to keep them the same and include Eliquis as non-preferred.

Shamim Nagy, MD, Chair: Any questions, comments? I need a motion.

Michael Hautekeet, RPh: I motion to accept the proposed PDL.

Adam Zold, Pharm.D.: Can I make a comment that Eliquis may have some benefits with some patients in this group. I have had some patients of mine from the pharmacy that have switched over from Xarelto and Pradaxa, I know it is pretty unique, but I think Eliquis can provide some benefit to these patients.

Michael Hautekeet, RPh: But Eliquis has not been taken off the list, they can still get it, but they have to try a preferred product first.

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Adam Zold, Pharm.D.: But they have to fail a therapy first, just a thought. I'm making a motion to add Eliquis to the preferred drug list.

Shamim Nagy, MD, Chair: Second?

Kevin Desmond, RPh: I second that. It decreases mortality as well, it is the only one that decreases mortality, it seems like it is superior.

Adam Zold, Pharm.D.: It is superior to the gold-standard, so I don't see why we wouldn't have it on the preferred list.

Kevin Desmond, RPh: It seems like it is on a level playing field with the others.

Weldon Havins, MD: Is there any difference shown between Pradaxa and Eliquis?

Carl Jeffery, Pharm.D.: Well, there are no head to head studies with Pradaxa and Eliquis, it is hard to compare. You're comparing two different trials that are set up differently, so it is hard to compare head to head.

Gabe Lither, Deputy Attorney General: So we currently have a motion to add Eliquis as preferred, and that has been seconded, any additional discussion?

Shamim Nagy, MD, Chair: Move to voting?

Board Votes unanimous, "Aye"

Shamim Nagy, MD, Chair: Motion approved.

VI. New Class

A. Ophthalmic Steroids

Shamim Nagy, MD, Chair: So we move to ophthalmic steroids, new class. No public comment.

Displayed on Screen:

Alrex®	FML®
Decadron	Lotemax®
Dexamethasone ophthalmic	Maxidex®
Durezol®	Omnipred
Flarex®	Pred Forte®
Fluorometholone ophthalmic	Pred Mild®
Fluor-Op®	Prednisolone acetate ophthalmic

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FML Forte®	Prednisolone sodium phosphate ophthalmic
FML Liquifilm®	Vexol®

Carl Jeffery, Pharm.D.: This is a new class we are introducing to our preferred drug list. Right now what is included in this class is dexamethasone, Durezol, Flarex, Alrex, Lotemax, Omnipred, Pred Forte, Prednisolone and the Vexol, are all included in this class. Ophthalmic steroids are mostly used postoperatively following ocular surgeries and uveitis, allergies and inflammation of the eye disease or associated with infection or disease or corneal injuries. The topical administration with eye drops is preferred because you get the medicine right where you need it most, where taking something systemically; you don't get the high concentrations where it will be most effective. There is no known mechanism of how steroid eye drops work on the eye, but there are some postulated ideas that it is inhibiting the phospholipase A2. Our recommendation is to consider all of them therapeutically and clinically alternatives.

Shamim Nagy, MD, Chair: Any questions? Or Discussion

Weldon Havins, MD: I move that we consider all of these medications listed at therapeutic alternatives.

David Fluitt, RPh: Second

Board votes unanimous, "Aye"

Motion carries.

Displayed on Screen:

Proposed PDL	Proposed NON PDL
Dexamethasone	Maxidex
Durezol	Flarex®
Fluorometholone	FML
Alrex®	Omnipred
Lotemax	Pred Forte®
Prednisolone	Pred Mild
	Vexol®

Carl Jeffery, Pharm.D.: In patients undergoing cataract surgery, the topical anti-inflammatory agents are used post-operatively to reduce the inflammation response and to treat the established cystoid macular edema. Topically applied non-steroidal anti-inflammatory drugs alone or in combination with corticosteroids are more effective than topical corticosteroids alone in preventing and treating cystoid macular edema. A short course of less than two weeks of a low-potency topical corticosteroid may be

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added to the allergic conjunctivitis treatment regimen if symptoms are not controlled despite treatment with an ophthalmic antihistamine with mast-cell stabilizing properties. Topical corticosteroids are effective in relieving allergy symptoms, however, their use should be limited to the acute suppression of symptoms due to the potential for adverse side effects with prolonged use. Low dose topical corticosteroids may be used for short-term, for less than two weeks, for suppression of irritation secondary to inflammation in moderate dry eye syndrome. Patients should be monitored for adverse side effects. When you look at the studies, there is really nothing, no head-to-head trials showing one agent is better than another. With this, we propose this preferred drug list with mostly the generics being preferred with addition of Alrex and Lotemax also as preferred to give prescribers a few more options.

Shamim Nagy, MD, Chair: Any questions?

Weldon Havins, MD: I move we accept the list as proposed for the preferred drug list.

Adam Zold, Pharm.D.: Second.

Board votes unanimous, "Aye"

Motion carries.

VII. Report by Catamaran on New Drugs to Market, New Generic Drugs to Market, and New Line Extensions

Carl Jeffery, Pharm.D.: In your binder is the Rx Outlook that talks about some of the new products and indications that are available. Not a whole lot this time around. A lot of new agents that are coming out now are anti-neoplastics, and we don't have agents on the PDL now, and I don't know if that is something we will venture into in the future, it can be a pretty touchy subject. I know some other states have tackled these classes. I will let you read through it, there really isn't anything in this I want to call out specifically for this program today.

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

Shamim Nagy, MD, Chair: Time for the next meeting?

Carl Jeffery, Pharm.D.: The fourth Thursday in June.

Coleen Lawrence: Does the board like this location? With microphones? Ok to stick with this location? June 27.

Gabe Lither, Deputy Attorney General: June 27, there has been some discussion that perhaps some board members might not be available on that date. We will have to make sure everyone knows if we are going to schedule for another time.

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Shamim Nagy, MD, Chair: So June 27 is tentative at this point. At this location.

IX. Public Comment

Shamim Nagy, MD, Chair: Any additional public comment before we adjourn? None, so the meeting is adjourned. Thank you all.

X. Adjournment

Meeting adjourned at 2:10PM.

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