



STATE MEDICAID P&T COMMITTEE MEETING
 FRIDAY, February 15, 2008
 7:00 a.m. to 8:30 a.m.
 Cannon Health Building
 Room 125



MINUTES

Committee Members Present:

Lowry Bushnell, M.D.
Karen Gunning, Pharm. D.
Raymond Ward, M.D.
David Harris, M.D.

Kort DeLost, R.Ph.
Thomas Miller, M.D.
Duane Parke, R.Ph.

Board Members Excused:

Jerome Wohleb, Pharm D.

Koby Taylor, Pharm D.

Dept. of Health/Div. of Health Care Financing Staff Present:

RaeDell Ashley
Jennifer Zeleny

Lisa Hulbert
Tim Morley

University of Utah Drug Information Center Staff Present:

Chris Beckwith, Pharm. D.

Linda Tyler, Pharm. D.

Other Individuals Present:

Reed Murdoch, Wyeth
 Rick Moulton, Graceway
 Maria Papayoti, AstraZeneca

Felicia Fuller, Brogen Idec
 Corey James, AstraZeneca
 Lori Howarth, Bayer

Perry Johnson, Graceway
 Linda Craig, AstraZeneca
 Lara Hardman, IHC

Note: Roll did not complete circulation - there were 20+ in attendance.

Meeting conducted by: Karen Gunning, Pharm. D., Chairperson.

1. Minutes for January 2008 were reviewed. Dr. Miller made a motion to approve the minutes. The motion was seconded by Kort DeLost. The motion passed with a unanimous vote by Dr. Harris, Dr. Miller, Dr. Bushnell, Dr. Ward, Dr. Gunning, and Duane Parke.
2. DUR Board update: Tim Morley addressed the Committee. There is not a great deal to report on. The DUR Board has taken up some issues that were raised by the P&T Committee, but found that they didn't have much merit. One issue was the oral hypoglycemics. Those were going to be considered for duplicate therapy, but as Medicaid studied the issue, there were no problems within the Medicaid program. On the previous

day, the DUR Board reviewed the issue of opiate analgesic quantity limits. The DUR Board wanted to do that in conjunction with the issues that were discussed by the P&T Committee. The Board requested some specific information from Medicaid, and will reconsider the issue of the quantity limits once the information is provided.

The Committee asked Duane Parke for the status of contracts for drugs that have been considered. Medicaid is currently pursuing contracts on three ARBs: Diovan, Avapro, and Benicar. The non-preferred ACE inhibitors (the two standalone brands) have not yet been programmed with the appropriate control code. That is still in process.

3. **Inhaled Beta Agonists:** Dr. Beckwith addressed the Committee. There are two types of agents: long acting and short acting. The short acting agents typically have an onset of action within 30 minutes and last anywhere from 4 to 5 hours. The long acting agents typically last at least 12 hours. These agents are used in asthma, exercise-induced bronchospasm, and COPD. They are thought to decrease inflammation of the lungs, and open up the airways by relaxing the smooth muscle. The short-acting agents include albuterol, levalbuterol, metaproteranol, and pirbuterol. This review was prepared by the Oregon Evidence Based Practice Center, and included two agents that are available in Canada, but not in the U.S. These will not be discussed during the review. The methods used by the Oregon Review are to identify key clinical questions for the disease states involved and conduct literature searches to identify studies that address key questions and outcomes of interest. Typically, they try to evaluate outcomes that are more related to health and quality of life, such as symptoms, quality of life, healthcare utilization, mortality, change in other medication use, and use of rescue medications. For safety they evaluated the overall adverse effects, withdrawals due to adverse effects, serious adverse events, and specific adverse events. They did not just evaluate pulmonary function tests or FEV1, because they felt that these are very short term outcomes that do not tell a lot about the patient's overall health. For the overall review of both the short acting and the long acting agents, the review found 6,647 articles. Of these, 771 were retrieved for evaluation. Out of those, they chose to include 104 publications within the review of the short acting and long acting agents. 84 of those were in asthma, 6 were in exercise-induced asthma, and 14 were in COPD. These were publications that looked at the appropriate key clinical questions and key clinical endpoints for these agents. There were not any systematic reviews or meta-analyses included in this review.

The first clinical question related to safety and effectiveness when used in adults with asthma or COPD. Are there differences in efficacy or effectiveness in the short acting agents when used in the outpatient setting? When used in children with asthma, are there differences in efficacy or effectiveness when used in the outpatient setting. This review looked at comparisons between two different agents. For albuterol versus levalbuterol in adults, there were two fair quality studies that were included. In patients who got levalbuterol, albuterol, or placebo, levalbuterol reduced rescue medication use compared to placebo. Albuterol showed a trend towards less rescue medication use than placebo, although it did not reach statistical significance. They did not compare the two agents with each other. There was no difference in asthma symptoms between albuterol and levalbuterol in this trial. Another study looked at hospital admission rates. The admission rates ranged from 0-8% with levalbuterol and 0-7% with albuterol. There were no statistical comparisons made between the groups. For albuterol versus metaproterenol, there are no effectiveness data. For albuterol versus pirbuterol, there are no effectiveness data. For metaproterenol versus pirbuterol there are no data. In children, for albuterol versus levalbuterol there were 3 trials

that were conducted in patients that were admitted to emergency rooms. Two of these studies found no difference in hospital admission rates. One study found that levalbuterol was more effective than albuterol in preventing hospital admission, however the rates were much higher than the other two studies, so there may have been something different about the patients in this study. For albuterol versus metaproterenol in exercise-induced asthma, the agents were equally effective in blocking bronchospasm. The duration of action was greater for albuterol than for metaproterenol, but the exact values were not recorded. For albuterol versus pirbutolol or pirbutolol versus metaproterenol, there were no effectiveness data on which to draw conclusions.

When used in adults with asthma or COPD, are there differences in safety or adverse events among the short-acting agents that were included in the review? This was in the outpatient study. The next question was, when used in children with asthma, are there differences in the rates of adverse effects among the agents? In adults, there is no difference in any adverse events when equivalent doses of the agents are used. There were two fair quality trials that were included for the albuterol versus levalbuterol comparison. Heart-rate usually increases from 5-15 beats per minute with use of these agents. One trial found that heart rate increased more with albuterol 2.5mg versus levalbuterol 0.63mg. These doses are not equivalent; an equivalent dose would have been albuterol 2.5mg and levalbuterol 1.25mg. Another study found that potassium decreased more with albuterol 2.5mg versus albuterol 0.63mg; again, these were not equivalent doses. When given in equivalent doses, these agents had similar effects on palpitations, tachycardia, blood pressure, blood glucose, anxiety, and tremor. For albuterol versus metoproterenol, there were no differences in adverse events. Similarly, there were no differences between metoproterenol and pirbutolol. For albuterol versus pirbutolol, there are no comparative adverse event data. In children, the first comparison was albuterol versus levalbuterol. Adverse events that led to withdrawals occurred in 0-4% of the albuterol patients and 0-12% of the levalbuterol patients. However, there was no statistical comparison made. For other adverse events, there was no difference between the two agents when given at equivalent doses. For the other comparisons between the agents (albuterol versus metoproterenol, albuterol versus pirbuterol, and pirbuterol versus metaproterenol) there are no data.

The next question involves sub-populations. Are there sub-populations of patients based on demographic characteristics such as age, racial groups, gender, other medications, comorbidities, or pregnancy for which one of the agents is more effective or efficacious or causes fewer adverse events than the others? For this question regarding the short acting agents, the only data available are from pulmonary function tests or FEV1, and the only subgroup that was evaluated well was older COPD patients. In these patients, albuterol and levalbuterol were equally effective and safe, albuterol and metaproterenol were equally effective and safe, albuterol and pirbuterol were equally effective and safe, and metaproterenol and pirbuterol were equally effective and safe. There were no evaluations that really looked at race or other comorbidities that found any other information.

Dr. Tyler addressed the Committee. There are two long acting inhaled beta agonists that are available in the United States, salmeterol and formeterol. There is also a new drug called arformeterol that will be discussed, but it is not available in the form of an inhaler for outpatient use. To be considered a long acting beta agonist, the drug needs to have a duration of action greater than 12 hours. Long acting beta agonists have a different role than the short acting ones, since they are used for long-term treatment and control of patients. They do not work and are not appropriate for short-term acute symptom control. Both are available

powdered inhaled formulations. Formeterol uses an aerolizer brand named device with a capsule. The salmeterol uses a discus inhaler device. Salmeterol has a half life of 5.5 hours, and formeterol has a half life of 10 hours. This is probably not a clinically relevant difference, since they both have a duration of action of 12 hours or more. The key questions for them are for safety, efficacy, and special populations such as children. There were 21 studies and 25 publications that compared salmeterol and formeterol. Looking at the efficacy for adults, there were 10 studies. There were no differences that were determined in the outcomes measured, in the amount of rescue medications used, in healthcare utilization, or quality of life studies. One study showed that formeterol had more symptom-free days than salmeterol at 4 weeks, but this difference was not sustained at 8 weeks. There were no differences in patient preferences in the studies that examined that. In children with asthma, there was 1 open-label study. The drugs were determined equal in efficacy in the number of poorly-controlled days, number of mild exacerbations, number of severe exacerbations, and school attendance. Formeterol was better than salmeterol in terms of clinically assessed score at night and patient assessed score at day. There was one study that examined it in exercise-induced asthma, and found that formeterol was better than salmeterol in terms of bronchodilation at 5, 30, and 60 minutes. However, it may have had a sooner onset. There were several studies that examined COPD. There were no differences determined between either of these agents at 1 and 4 hours and no differences in dyspnea symptoms.

In terms of adverse effects, the rate of withdrawal in adults was similar between the two agents. The effect on heart rate was similar between the two agents. One study that used a single dose study found a difference between the agents, but because it is a single dose study, it does not have much bearing. One study comparing the agents in children found that the withdrawal with formeterol was 27% versus salmeterol at 16%. There was also a difference in adverse effects with 1% versus 5%. There was likewise a difference with headache. Formeterol was 18% and salmeterol was 22%.

In the key question about sub-populations, the agents were similar. While there were slight differences, none of them were viewed as clinically relevant. In summary, these agents are similar in almost all regards for clinically relevant questions. The one study in pediatrics that found a clinically relevant difference between salmeterol and formeterol was of poor quality and difficult to assess.

Arformoterol is a selective beta-2 adrenergic agent that is also labeled for the long-term maintenance of treatment of bronchoconstriction. This is nebulized dosing form, so it may be used on an outpatient basis, but it is a different dosage form than the other two agents. Arfomoterol is an active isomer of racemic formeterol and has a half-life of 26 hours. In the studies that have been done in COPD, areformoterol is at least as effective as salmeterol metered dose inhalers. There were no statistical comparisons that were conducted with this agent. The dosing is 15mcg bid in the morning and evening.

Dr. Beckwith addressed the Committee. The Oregon review that evaluated these studies included all dosage forms. They did not differentiate nebulized solutions versus metered dose inhalers, or discuss the different propellants used in the inhalers.

The next part of the discussion has to do with the propellants used in the metered dose inhalers. With the short acting beta agonists, they are available both as solutions for nebulizer and as metered dose inhalers. The metered dose inhalers use a propellant to disperse and deliver the active drug. Most inhalers that have been out on the market for years

have contained chlorofluorocarbon (CFC) propellants. Over the last year or two, most of the albuterol inhalers that have contained CFC's have been discontinued. Previously, they were available both as brand and generic products. Since about 2005, most manufacturers have discontinued production of the CFC-containing products. There is now a hydrofluoroalkane (HFA) propellant that is available, but only in brand name products. There is still one product on the market that contains a CFC, but because of the FDA ban on the use of CFC propellant, that product will also be going off the market by the end of this year. At the time that the ban was put into place, medications were initially exempted from it. Over time, this has changed. In 2005, the FDA and EPA ruled that albuterol inhalers must be off the market if they contain CFC's by the end of 2008. Another rule that was proposed in 2007 would effect other prescription medication products. This rule states that for other inhaled bronchodilators, they must either change to a non-CFC propellant, or they must be off the market by 2009. This ruling has not yet gone into effect; it is a proposed rule.

Dr. Ward asked how many still have CFCs versus another propellant. For the short-acting agents, there are 2 albuterol HFA inhalers available, but they are brand name only. There is also a solution available. For levalbuterol, there is an HFA inhaler and a solution available. For metaproterenol, there is a generic product and a brand name product that contain CFCs. For pirbuterol, there is a brand name product that contains a CFC propellant. This has been summarized in a table provided to the Committee. For the long acting agents, they are available as solution for nebulizer use or as dry powder inhalers. With dry powder inhalers, the medication is intact in a capsule, and the capsule is either stored within the device or gets put into the device and pins inside the device puncture the capsule. The medication is then dispersed when the patient inhales through the device. The two available agents have different devices that they use. Arformoterol is available as a solution for nebulizer, formoterol is available as a dry powder inhaler and nebulized solution, and salmeterol is available only as a dry powder inhaler. With the combination corticosteroid and long acting beta agonists, they are available as metered dose inhalers with an HFA propellant or as a dried powder inhaler.

Dave Young and pharmacy resident Kayla from the University of Utah College of Pharmacy addressed the Committee about the different available inhalation devices. Dave Young works in the University of Utah Adult Asthma Center. Studies that examine device use have shown that both patients and health care providers do rather poorly in how they use the devices. The Committee was provided with instruction sheets on how to use the different inhalers. The albuterol HFA inhalers (ProAir and Ventolin) actually have counters on them to show patients how many doses are left. These inhalers need to have the cap removed and be shaken prior to use. The patient then needs to breathe in deep and slow while depressing the canister. This can be used with a spacer. Most of the metered dose inhalers work like this. Some of the best studies show that 75% of healthcare providers do this correctly. The Xopenex HFA works by the same process. The next short-acting inhaler is the Maxair. This is the same process; it is a metered dose inhaler. On this one a lever is lifted up, and the patient can tell that the drug is delivered because it clicks when it is inhaled correctly. The Foradil device requires that a patient place a capsule into the device, close it, puncture the capsule, and inhale. If there is any powder left, it may require a second inhalation. The device can be confusing and difficult to maneuver, particularly for the elderly. A major counseling point is that patients is that the powder from the capsule can get on the hands. If that happens, they need to wash their hands thoroughly. The Serevent Discus and Advair are both similar. The patient opens them, clicks the lever, inhales, and closes the device. The Symbicort is an MDI device that combines a corticosteroid and a long acting beta

agonist. Advair also has an HFA formulation.

The HFA's and CFC's require initial priming. For medications that are taken regularly, such as Symbicort, they do not need to be primed if patients are taking them regularly as prescribed. In the short acting beta agonists, patients can run into issues with the inhalers not being primed if they are not used for more than a couple of days.

The short acting inhalers, except for Maxair, contain 200 doses. Maxair contains 400 doses. Ventolin has a dose counter. The discus devices also contain dose counters. The dose counters are helpful, because it helps patients know how much medication is left in an inhaler. Many of the inhalers are overfilled, but the manufacturers cannot guarantee the dose of the medication left in the inhaler beyond the 200 or 400 puffs. This can be dangerous for patients who are continuing to use their inhalers beyond their intended number of doses. Manufacturers provide very accurate weight charts to determine how many doses are left based on the weight of the inhaler, but patients do not have access to the scales that measure such small masses with enough accuracy. There was a company that was selling devices to go on top of the inhaler to keep track of doses, but they were expensive and the batteries could not be replaced. The water method is not effective for determining if an inhaler is still full, because the HFA inhalers are not designed to be popped out and placed into water, and there have never been studies to back that up.

The Committee asked if there are any studies available on differences in efficacy of delivery. There are no differences in efficacy of delivery as long as patients are using correct technique. Counseling on correct technique has proven to be the most effective strategy in managing patients in the Adult Asthma Clinic. As far as ease of use, different companies have looked at this individually in their own studies. However, there have not been head-to-head studies between the different devices.

The Committee stated that it is helpful when companies bring placebo inhalers so that they patients can be taught proper technique in a hand-on manner. The Committee was also bothered by the fact that insurance companies do not pay for spacers. Dr. Young was asked what kind of a difference spacers make.

The puff speed on the CFC devices was faster than on the new HFA devices. With good technique, there is no difference. Most people do not have good technique, so patients are routinely sent home with a spacer if they have an MDI prescribed to them. The spacer provides an extra bit of time so that the patient does not have to coordinate between when they spray the inhaler and when they inhale. However, they teach the patients to use the same technique whether or not the spacer is used, so that the drug does not settle in the chamber. There are many spacers on the market, and there are studies with them. The University happens to use one that is about half of the cost of the others. The studies are not so strong on the others that it would justify having patients pay twice the cost when they are paying out-of-pocket. For children under the age of 4, the spacers are necessary.

The Committee asked about spacers where the patient can breathe in and out. The spacer that the University recommends is ventilated to allow that. Patients should still be careful not to let the medication sit for too long and settle in the chamber.

The Committee asked if spacers are covered on Medicaid. Spacers are a covered benefit, so the Committee does not need to worry about them.

Karen Gunning asked Dr. Young to comment on nebulizers versus MDI's, since Medicaid has a large population on nebulized solutions. There are many issues associated with nebulizer solution. Looking at the amount of drug that is delivered via nebulizer versus MDI, as in per cent delivery, they are basically equal if the patient has good technique. If someone is really struggling with technique, the patient should first get a spacer. If a patient believes that a nebulizer is better, they are usually referring to the dose. For example, one puff of an albuterol MDI is 90 mcg, but one vial of albuterol for nebulizer is 2.5mg.

Karen Gunning asked if there are any issues of concern regarding nebulizer use and technique. Dr. Young stated that most of the areas of concern have to do with care and cleaning of the nebulizer.

Dr. Harris stated that in pediatrics it is common for patients to have both MDI and a nebulizer because of the perception that a nebulizer is more effective for delivering medication. There are protocols centered around this. For example, if a mother thinks that the attack is mild, they will go with an inhaler and if it is more severe, they will go with a nebulizer. A nebulizer also allows the child to calm down, because they have to sit and breathe deeply for 20 minutes.

The Committee asked Dr. Young how he decides to use an MDI with a spacer versus a powdered form. Right now, there is not a short acting powder. There used to be a device called a Ventolin Rotocap, which was a dry powder short acting. Right now, short acting inhalers are all MDI. There are some long-acting nebulized solutions, but these are new.

The Committee asked why different medications are developed in different dosage forms, i.e., short acting MDIs and long acting powder inhalers. There is no good reason for this. However, companies were probably aware that CFCs were going to be phased out as the long acting beta agonists were being researched and developed for the market. This may have something to do with it.

The Committee asked if there was any dry powder inhalers for short acting beta agonists were going to become available. This is not known. The Ventolin Rotocap device was not easy to use. Devices are very important to people - some people will fail to pop a dry powder capsule, fail to squeeze an inhaler due to weakness or frailty, spray an inhaler somewhere other than in their mouth, etc. Counseling and reinforcement are the key. All of the devices come with some instructions, but they are tiny and in microscopic print. The American College of Chest Physicians provides written instructions with pictures for the different inhaler devices.

Dr. Ward asked if the agents were vastly different in cost. There used to be a big cost difference when the albuterol with a CFC propellant was available as a generic. Now that many of the albuterols are off the market, the differences are not as great. It is a moot point anyway, since the rest of the CFC-containing inhalers will be going off the market soon.

Perry Johnson with Graceway Pharmaceuticals addressed the Committee. The real advantage that this product provides is helping people to use it correctly. People who are going through an attack are going to be nervous and have a harder time using a press-and-breathe inhaler correctly. The Maxair will help that, because it takes away a lot of the coordination. All that the patient needs to do is to raise the lever, shake it, and breathe. There is no need for a spacer. One of the things that the spacer does is to slow down the

spray. This already has about half of the propellant that the other short acting beta-2's have, so it is a very soft spray. There is a small study in older patients looking at how well they could use a press-and-breathe inhaler. In the observers' opinion, 79% of the patients used the autohaler correctly versus 60% on the press-and-breathe. Using objective measurements, that dropped to 64% and 39% in favor of the Maxair autohaler. The Maxair autohaler does have CFC's in it, and Graceway has applied to the FDA to get an extension on the 2009 date, until they can reformulate the inhaler with another propellant. The Maxair has 400 doses, and the other have 200 doses. Rescue medications should not need to be used more than a couple of times per week, so this inhaler should last a long time. There is no counter on the device, but the device can be test-sprayed. There is also an anecdotal way to tell that the medication is out - the device has more of a hollow sound to it when fired.

Dr. Douglas Ethel of GSK addressed the Committee. None of the short acting beta agonists should be used very often. In the past, it was not considered very critically how much generic albuterol was being used because of the cost. By December 2008, all of the CFC albuterol is gone. The dose counter is the key. In an article published in the Annals of Allergy, Asthma, and Immunology in 2006, out of 500 asthma patients from the Mothers of Asthmatics Group, 54% of the bronchodilators were being used in excess of the recommended guidelines. Only 36% of the bronchodilator users remember ever being told that they should keep track of the number of doses. Unfortunately, only 6% of those were told by a pharmacist. 25% of these patients found their inhaler to be empty during an asthma exacerbation. The only way to prevent that is with a dose counter. The problem with floating testing the HFA products is that they have a different seal that water will degrade. The reason that there are no dry powder inhalers for short acting beta agonists is due to cost. Those devices are very expensive to manufacture, and an MDI is cheap.

Karen Gunning stated that there do not seem to be any significant differences among the short acting beta agonists in safety and efficacy. The discussion revolves around education, which the Committee does not have control over.

Dr. Ward recommended that both nebulized forms and MDI forms be included on the PDL. Dr. Ward asked if the Committee felt that at least one HFA-containing inhaler be included on the PDL. Generic CFC-containing albuterol is not available on a consistent basis, but other CFC-containing inhalers are. The FDA has not yet implemented a hard deadline for removing CFC-containing inhalers other than albuterol from the market.

The Committee felt that the counting device on ProAir is a valuable device.

Duane Parke made a motion that the short acting beta agonists are equally safe and efficacious, and that at least one nebulized dosage form and one MDI dosage form be available on the PDL.

The Committee asked Dr. Young about how often the Maxair autohaler device is used at the Adult Asthma Clinic. That device is useful when a patient cannot use an MDI properly despite extensive training. The elderly who cannot spray an inhaler can also be taught to activate the lever by pushing it against a table. They do not generally start out with the Maxair autohaler because patients preferred to have a lower-cost generic albuterol when it was available.

Karen Gunning seconded the motion proposed by Duane. The motion passed with a

unanimous vote by Dr. Harris, Dr. Miller, Kort DeLost, Dr. Bushnell, Dr. Ward, Dr. Gunning, and Duane Parke.

For the long acting beta agonists, Karen Gunning felt that the device is unweildy. Dr. Hardman, a local pulmonologist, felt that patients can use it once they are taught proper technique.

Dr. Ward felt that the data in the Oregon review did not demonstrate that one of the long acting beta agonists was better than the other. The Committee asked if the half-life of the agents had any bearing on efficacy. Dr. Hardman stated that patients like the formeterol better because it has a faster onset and they can feel it working. As far as efficacy, they are the same.

Kort Delost made a motion that there is little clinically significant difference between the long acting beta agonists, and Medicaid should choose an agent based on cost. Dr. Harris seconded the motion. The motion passed with a unanimous vote by Dr. Harris, Dr. Miller, Kort DeLost, Dr. Ward, Dr. Gunning, and Duane Parke.

4. Inhaled Beta Agonist/Steroid Combinations: Dr. Beckwith addressed the Committee. For the inhaled beta agonist/steroid combinations, there are two products available. Budesonide/formeterol is available as Symbicort and fluticasone/salmeterol is available as Advair. Advair is available as HFA and discus. Symbicort is labeled for use in asthma for long-term maintenance. It is also used off-label for COPD. Advair HFA is labeled for use in asthma. Advair Discus is labeled for use in asthma and COPD. The methods used by the University of Utah Drug Information Service were similar to the methods used by Oregon. They searched relevant databases to look for trials that directly compared the two products in combination with each other. The key endpoints that they looked for were exacerbations in symptoms and symptom free days. There are two clinical trials that have compared these two products in patients with asthma. One was a 24 week trial of almost 1400 adults. The authors found no significant differences in these groups in changes in pulmonary function tests, number of symptom-free days, or number of rescue medicine-free days. The next study had a 4 week double blind phase in 658 patients. There were similar numbers of patients that achieved a week of well controlled asthma with either the Symbicort or Advair. In the open label extension, which was 6 months long, the exacerbation rate was similar in the two groups. In COPD, there are no studies that have evaluated long term results in evaluating these two agents. There are two single-dose studies to get an idea of short term effects. They both found equivalent effects on pulmonary function tests with the two agents.

As far as comparative safety between the two products, the adverse effects and discontinuation due to adverse effects were similar between the two groups in the comparative trials that were assessed. They both have similar black box warnings.

Dr. Ethel from GSK addressed the Committee about Advair. Advair Discus is indicated down to age 4 and for COPD. Advair HFA is not indicated for COPD or children at this time. There will hopefully be a pediatric indication for Advair HFA by this summer. According to guidelines, these dual controllers are to be used for moderate persistent asthmatics. They start on a corticosteroid. If that is not helpful, they can either increase the steroid or go to the dual controller product. Looking at the median dose of the steroids, the budesonide products barely get into the median dose range, whereas the fluticasone products get into the top end of the median dose range. There is a considerable difference in these

products steroid-wise.

Dr. Ward asked if there is a significant difference in cost between the Advair products. Kort did not know since he has not seen prescriptions written for the HFA product. Dr. Hardman stated that she knows that there is a difference between the different strengths of Advair.

Maria Pappayoti of AstraZeneca addressed the Committee. High dose Symbicort studies did include patients with moderate to severe asthma. Many of the patients were on the 500mg Advair, and were well controlled with the Symbicort. The best benefit from inhaled corticosteroids comes from low to medium doses. There is a drop in benefits and a very high increase in adverse events with higher doses. This is why AstraZeneca only makes the two strengths of Symbicort. Symbicort is in an MDI form. There were about 9,000 patients in the studies. They didn't need a spacer, they were just instructed using the patient instructions in the dosing information. There was an in-vitro study with spacers showing that when used properly there are fine particle fractions consistent with appropriate dosing. Symbicort is different because budesonide is the inhaled corticosteroid. This is unique because the molecule is a pregnancy category of B. There were about 2,500 infants that were born to mothers using inhaled budesonide, and no increase in congenital fetal malformation was seen. Formoterol lasts for 12 hours and has a rapid onset of action. This prods the asthmatic to take the controller medication.

Dr. Lara Hardman addressed the Committee. She is a pulmonologist in Salt Lake City. She uses both products, and has no financial ties to disclose. If both products will be on formulary, that would be great. She has reasons that she would choose one over the other. Karen Gunning and Dr. Ward explained that the state will ultimately make the decision of what to include on the PDL, and that the PDL could be overridden by the prescriber. There are many patients that have been on Advair Discus for a long time, and have not been able to learn to use an MDI. Formoterol is a little better than Serevent because of the shorter duration of onset and the hydrophilic versus hydrophobic properties. Outcomes are very similar. Fluticasone and budesonide are not, however similar - fluticasone is clearly more potent. Having fluticasone as an option for the more severe patients has kept patients out of the ER. Having Serevent come out was also huge, and the ease of use of the Advair Discus was huge, and has kept costs of care down for her patients. Symbicort is also a good product, and is useful for managing COPD patients. Having a fluticasone product for difficult asthmatics is important.

The Committee asked Dr. Hardman if her opinion is based on her experience or data. It is based on both.

The Committee asked about patients' preference of formoterol. Patients to get the feedback of feeling the rapid onset of action. Serevent is much more smooth in its onset because of its hydrophilic property. However, this creates a hypothetical worry for the patients that are not seen and educated regularly possibly using it as a short-acting.

Dr. Ward stated that there were several letters sent to the P&T Committee. All of the letters were very similar and have received a written response. Karen Gunning summarized the letters for the meeting. There were 16 letters received. There is apparently a misunderstanding about the process involved with the PDL. Many physicians are concerned about the possibility of a PA. The PDL does not have the ability to impose a PA requirement, as per the legislation. There is also a sense that there is only one available

controller medication, and that if Advair is taken away asthma cannot be treated. This has not been borne out by the discussion today.

The Committee stated that there needs to be an agent available with a pediatric indication. Symbicort currently does not have one. Maria Pappayoti stated that Symbicort is currently seeking a pediatric indication, a COPD indication, and plans on having a dose counter very soon.

Karen Gunning asked the Committee if there is a need for both the HFA and the Discus dosage form of Advair as a preferred status. The HFA is not indicated for pediatric use.

Kort DeLost made a motion that the agents are equal in safety and efficacy, but there does need to be an agent available with a pediatric indication. Dr. Harris seconded the motion. The motion passed with a unanimous vote by Dr. Harris, Dr. Miller, Kort DeLost, Dr. Ward, Dr. Gunning, and Duane Parke.

Next Meeting Set for Friday, March 21, 2008. The Committee asked why cholinergic agents were not included in the scheduled asthma discussions. There are two cholinergic agents available, and their half-lives are so distinct that they do not lend well to the PDL. As an educational item, Karen Gunning stated that there is an area of educational concern that she has noticed in the state. She and Dave Young are involved in the Asthma Friendly Pharmacist Program through the University. For every 5 albuterol inhalers that are dispensed in the state, there is 1 controller inhaler dispensed. There are some other uses for albuterol, but this is still an area of concern. This disconnect may be an area that the DUR Board could study. Medicaid does have a limit of 2 inhalers per month. Meeting Adjourned.

Minutes prepared by Jennifer Zeleny