

Minutes of Meeting

Alabama Medicaid Agency Pharmacy and Therapeutics Committee

August 14, 2013

Members Present: Vice chairperson-Ms. Janet Allen, Dr. Frances Cohenour, Dr. Kelli Littlejohn, Ms. LaTonage Porter, Dr. Melinda Rowe, and Dr. Chivers Woodruff

Members Absent: Chairperson-Dr. Gerard Ferris, Dr. Julia Boothe, and Dr. Donald Marks

Patient Care Networks of Alabama (PCNA) Staff Present: Mr. Chris Barwick, Dr. Amy Donaldson, Dr. Joshua Lee, Dr. Holley Rice, and Dr. Kristian Testerman

Presenters: Dr. James Gagnon and Dr. Mark Kohn

Presenters Present via teleconference: None

1. OPENING REMARKS

Vice chair Allen called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 9:15 a.m.

2. APPROVAL OF MINUTES

Vice chair Allen asked if there were any corrections to the minutes from the May 15, 2013 P&T Committee Meeting.

There were no objections. Dr. Woodruff made a motion to approve the minutes as presented and Dr. Cohenour seconded to approve the minutes. The minutes were unanimously approved.

3. PHARMACY PROGRAM UPDATE

Dr. Littlejohn oriented the Committee members to the Provider Alerts that are available on the Agency's website. She noted that the Regional Care Organization developments are posted on the Agency website. Dr. Littlejohn highlighted changes to the pharmacy program effective October 1, 2013. These changes include a monthly prescription limit for adults, a three month supply on certain therapeutic classes and discontinued coverage of most over-the-counter products. In addition, a large educational effort concerning these changes will begin soon. Dr. Littlejohn noted that Drug Enforcement Agency (DEA) edits, compounding changes, and copay increases were implemented in July, 2013.

4. ORAL PRESENTATIONS BY MANUFACTURERS/MANUFACTURERS' REPRESENTATIVES

Five-minute verbal presentations were made on behalf of pharmaceutical manufacturers. The process and timing system for the manufacturers' oral presentations was explained. The drugs and corresponding manufacturers are listed below with the appropriate therapeutic class. There were a total of five manufacturer verbal presentations at the meeting.

5. PHARMACOTHERAPY CLASS REVIEWS (Please refer to the website for full text review.)

The pharmacotherapy class reviews began at approximately 9:25 a.m. There was one new drug class review, as the androgens were reviewed for the first time.

Androgens, AHFS 680800

Manufacturer comments on behalf of these products:

AndroGel[®] - Abbvie

Dr. Kohn stated that the androgens are a new pharmacotherapy class review. The agents in this class include danazol, fluoxymesterone, methyltestosterone, oxandrolone, oxymetholone, buccal testosterone, testosterone transdermal system, testosterone topical gel, testosterone topical solution, testosterone enanthate and testosterone cypionate. Danazol is an oral synthetic derivative of ethisterone with a weak androgenic activity. Oxandrolone and oxymetholone are anabolic steroids. Oxandrolone suppresses gonadotropic functions of the pituitary gland and exhibits direct action on the testes. It also increases low-density lipoprotein and decreases high-density lipoprotein. Testosterone is an endogenous androgen that plays a role in the normal growth and development of the male sex organs as well as the maintenance of secondary sex characteristics.

With the exception of danazol, oxandrolone, and oxymetholone, all agents in this review are Food and Drug Administration (FDA)-approved for the management of male hypogonadism. The oral synthetic testosterone and injectable testosterone are also FDA-approved for the treatment of delayed puberty in males and metastatic mammary cancer in females. Danazol is FDA-approved for the treatment of endometriosis, fibrocystic breast cancer and hereditary angioedema, though it is not indicated for the management of male hypogonadism. Oxandrolone is approved for adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and in some patients who without definite pathophysiologic reasons fail to gain or to maintain normal weight. Oxymetholone is approved for the treatment of anemias caused by deficient red cell production. Currently, danazol, methyltestosterone, oxandrolone, testosterone cypionate, and testosterone enanthate are available generically.

Hypogonadism is a defect of the reproductive system which results in a lack of function of the gonads (testes). Primary hypogonadism is hypogonadism resulting from a defect of the gonads while secondary hypogonadism, also known as hypogonadotropic hypogonadism, results from defects in the hypothalamus or pituitary. Male hypogonadism may manifest with testosterone deficiency and/or infertility. Clinical signs and symptoms depend primarily on the age at the onset of the condition.

According to current guidelines, testosterone replacement therapy is recommended for symptomatic men with classical androgen deficiency syndromes to induce and maintain secondary sex characteristics and to improve sexual function, sense of well-being, muscle mass, strength and bone mineral density. The available intramuscular, subdermal, transdermal, oral and buccal preparations of testosterone are safe and effective. The selection of the preparation should be a joint decision of the patient and physician. Short-acting preparations may be preferred over long-acting depot preparations in the initial treatment of patients with late-onset hypogonadism because of the possible development of an adverse event that may require rapid discontinuation of testosterone replacement therapy. The orally administered alkylated androgen preparations are generally not recommended due to poor androgen effects, adverse lipid changes and hepatic side effects. In women with pelvic pain associated with endometriosis, danazol is one of several medical treatments that have been employed for the treatment of endometriosis. For the treatment of hereditary angioedema, long-term prophylactic treatment is appropriate for patients in whom on-demand acute treatment was inadequate. The 17- α -alkylated androgens (e.g., danazol) can be considered in patients ≥ 16 years of age and women who are not pregnant or breastfeeding.

In clinical studies, testosterone buccal and topical products have been shown to increase serum testosterone levels and/or improve lean body mass, decrease body fat and improve sexual function in men with hypogonadism. Head-to-head studies comparing testosterone topical gel to testosterone transdermal system have shown greater improvement in serum testosterone levels, lean body mass and sexual function as well as fewer adverse events with testosterone gel compared to testosterone patches in men with hypogonadism. Severe hepatotoxicities have been associated more commonly with oral androgen than topical androgen therapy and liver function tests should be monitored periodically. In a meta-analysis of studies evaluating the role of danazol in women with heavy menstrual bleeding, there was no significant improvement in menstrual blood loss with danazol compared to progestins. In addition, there was no significant improvement in dysmenorrhea with danazol compared to mefenamic acid.

Overall, there is insufficient evidence to support that one brand androgen is safer or more efficacious than another. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand androgens within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand androgen is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

6. PHARMACOTHERAPY CLASS RE-REVIEWS (Please refer to the website for full text reviews.)

There were a total of 10 drug class re-reviews. The inhaled antimuscarinics, respiratory β -adrenergic agonists, leukotriene modifiers, inhaled mast-cell stabilizers, respiratory agents-corticosteroids, respiratory smooth muscle relaxants, intranasal corticosteroids, eye, ear, nose and throat preparations-antiallergic

agents, eye, ear, nose and throat preparations-antibacterials, and eye, ear, nose and throat preparations-vasoconstrictors were last reviewed in February 2011.

Inhaled Antimuscarinics: American Hospital Formulary Service (AHFS) 120808

Manufacturer comments on behalf of these products:

Spiriva HandiHaler[®] - Boehringer Ingelheim

Dr. Gagnon commented that the inhaled antimuscarinics that are included in this review are listed in Table 1. Since the last review acclidinium was approved by the FDA. The fixed-dose combination product containing ipratropium/albuterol is included in the respiratory beta-adrenergic agonists class review. The inhaled antimuscarinics are approved for the maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Tiotropium is also approved to reduce exacerbations in patients with COPD. Tiotropium has a longer duration of action than ipratropium and can be dosed once daily. Acclidinium was the most recently FDA-approved inhaled antimuscarinic in July 2012. Similar to tiotropium, acclidinium is a long-acting inhaled antimuscarinic but requires twice daily dosing. Ipratropium inhalation solution is the only product, in this class, that is available in a generic formulation.

Treatment guidelines that incorporate the use of the inhaled antimuscarinics are summarized in Table 2. For the treatment of mild airflow obstruction, the use of a short-acting bronchodilator as needed is recommended for the relief of breathlessness and exercise limitation. For patients who require daily maintenance therapy to control symptoms, a long-acting inhaled bronchodilator is recommended, such as a β_2 -agonist or antimuscarinic. Guidelines do not indicate a preference as there is insufficient evidence to favor one long-acting bronchodilator over another. When selecting an inhaled antimuscarinic, a long-acting agent is preferred over a short-acting agent due to differences in efficacy.

Tiotropium has been shown to significantly reduce COPD exacerbations, improve spirometric indices, and lead to improvements in health-related quality of life and symptom scales compared to treatment with ipratropium. Acclidinium has been shown to significantly improve spirometric indices and lead to improvement in health related quality of life and symptom scores compared to treatment with placebo.

Therefore, all brand short-acting inhaled antimuscarinics within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use. Acclidinium and tiotropium offer significant clinical advantages in general use over short-acting inhaled antimuscarinics.

No brand short-acting inhaled antimuscarinic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

At least one long-acting inhaled antimuscarinic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Respiratory Beta-Adrenergic Agonists: AHFS 121208

Manufacturer comments on behalf of these products:

Combivent Respimat[®] - Boehringer Ingelheim

Dr. Gagnon commented that the respiratory β_2 -agonists that are included in this review are listed in Table 1. Since the last review, indacaterol dry powder inhaler and a fixed dose ipratropium/albuterol solution inhaler were approved by the FDA. All of the β_2 -agonists elicit a similar biologic response; however, they differ in their dosing requirements, pharmacokinetic parameters and adverse events. Short-acting β_2 -agonists include albuterol, ipratropium/albuterol, levalbuterol, metaproterenol, pirbuterol and terbutaline. These agents increase airflow within 30 minutes and the effects may last up to four to five hours. Long-acting β_2 -agonists include albuterol (extended-release tablets), arformoterol, formoterol and salmeterol. They are administered twice daily for the maintenance treatment of bronchospasm associated with asthma and COPD. Indacaterol (Arcapta[®]), a long-acting β_2 -agonists, was FDA-approved in July 2011 for the long term, once-daily maintenance bronchodilator treatment of airflow obstruction in people with COPD including chronic bronchitis and emphysema. Also approved in 2011 (October) was Combivent Respimat[®] a new fixed-dose combination of (ipratropium/albuterol) for patients with COPD on a regular aerosol bronchodilator who continue to have evidence of bronchospasm and who require a second bronchodilator. Albuterol (immediate-release tablets, inhalation solution, sustained-release tablets and syrup), ipratropium/albuterol (inhalation solution), levalbuterol (inhalation solution), metaproterenol (syrup and tablets) and terbutaline (tablets) are available in a generic formulation.

Treatment guidelines that incorporate the use of the β_2 -agonists are summarized in Table 2. For the treatment of asthma, guidelines consistently recommend the use of a short-acting inhaled β_2 -agonist for all stages of the disease. They should be used on an as needed basis for symptom control and for the pre-treatment of exercise-induced bronchospasm. For the long-term maintenance treatment of asthma, the inhaled corticosteroids are recommended as first-line therapy. When additional therapy is needed, guidelines recommend the addition of an inhaled long-acting β_2 -agonist in patients five years of age and older. Long-acting β_2 -agonists should not be used as monotherapy since they do not affect airway inflammation. Guidelines do not give preference to one short- or long-acting β_2 -agonist over another for the treatment of asthma.

For the treatment of mild airflow obstruction associated with COPD, guidelines recommend the use of a short-acting bronchodilator as needed to relieve breathlessness and exercise limitation. For patients who require daily maintenance therapy to control symptoms, the use of an inhaled long-acting bronchodilator is recommended, such as a β_2 -agonist or antimuscarinic. Guidelines do not indicate a preference as there is insufficient evidence to favor one long-acting bronchodilator over another.

An increased risk of asthma-related death has been reported with the use of the inhaled long-acting β_2 -agonists. The data are insufficient to determine whether concurrent use of inhaled corticosteroids mitigates the increased risk of asthma-related death. According to the prescribing information, the use of an inhaled long-acting β_2 -agonist should only be considered as additional therapy for patients who are not adequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid. Once asthma control is achieved and maintained, therapy should be stepped down (e.g., discontinue the long-acting β_2 -agonist) if possible. The inhaled long-acting β_2 -agonists should not be used for patients whose asthma is adequately controlled on a low or medium dose of an inhaled corticosteroid. The available data also suggest that the inhaled long-acting β_2 -agonists increase the risk of asthma-related hospitalization in pediatric and

adolescent patients. For pediatric and adolescent patients with asthma who require the addition of an inhaled long-acting β_2 -agonist to an inhaled corticosteroid, a fixed-dose combination product should be considered to ensure adherence with both drugs. If the use of a separate long-term asthma control medication (e.g., inhaled corticosteroid) and an inhaled long-acting β_2 -agonist is clinically indicated, appropriate steps must be taken to ensure adherence with both treatments.

For the treatment of asthma, several comparative studies have demonstrated similar improvements in respiratory endpoints with the use of short-acting β_2 -agonists; however, a few studies have demonstrated greater efficacy with one agent over another. The long-acting β_2 -agonists have been shown to be more effective than the routine use of short-acting β_2 -agonists for the maintenance treatment of asthma. Clinical studies directly comparing the long-acting β_2 -agonists have also demonstrated similar outcomes for the majority of the endpoints assessed, including their ability to control asthma symptoms, prevent exacerbations, improve quality of life, and prevent hospitalizations or emergency visits in patients with persistent asthma not controlled on inhaled corticosteroids alone. There does not appear to be a difference in adverse events with the long-acting β_2 -agonists.

For the treatment of COPD, regular treatment with long-acting bronchodilators are more effective than treatment with short-acting bronchodilators. Studies directly comparing the long-acting β_2 -agonists have demonstrated similar improvements in some, but not all, respiratory endpoints. Some studies suggest that formoterol may have a faster onset of action than salmeterol. Tiotropium may provide a greater clinical benefit than long-acting β_2 -agonists with regards to spirometric endpoints, dyspnea, exacerbations, quality of life, and health care resource utilization. Data are not available to determine whether the rate of death in patients with COPD is increased by long-acting β_2 -agonists.

Therefore, all brand short-acting respiratory beta-adrenergic agonists within the class reviewed are comparable to each other and to the generics and OTC products (if available) and offer no significant clinical advantage over other alternatives in general use. The brand long-acting respiratory beta-adrenergic agonists offer significant clinical advantages over the short-acting respiratory beta-adrenergic agonists, generics and OTC products (if available) and are comparable to each other. However, for patients with asthma, the long-acting respiratory beta-adrenergic agonists are not recommended as first-line therapy. For patients with COPD, the long-acting respiratory beta-adrenergic agonists do not offer significant clinical advantages over other long-acting inhaled bronchodilators (e.g., inhaled antimuscarinics). Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

No brand respiratory beta-adrenergic agonist is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Leukotriene Modifiers: AHFS 481024

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that the leukotriene modifiers that are included in this review are listed in Table 1. Montelukast and zafirlukast are classified as leukotriene receptor antagonists, whereas zileuton is classified as a 5-lipoxygenase inhibitor. All of the agents are approved for the long-term management of asthma. Montelukast is also approved for the treatment of allergic rhinitis, as well as for the prevention of exercise-induced bronchoconstriction. Montelukast and zafirlukast are available in generic formulations.

Treatment guidelines that incorporate the use of the leukotriene modifiers are summarized in Table 2. For the treatment of asthma, guidelines note that inhaled corticosteroids are currently the most effective anti-inflammatory medications for the treatment of persistent asthma for patients of all ages. Concerning the leukotriene modifiers specifically, current guidelines note that these agents are generally less effective than low doses of inhaled corticosteroids and therefore may be used as an alternative treatment in patients with mild persistent asthma. Additionally, some patients with aspirin-sensitive asthma respond well to leukotriene modifiers. Current guidelines also note that leukotriene modifiers used as add-on therapy may reduce the dose of the inhaled corticosteroids required by patients with moderate to severe asthma, and may improve asthma control in adult patients whose asthma is not controlled with low or high doses of inhaled corticosteroids. Several studies have demonstrated that leukotriene modifiers are less effective than long-acting β_2 -agonist as add-on therapy. Guidelines do not give preference to one leukotriene modifier over another for the treatment of asthma.

Clinical trials have demonstrated that the leukotriene receptor modifiers have been shown to be useful for the treatment of allergic rhinitis, either alone or in combination with antihistamines. In clinical trials, there was no difference in efficacy between montelukast and second-generation antihistamines; however, montelukast was found to be less effective than treatment with intranasal corticosteroids.

Clinical trials have also demonstrated that the leukotriene modifiers improve asthma outcomes, including pulmonary function, daytime symptoms, nocturnal awakening, β_2 -agonist use, exacerbations and quality of life. However, they have generally been shown to be less effective than inhaled corticosteroids and long-acting β_2 -agonists. There are very few studies that directly compare the leukotriene modifiers for the treatment of asthma.

There is insufficient evidence to support that one brand leukotriene modifier is more efficacious than another. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand leukotriene modifiers within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand leukotriene modifier is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Inhaled Mast-Cell Stabilizers: AHFS 481032

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that cromolyn sodium inhalation solution is the only inhaled mast-cell stabilizer that is currently available in this class. It is approved for the maintenance treatment of asthma, as well as for the prophylaxis of acute bronchospasm induced by exercise, exposure to cold air, or other environmental agents. It is available in a generic formulation. There have been no major changes in the prescribing information, treatment guidelines or clinical studies since this class was last reviewed.

Therefore, all brand inhaled mast-cell stabilizers within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand inhaled mast-cell stabilizer is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Respiratory Agents-Corticosteroids: AHFS 481008

Manufacturer comments on behalf of these products:

Pulmicort Flexhaler[®] - AstraZeneca

Symbicort[®] - AstraZeneca

Dr. Gagnon commented that the inhaled corticosteroids that are included in this review are listed in Table 1. They are available as single entity agents. Budesonide, fluticasone, and mometasone are also available in combination with a long-acting β_2 -agonist. All of the agents are approved for the maintenance treatment of asthma. The fixed-dose combination products containing budesonide/formoterol and fluticasone/salmeterol are also approved for the treatment of COPD, including chronic bronchitis and emphysema. Budesonide inhalation solution is the only product that is currently available in a generic formulation.

Treatment guidelines that incorporate the use of the inhaled corticosteroids are summarized in Table 2. These agents are the most effective long-term medications for the treatment of asthma and are consistently recommended as first-line therapy. Guidelines do not give preference to one inhaled corticosteroid over another. When additional therapy is needed, it is recommended that a long-acting β_2 -agonist be added to an inhaled corticosteroid in patients five to 12 years of age.

For the treatment of mild airflow obstruction associated with COPD, guidelines recommend the use of a short-acting bronchodilator as needed to relieve breathlessness and exercise limitation. For patients who require daily maintenance therapy to control symptoms, the use of an inhaled long-acting bronchodilator is recommended, such as a β_2 -agonist or antimuscarinic. The inhaled corticosteroids have been shown to

reduce the frequency of exacerbations and improve health status in symptomatic patients with an forced expiratory volume in one second (FEV₁) <50% predicted. Therefore, they are recommended in patients with more advanced disease and for those with repeated exacerbations. The combination of an inhaled corticosteroid and a long-acting β 2-agonist is more effective than monotherapy in reducing exacerbations, improving lung function and improving health status. Guidelines do not give preference to one inhaled corticosteroid over another for the treatment of COPD.

Dr. Gagnon noted that the safety concerns associated with the long-acting β 2-agonist are applicable to the inhaled corticosteroid/long-acting β 2-agonist fixed dose combination products.

Numerous trials have been conducted with the inhaled corticosteroids. They have been shown to improve pulmonary function, prevent symptoms and exacerbations, reduce the need for emergency department treatment, and reduce asthma mortality compared to other maintenance therapies. When administered at equipotent doses via comparable delivery devices, the inhaled corticosteroids do not appear to differ in their ability to control asthma symptoms, prevent exacerbations, or reduce the need for rescue medication use. Several studies have demonstrated similar outcomes with the fixed-dose combination inhalers compared to the coadministration of their individual components as separate inhalers. Studies directly comparing the fixed-dose combination products have shown conflicting results with regards to asthma outcomes.

Given the role of the single entity inhaled corticosteroids in the management of asthma, one or more brand products within the class reviewed offers significant clinical advantage in general use over the generics and OTC products (if applicable), but is comparable to all other brands in the same class. All brand fixed-dose combination inhaled corticosteroids within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use. The fixed-dose combination inhaled corticosteroids should be available through the medical justification portion of the prior authorization process for patients who require the combination of an inhaled corticosteroid and long-acting β 2-agonist to control their respiratory symptoms.

Alabama Medicaid should work with manufacturers of brands in the class on cost proposals so that at least one single entity brand inhaled corticosteroid is selected as a preferred agent.

No brand fixed-dose combination inhaled corticosteroid is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Respiratory Smooth Muscle Relaxants: AHFS 861600

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that the respiratory smooth muscle relaxants that are included in this review are listed in Table 1. They are approved for the treatment of asthma, chronic bronchitis and emphysema. All of the products are available in a generic formulation, with the exception of dyphylline. There have been no

major changes in the prescribing information, treatment guidelines or clinical studies since this class was last reviewed.

There is insufficient evidence to support that one brand respiratory smooth muscle relaxant is safer or more efficacious than another. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand respiratory smooth muscle relaxants within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand respiratory smooth muscle relaxant is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Intranasal Corticosteroids: AHFS 520808

Manufacturer comments on behalf of these products:

None

Dr. Kohn commented that since the last review of the intranasal corticosteroids beclomethasone (QNASL[®]) and ciclesonide (Zetonna[®]) nasal aerosols have been approved and are the only two intranasal corticosteroid products formulated as a “dry” nasal aerosol; all other products in within the class are formulated as aqueous suspensions. In addition, Dymista[®] was approved and contains the antihistamine azelastine and the steroid fluticasone in combination to manage the symptoms of allergic rhinitis. Intranasal corticosteroids are used for the management of allergic rhinitis, some forms of nonallergic rhinitis and nasal polyps. They are generally well tolerated and are associated with limited drug interactions due to their localized administration and limited systemic absorption. Like other corticosteroids, intranasal corticosteroids carry warnings regarding the use in patients with active infection and the development of signs of adrenal insufficiency with the administration of higher than recommended doses. Flunisolide, fluticasone propionate and triamcinolone are currently available generically.

Intranasal corticosteroids are considered first-line agents for the treatment of allergic rhinitis, especially for patients with moderate to severe symptoms. Consensus guidelines do not recommend the use of one intranasal corticosteroid product over another. All ten available intranasal corticosteroids have demonstrated safety and efficacy for their respective indications. These agents have been shown to be effective in reducing rhinitis-related nasal symptoms such as congestion, rhinorrhea, sneezing, nasal itch, and postnasal drip.

Fluticasone furoate, mometasone and triamcinolone are FDA-approved for use in children two years of age and older and fluticasone propionate is FDA-approved for use in children four years of age and older. Beclomethasone, budesonide, ciclesonide, and flunisolide are approved for use in children six years of age and older. The newer nasal aerosol formulations of beclomethasone (QNASL[®]) and ciclesonide (Zetonna[®])

may be preferred by patients as the other intranasal corticosteroid products are formulated as aqueous suspensions which have the potential to drip down or out of the nose following administration.

Comparative clinical trials have demonstrated similar efficacy with the intranasal steroids for the majority of the endpoints assessed in patients with allergic rhinitis. The differences in potencies, systemic bioavailabilities and onset of action did not translate to improved efficacy. However, there were subtle differences reported among the various agents in tolerability and patient preference.

There is insufficient evidence to support that one brand intranasal corticosteroid is safer or more efficacious than another. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand intranasal corticosteroids within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand intranasal corticosteroid is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Eye, Ear, Nose, and Throat Preparations: Antiallergic Agents: AHFS 520200

Manufacturer comments on behalf of these products:

None

Dr. Kohn commented that the eye, ear, nose, and throat (EENT) antiallergic agents that are included in this review are listed in Table 1. Since the last review, alcaftadine ophthalmic solution (Lastacaft[®]) was approved by the FDA and epinastine (Elestat[®]) became available generically. The EENT antiallergic agents are approved for the treatment of allergic conjunctivitis and rhinitis. They are available in both nasal and ophthalmic formulations. Emedastine is a relatively selective, histamine H1-receptor antagonist. Cromolyn, lodoxamide, nedocromil and pemirolast are mast cell stabilizers. Azelastine, bepotastine, epinastine, ketotifen and olopatadine have dual actions that offer a combination of these two mechanisms (i.e., they are antihistamines with mast cell stabilizing properties). The ophthalmic products that are available in a generic formulation include azelastine, cromolyn, epinastine and ketotifen. The nasal products that are available in a generic formulation include azelastine and cromolyn.

Treatment options for allergic rhinitis include anticholinergics, antihistamines, corticosteroids, decongestants, leukotriene receptor antagonists and mast cell stabilizers. Many of these agents can also benefit associated symptoms of allergic conjunctivitis. The selection of therapy should be individualized and take into consideration the severity and duration of the disease, patient preference, efficacy and safety. In general, guidelines do not give preference to one EENT antiallergic agent over another. Ophthalmic products may be preferred to oral formulations if ocular symptoms are the primary manifestation of the disease as they are faster-acting and are less likely to cause systemic adverse events. The dual action antiallergic agents treat signs and symptoms of allergic conjunctivitis during the acute phase (antihistaminic

action) and prevent mast cell degranulation (membrane stabilizing action). Thus, they are suitable for both the acute and long-term management of allergic conjunctivitis. The onset of action for mast cell stabilizers is five to fourteen days; therefore, they are not useful for treating acute symptoms.

There are relatively few comparative studies that have been conducted with the EENT antiallergic agents in a 'real-life' setting. While some of these trials have demonstrated similar outcomes with regards to ocular symptoms, nasal symptoms and patient preference, other studies have demonstrated greater efficacy with one agent over another. Many comparative studies have been performed using environmental challenge chambers. However, the antiallergic agents are typically administered as a single dose and the clinical outcomes are assessed after several minutes or hours.

There is insufficient evidence to support that one brand EENT antiallergic agent is safer or more efficacious than another. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand EENT antiallergic agents within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand eye, ear, nose, and throat (EENT) antiallergic agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Eye, Ear, Nose, and Throat Preparations: Antibacterials: AHFS 520404

Manufacturer comments on behalf of these products:

None

Dr. Kohn commented that the EENT antibacterials that are included in this review are listed in Table 1. Since the last review ophthalmic moxifloxacin (Moxeza[®]) was approved and is indicated for the treatment of bacterial conjunctivitis. The EENT antibacterials effectively treat a variety of infections. There is at least one single entity ophthalmic aminoglycoside, macrolide, quinolone, sulfonamide and miscellaneous antibacterial available in a generic formulation. For the single entity otic products, ofloxacin is also available generically. There are several ophthalmic and otic antibacterial/corticosteroid combination products that are available in a generic formulation.

Clinical guidelines addressing the role of the antibacterials in the management of various infections are described in Table 4. For the treatment of blepharitis, initial use of bacitracin or erythromycin ointment is recommended. Corticosteroids may also be used to control inflammation and maintain patient comfort; however, adverse effects should be considered. Bacterial conjunctivitis is often self-limiting and resolves spontaneously without specific treatment. The use of topical antibacterial therapy may lead to earlier clinical and microbiological remission. The choice of antibiotic is usually empirical and guidelines do not give preference to one ophthalmic antibacterial agent over another. Soft contact lens wearers with conjunctivitis have a high incidence of infection with Pseudomonas and quinolones are the preferred treatment in these

patients. For the empiric treatment of bacterial keratitis, topical broad-spectrum antibacterials are used initially. Guidelines recommend use of quinolones if the organism is unknown or if multiple types of organisms are identified. Numerous clinical trials have demonstrated similar clinical cure rates with the ophthalmic antibacterial agents.

For the treatment of acute otitis externa, guidelines recommend the use of a topical antibacterial agent without preference of one agent over another as there is minimal or no difference in clinical or bacteriologic cure rates among the agents. Topical preparations that contain alcohol or have a low pH, as well as aminoglycosides, should be avoided in patients with tympanostomy tubes or perforated tympanic membranes due to the risk of ototoxicity. Guidelines recommend the use of an oral antibacterial agent for the treatment of acute otitis media. Topical antibacterials may be used as an alternative treatment option in patients with perforated tympanic membranes, tympanostomy tubes, or chronic suppurative otitis media. Several clinical trials have demonstrated similar cure rates with the otic antibacterials. Relatively few studies have demonstrated greater efficacy with one agent over another.

Mupirocin is indicated for the eradication of nasal colonization with methicillin-resistant *S aureus* (MRSA) in adult patients and health care workers during institutional outbreaks. Most published trials evaluating mupirocin utilized placebo or no treatment as a comparator. Several clinical trials have demonstrated that mupirocin eradicates *S aureus* and MRSA nasal colonization in a variety of patient populations immediately following therapy. These studies do not consistently document a long-term benefit on nasal decolonization, nor do they consistently show a reduction in the incidence of *S aureus* or MRSA infections. There is insufficient evidence that mupirocin prevents autoinfection of patients from their own nasal colonization with *S aureus*. Mupirocin nasal ointment is not available generically.

There is insufficient evidence to support that one brand EENT antibacterial is safer or more efficacious than another within its given indication. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand EENT antibacterials within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand eye, ear, nose, and throat (EENT) vasoconstrictor is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

Eye, Ear, Nose, and Throat Preparations: Vasoconstrictors: AHFS 523200

Manufacturer comments on behalf of these products:

None

Dr. Kohn commented that the EENT vasoconstrictors that are included in this review are listed in Table 1. The EENT vasoconstrictors are approved for use in a variety of ophthalmic conditions/procedures and to treat nasal congestion. The ophthalmic products that are available in a generic formulation include

naphazoline and phenylephrine. There are no nasal products that are currently available in a generic formulation.

Clinical guidelines addressing the role of the vasoconstrictors in various ophthalmic conditions/procedures are described in Table 2. Treatment options for allergic rhinitis include anticholinergics, antihistamines, corticosteroids, decongestants, leukotriene receptor antagonists and mast cell stabilizers. The selection of therapy should be individualized and take into consideration the severity and duration of the disease, patient preference, efficacy and safety. The intranasal corticosteroids are the most effective agents for the treatment of allergic rhinitis. Antihistamines treat rhinorrhea, sneezing, itching, and allergic conjunctivitis but have little effect on nasal congestion. They are also less effective than intranasal corticosteroids. Oral decongestants effectively treat nasal congestion; however, they may cause insomnia, irritability and palpitations. Topical decongestants are also effective for the short-term treatment of nasal congestion. Chronic use of topical decongestants may cause rhinitis medicamentosa and should be avoided.

The scientific evidence regarding the efficacy of the EENT vasoconstrictors is extremely limited. There were no studies found in the medical literature that directly compared the safety and efficacy of the ophthalmic or nasal EENT vasoconstrictors.

There is insufficient evidence to support that one brand EENT vasoconstrictor is safer or more efficacious than another. Formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand EENT vasoconstrictors within the class reviewed are comparable to each other and to the generics and OTC products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand eye, ear, nose, and throat (EENT) vasoconstrictor is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Vice chair Allen asked the P&T Committee members to mark their ballots.

7. RESULTS OF VOTING ANNOUNCED

The results of voting for each of the therapeutic classes were announced; all classes were approved as recommended. Results of voting are described in the Appendix to the minutes.

8. NEW BUISNESS

Dr. Littlejohn acknowledged Chairperson Ferris and Dr. Woodruff for their service to the Alabama Medicaid P&T Committee. Dr. Littlejohn asked the P&T Committee members to vote for a new Vice Chair (current Vice chairperson Allen will become Chairperson). The results of the vote will be distributed at a later date. UPDATE: Ms. LaTonage Porter was voted the new Vice Chairperson.

The dates for the 2014 Alabama Medicaid P&T Meetings were provided and are as follows: February 12, 2014, May 14, 2014, August 13, 2014, and November 19, 2014.

After discussion with the P&T Committee members, going forward they will receive the clinical information on a jump drive vs a CD.

9. NEXT MEETING DATE

The next P&T Committee Meeting is scheduled for November 13, 2013 at the Medicaid Building in the Commissioner's Board Room.

10. ADJOURN

There being no further business, Dr. Woodruff moved to adjourn and Ms. Porter seconded. The meeting adjourned at 10:30 a.m.

Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
August 14, 2013

A. **Recommendation:** No brand androgen is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda S. Rowe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A Approve Approve as amended Disapprove No action
Acting Commissioner

B. **Recommendation:** No brand short-acting inhaled antimuscarinic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

At least one long-acting inhaled antimuscarinic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda S. Rowe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A Approve Approve as amended Disapprove No action
Acting Commissioner

C. Recommendation: No brand respiratory beta-adrenergic agonist is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda A. Doucette Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. [Signature] Approve Approve as amended Disapprove No action
Acting Commissioner

D. Recommendation: No brand leukotriene modifier is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda A. Doucette, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. [Signature] Approve Approve as amended Disapprove No action
Acting Commissioner

E. Recommendation: No brand inhaled mast-cell stabilizer is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda S. Rowe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. Approve Approve as amended Disapprove No action
Acting Commissioner

F. Recommendation: Alabama Medicaid should work with manufacturers of brands in the class on cost proposals so that at least one single entity brand inhaled corticosteroid is selected as a preferred agent.

No brand fixed-dose combination inhaled corticosteroid is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda S. Rowe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. Approve Approve as amended Disapprove No action
Acting Commissioner

G. Recommendation: No brand respiratory smooth muscle relaxant is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda A. Rowe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. Approve Approve as amended Disapprove No action
Acting Commissioner

H. Recommendation: No brand intranasal corticosteroid is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda A. Rowe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. Approve Approve as amended Disapprove No action
Acting Commissioner

I. **Recommendation:** No brand eye, ear, nose, and throat (EENT) antiallergic agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda S. Rowan Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. Approve Approve as amended Disapprove No action
Acting Commissioner

J. **Recommendation:** No brand eye, ear, nose, and throat (EENT) antibacterial is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda S. Rowan Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. Approve Approve as amended Disapprove No action
Acting Commissioner

K. Recommendation: No brand eye, ear, nose, and throat (EENT) vasoconstrictor is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda D. Rowe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie H. Approve Approve as amended Disapprove No action
Acting Commissioner

Respectfully submitted,



James Gagnon, Pharm.D., BCPS

August 19, 2013

Date