

Minutes of Meeting

Alabama Medicaid Agency Pharmacy and Therapeutics Committee

February 11, 2015

Members Present: Ms. Janet Allen, Dr. Frances Cohenour (Vice-chair), Dr. Elizabeth Jacobson, Dr. Kelli Littlejohn Newman, Dr. Pilar Murphy, Dr. Melinda Rowe, and Dr. Robert Smith

Members Absent: Dr. Lee Carter, Dr. David Harwood (Chair)

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

Presenters: Dr. Rachel Bastien and Ms. Amy Levy

Presenters Present via teleconference: None

1. OPENING REMARKS

Vice chairperson Cohenour called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 9:03 a.m.

2. APPROVAL OF MINUTES

Vice chairperson Cohenour asked if there were any corrections to the minutes from the November 12, 2014 P&T Committee Meeting.

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

3. PHARMACY PROGRAM UPDATE

Dr. Littlejohn Newman oriented the Committee members to the eleven organizations approved as probationary Alabama Regional Care Organizations that are available on the Agency's website (http://medicaid.alabama.gov/news_detail.aspx?ID=9371), along with the Letters of Intent/Health Home updates (http://medicaid.alabama.gov/news_detail.aspx?ID=9392).

Dr. Littlejohn Newman reminded the committee that a routine PDL update became effective January 2015 (http://medicaid.alabama.gov/news_detail.aspx?ID=9343). New phone numbers for HP provider representatives are now available (http://medicaid.alabama.gov/news_detail.aspx?ID=9390). Changes to the Plan First Program also

occurred in January (http://medicaid.alabama.gov/news_detail.aspx?ID=9406). In December 2014, Alabama Pharmacy Association announced that pharmacy is carved out of Medicaid RCOs (<http://www.aparx.org/news/207843/-BREAKING-NEWS-Pharmacy-Carved-Out-of-Medicaid-RCO-System.htm>), reading “APA has been informed that the Governor’s office has made the decision to exclude pharmacy services from the Medicaid Regional Care Organization (RCO) program currently under development.”

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 were explained. The drugs and corresponding manufacturers are listed below with the appropriate therapeutic class. There were a total of four manufacturer verbal presentations at the meeting.

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

The pharmacotherapy class reviews began at approximately 9:09 a.m. There were a total of 15 drug class re-reviews. The first generation antihistamines; estrogens; alpha glucosidase inhibitors; amylinomimetics; biguanides; dipeptidyl peptidase-4 inhibitors; incretin mimetics; insulins; meglitinides; sodium-glucose cotransport 1 inhibitors; sodium-glucose cotransport 2 inhibitors; sulfonylureas; thiazolidinediones; antidiabetic agents, miscellaneous; and prenatal vitamins were all last reviewed in November 2012. There was one new drug review: Aerospan™.

First Generation Antihistamines: Ethanolamine Derivatives, AHFS 040404; Ethylenediamine Derivatives AHFS 040408; and Propylamine Derivatives AHFS 040420

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the first generation antihistamines included for this review are listed in Table 1. This review encompasses all systemic dosage forms and strengths. The first generation antihistamines are approved for use in several allergic and nonallergic conditions; however, these agents are primarily utilized for the treatment of allergic rhinitis. The eye, ear, nose and throat anti-allergic agents (American Hospital Formulary Service 520200) were previously reviewed and not included in this review. The majority of these agents are available in a generic formulation. Cough and cold agents are excludable/ optional drug class in accordance with the Omnibus Budget Reconciliation Act of 1990 (OBRA90). Brand cough and cold products are not covered by Alabama Medicaid; therefore these products are not included in this review. Covered generics (unless otherwise specified) do not require prior authorization. This class was last reviewed in November of 2012. There have been no major changes in prescribing information, treatment guidelines, or clinical studies since the class was last reviewed.

The first generation antihistamines are approved for the treatment of allergic and non-allergic conditions; however, they are primarily used for the management of allergic rhinitis, urticaria, and angioedema. They are available as single entity agents, as well as in combination with other first generation antihistamines and oral decongestants. Many of the products are available in a generic formulation. Due to their pharmacokinetic properties (prolonged half-life and active metabolites), the central nervous system effects cannot be eliminated by administering these agents at bedtime. For the treatment of urticaria, antihistamines are the cornerstone of therapy. Second generation antihistamines are generally preferred; however, first generation agents can also be effective and well-tolerated by patients. The addition of a sedating first generation antihistamine to a second generation antihistamine may help patients sleep better. For the treatment of atopic dermatitis, topical corticosteroids are the standard of care. Antihistamines may help relieve pruritic symptoms, especially in those with concomitant urticaria or allergic rhinitis. First generation antihistamines may also be useful in patients with sleep disturbances due to pruritus. For the management of allergic/atopic conjunctivitis, topical antihistamines are an effective treatment option; however, oral antihistamines may also be considered. Antihistamines are not recommended for the treatment of acute sinusitis. They may have a role in the management of chronic sinusitis if allergic rhinitis is an underlying risk factor. The available guidelines do not give preference to one particular first generation antihistamine over another.

There is insufficient evidence to support that one brand first generation antihistamine 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 products within the class reviewed are comparable to each other and to the generic products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand first generation antihistamine 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Estrogens: AHFS 681604

Manufacturer comments on behalf of these products:

Duavee® - Pfizer

Premarin® vaginal cream - Pfizer

Ms. Levy commented that the estrogens are approved for the treatment of vasomotor symptoms associated with menopause, vulvar and vaginal atrophy, abnormal uterine bleeding, hypoestrogenism, prevention of postmenopausal osteoporosis, as well as for the palliative treatment of prostate and breast cancer. The menopausal transition period is associated with irregular or heavy bleeding, hot flashes, sleep disturbance, vaginal dryness, sexual dysfunction, incontinence, urinary tract infections, depression, and other clinical manifestations. For most

women, these symptoms are usually mild and of short duration. The use of hormone therapy helps to alleviate these symptoms. Estrogen can be used alone in women who have had a hysterectomy; however, a progestin should be added to the regimen for women with an intact uterus as it reduces the risk of endometrial cancer.

The estrogens are available in a variety of dosage forms, including injectable, oral, topical, transdermal, and vaginal preparations. Oral estrogens have a greater effect on the liver than topical formulations due to first-pass metabolism following gastrointestinal absorption. Oral estrogens may increase the production of cholesterol (triglycerides and high density lipoprotein cholesterol) and clotting factors, which is only minimally affected by topical, transdermal, and vaginal preparations.

Conjugated estrogens-bazedoxifene bind to and activate estrogen receptors alpha and beta, which vary in proportion from tissue to tissue. Bazedoxifene is a third generation selective estrogen receptor modulator which acts as an agonist in some tissues and as an antagonist in the uterus. The pairing of conjugated estrogens with bazedoxifene produces a composite effect specific to each tissue. The addition of bazedoxifene reduces the risk of endometrial hyperplasia associated with the conjugated estrogens component.

The estrogens that are included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. Estradiol, estradiol valerate, estradiol-norethindrone and estropipate are available in a generic formulation. This class was last reviewed in November 2012.

The estrogens are approved for the treatment of vasomotor symptoms associated with menopause, vulvar and vaginal atrophy, abnormal uterine bleeding, hypoestrogenism, prevention of postmenopausal osteoporosis, as well as for the palliative treatment of prostate and breast cancer. They are available in a variety of dosage forms, including injectable, oral, topical, transdermal, and vaginal preparations. Estradiol, estradiol valerate, estradiol/norethindrone, and estropipate are available in a generic formulation.

The recommendations for the use of hormone therapy have changed since the Women's Health Initiative studies were published. The use of hormone therapy was associated with an increased risk of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis. The long-term use of hormone therapy is no longer recommended for the prevention of chronic diseases, such as cardiovascular disease, cerebrovascular disease or dementia. Hormone therapy may be considered for the prevention of osteoporosis when other therapies are not appropriate or when the benefits outweigh the risks. Hormone therapy remains the most effective treatment for moderate-to-severe menopausal symptoms.

It is recommended that the lowest possible dose be used for the shortest amount of time. Vaginal formulations are recommended for women who only have symptoms of vulvar and vaginal atrophy. Systemic progestogen is required for endometrial protection of unopposed estrogen therapy.

A variety of clinical trials have been conducted with the estrogens, which have evaluated efficacy, safety, tolerability, as well as pharmacokinetic and pharmacodynamic end points. Numerous

studies have demonstrated a similar improvement in menopausal symptoms with the various estrogen preparations. There were no studies found in the medical literature that compared the continuous administration of a combination product versus the concomitant administration of the individual components. There is no evidence that natural estrogens are more or less hazardous than synthetic estrogens at equivalent doses.

The efficacy and safety of bazedoxifene with conjugated estrogens have been evaluated in the phase 3 Selective estrogens, Menopause And Response to Therapy (SMART) trials conducted in generally healthy postmenopausal women. Bazedoxifene-conjugated estrogens have shown an improvement in menopausal symptoms and bone loss and a favorable safety profile when compared to placebo. There were no studies found that compared bazedoxifene-conjugated estrogens to another selective estrogen receptor modifier and estrogen combination regimen.

There is insufficient evidence to support that one brand estrogen 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 products within the class reviewed are comparable to each other and to the generic products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand estrogen 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Alpha Glucosidase Inhibitors: AHFS 682002

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the alpha-glucosidase inhibitors are approved for use as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. The antihyperglycemic action of acarbose results from a competitive, reversible inhibition of pancreatic alpha-amylase and membrane-bound intestinal alpha-glucoside hydrolase enzymes. The antihyperglycemic action of miglitol results from a reversible inhibition of membrane-bound intestinal alpha-glucoside hydrolase enzymes. This enzyme inhibition leads to a delay in glucose absorption and subsequent lowering of postprandial hyperglycemia.

The alpha-glucosidase inhibitors that are included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. Acarbose is available in a generic formulation. This class was last reviewed in November 2012.

The alpha-glucosidase inhibitors are approved for use as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Acarbose is currently the only agent available in a generic formulation.

According to current clinical guidelines for the management of type 2 diabetes, metformin remains the cornerstone to most antidiabetic treatment regimens. Additionally, patients with a high glycosylated hemoglobin (HbA1c) will most likely require combination or triple therapy in order to achieve glycemic goals. At this time, uniform recommendations on the best agent to be combined with metformin cannot be made; therefore, advantages and disadvantages of specific antidiabetic agents for each patient should be considered. In general, the α -glucosidase inhibitors are not recommended for use in the management of patients with a high HbA1c (7.6 to 9.0%), mainly due to the limited HbA1c lowering potential associated with the medication class compared to other available antidiabetic medications. The α -glucosidase inhibitors may be utilized as monotherapy in the management of patients with a low HbA1c (6.5 to 7.5%); however, metformin remains the most appropriate initial choice for monotherapy in all patients. In addition, clinical guidelines recognize the potential use of α -glucosidase inhibitors when postprandial hyperglycemia is present. Among all current clinical guidelines, preference of one α -glucosidase inhibitor over another is not stated.

A variety of clinical trials have been conducted with the alpha-glucosidase inhibitors. A clinical trial directly comparing acarbose and miglitol does not evaluate glycemic control among type 2 diabetics; rather the results demonstrate that there is no significant difference between the two agents with regards to glucose variability during pre- and post-prandial periods. The majority of the clinical trials have compared active treatment to placebo or compared combination therapy to monotherapy. In these studies, the more aggressive treatment regimens improved glycemic parameters to a greater extent than the less-intensive treatment regimens. When comparing similar monotherapy treatment regimens, sulfonylureas have been shown to be more effective than the alpha-glucosidase inhibitors.

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with the alpha-glucosidase inhibitors or any other antidiabetic drug.

There is insufficient evidence to support that one brand alpha-glucosidase inhibitor 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.

No brand alpha-glucosidase inhibitor 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.

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

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

Amylinomimetics: AHFS 682003

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that Pramlintide is the only amylinomimetic agent that is currently available. It is approved for use as an adjunctive treatment in patients with type 1 and type 2 diabetes mellitus who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy. Amylin is co-secreted with insulin by pancreatic beta cells in response to food intake. It affects postprandial glucose levels by slowing gastric emptying, suppressing glucagon secretion, and regulating food intake via modulation of appetite. Patients with type 1 and type 2 diabetes have dysfunctional beta cells, which leads to a reduced secretion of insulin and amylin in response to food.¹ Pramlintide is a synthetic analog of human amylin, which has been shown to modulate gastric emptying, decrease postprandial glucagon concentrations in patients using insulin, and reduce caloric intake.

The amylinomimetics that are included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. There are no generic products available. This class was last reviewed in November 2012.

Pramlintide is the only amylinomimetic agent that is currently available. It is approved for use as an adjunctive treatment in patients with type 1 and type 2 diabetes mellitus who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy. It is not available in a generic formulation.

Several guidelines provide recommendations on the treatment of type 2 diabetes. According to the American Diabetes Association/ European Association for the Study of Diabetes treatment algorithm, metformin is recommended as first-line therapy, followed by a second oral agent, a glucagon-like peptide-1 (GLP-1) receptor agonist, or basal insulin. Notably the higher the glycosylated hemoglobin (HbA1c), the more likely insulin will be required. Pramlintide may be used as an adjunct to prandial insulin therapy to reduce postprandial hyperglycemia, HbA1c, and weight. In general, current clinical guidelines do not support the use of amylin analogs in the management of type 2 diabetes.

For the treatment of type 1 diabetes, the American Diabetes Association recommends the use of multiple dose insulin injections or continuous subcutaneous insulin infusion therapy. The addition of pramlintide to intensive insulin therapy should be considered to enhance glycemic control and to assist with weight management.

Several clinical trials have been conducted with pramlintide in patients with type 1 and type 2 diabetes mellitus. Data from clinical trials demonstrate that treatment with pramlintide is associated with significant baseline reductions in HbA1c compared to treatment with placebo in type 1 and 2 diabetics already receiving insulin. Furthermore, treatment with pramlintide is associated with significant baseline reductions in fasting plasma glucose levels, post-prandial glucose levels, insulin use, and body weight. However, compared to other available antidiabetic

agents, pramlintide is associated with modest HbA1c lowering ability, and its use is often limited by adverse events.

Pramlintide does not cause hypoglycemia when used alone; however, it is intended to be coadministered with insulin therapy. In this setting, pramlintide increases the risk of insulin-induced severe hypoglycemia, especially in patients with type 1 diabetes mellitus. To minimize this risk, patients must be carefully selected, proper education must be provided, and glucose levels must be carefully monitored. Therapy should only be considered in patients with insulin-using type 1 or type 2 diabetes who fulfill the following criteria: 1) have failed to achieve adequate glycemic control despite individualized insulin management; and 2) are receiving ongoing care under the guidance of a healthcare professional skilled in the use of insulin and supported by the services of diabetes educator(s).

There is insufficient evidence to support that one brand amylinomimetic is safer or more efficacious than another within its given indication. Since pramlintide is only approved for use as an adjunctive treatment in patients with type 1 and type 2 diabetes mellitus, it should be managed through the existing medical justification portion of the prior authorization process.

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

No brand amylinomimetic 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Biguanides: AHFS 682004

Manufacturer comments on behalf of these products:

None

Dr. Bastien commented that metformin remains the only biguanide that is currently available and it is FDA-approved for use as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes. Metformin is available as an immediate-release tablet, extended-release tablet, and solution. Both the immediate- and extended-release tablets are available generically.

Metformin remains the recommended first-line therapy for most antidiabetic treatment regimens and remains the cornerstone to most combination dual and triple therapy regimens. Among current treatment guidelines, preference of one formulation of metformin over another is not stated.

Metformin is associated with a boxed warning regarding the risk of lactic acidosis which is a rare but serious complication that can occur due to accumulation of metformin.

The safety and efficacy of metformin in the management of type 2 diabetes, either as monotherapy or in combination with other antidiabetic agents, are well established. Recently published clinical trials evaluating metformin have not produced clinically different results compared to clinical trials included in the previous review. Clinical trials comparing different formulations of metformin have demonstrated comparable efficacy.

There is insufficient evidence to support that one brand biguanide 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.

All brand products within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class and offer no significant clinical advantage over other alternatives in general use.

No brand biguanide 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors: AHFS 682005

Manufacturer comments on behalf of these products:

None

Dr. Bastien commented that since the last time the DPP-4 inhibitors were reviewed, alogliptin and alogliptin combination products have been approved by the FDA. The DPP-4 inhibitors are approved for use as an adjunct therapy to diet and exercise to improve glycemic control in adults with type 2 diabetes. In general, all of the DPP-4 inhibitors fixed-dose combination products are available for use when treatment with both drug components is appropriate. There are no generic DPP-4 inhibitors available; however, metformin and pioglitazone are available generically in a separate formulation.

Current treatment guidelines recommend the DPP-4 inhibitors as a potential second-line treatment option to be added to or used in combination with metformin in patients not achieving glycemic control. Due to their mechanism of action, the DPP-4 inhibitors are associated with a lower rate of hypoglycemia compared to other antidiabetic agents, and they also have a well established efficacy and safety profile when used in combination with metformin. The DPP-4 inhibitors may also be a potential treatment option for initial therapy in patients who have a contraindication to metformin. Among all current treatment guidelines, preference of one DPP-4 inhibitor over another is not stated.

Recently published clinical trials evaluating the DPP-4 inhibitors in the treatment of type 2 diabetes have not produced clinically different results compared to clinical trials included in the previous review. As a class, the clinical efficacy and safety of the DPP-4 inhibitors are well established; however, head-to-head trials comparing the various DPP-4 inhibitors are limited. The

majority of available clinical trials evaluate the use of a DPP-4 inhibitor as add-on therapy to metformin or another background antidiabetic therapy, and data consistently demonstrates that the more aggressive treatment regimens improve glycemic parameters to a greater extent compared to less intensive therapy.

At this time, due to a lack of robust head-to-head clinical trial data, there is insufficient evidence to support that one brand DPP-4 inhibitor is safer or more efficacious than another. Since DPP-4 inhibitors are not recommended as first-line therapy for the treatment of type 2 diabetes, they should be managed through the medical justification portion of the prior authorization process.

All brand products within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class and offer no significant clinical advantage over other alternatives in general use.

No brand DPP-4 inhibitor 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Incretin Mimetics: AHFS 682006

Manufacturer comments on behalf of these products:

Bydureon[®] - AstraZeneca

Dr. Bastien commented that incretin mimetics are FDA approved for use as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. The incretin mimetics that are included in this review are listed in Table 1. Byetta[®] and Bydureon[®] contain the same active ingredient, exenatide. Bydureon[®] is a long-acting formulation of exenatide. There are no incretin mimetics available generically.

Current treatment guidelines recommend incretin mimetics as a potential second-line treatment option to be used in combination with metformin in patients not achieving glycemic control. Similar to the DPP-4 inhibitors, the incretin mimetics are associated with a lower rate of hypoglycemia compared to other antidiabetic agents, and they have a well established safety and efficacy profile when used in combination with metformin. An advantage of the incretin mimetics over other available antidiabetic agents is their ability to induce weight loss which is beneficial in patients with diabetes. Because of this beneficial effect, the incretin mimetics may also be a potential first-line therapy in patients where weight loss is seen as an essential aspect of therapy. Among current treatment guidelines, preference of one incretin mimetic over another is not stated.

Extended-release exenatide, albiglutide, and liraglutide are associated with a boxed warning regarding an observed incidence of thyroid tumors in rats and mice. It is not known if these agents can cause such tumors in humans; however, patients should be counseled regarding the risk and symptoms of thyroid tumors.

As a class, the incretin mimetics are similar with regards to their efficacy and safety; the main difference among the individual agents appears to be in their dosing. All of the incretin mimetics are available for subcutaneous injection; however, Bydureon[®] is administered once weekly without regard to meals. Byetta[®] is administered twice daily, 60 minutes prior to a meal, Victoza[®] is administered once daily without regard to meals, and Tanzeum[™] is administered once weekly without regard to meals.

A variety of clinical trials have been conducted evaluating the incretin mimetics. The majority of available clinical trials evaluate incretin mimetics as add-on therapy to metformin or other background antidiabetic therapies, and results consistently demonstrate that more aggressive treatment regimens improved glycemic parameters to a greater extent compared to less intensive regimens. While the majority of clinical evidence supports the use of incretin mimetics as part of combination or triple therapy treatment regimens, there is limited evidence available evaluating the incretin mimetics as initial monotherapy in drug-naïve patients. There is an overall lack of head-to-head clinical trials comparing the individual incretin mimetics. In one trial, add-on treatment with extended-release exenatide to metformin resulted in significantly greater reductions in HbA_{1c} compared to exenatide. In two clinical trials, incretin mimetic therapy was added to existing metformin therapy and liraglutide resulted in significantly greater reductions in HbA_{1c} compared to exenatide, with weight loss comparable between treatment groups.

At this time, there is insufficient evidence to support that one brand incretin mimetic is safer or more efficacious than another. Since incretin mimetics are not recommended as first-line therapy for the treatment of type 2 diabetes, they should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand products within the class reviewed are comparable to each other and offer no significant clinical advantage over other alternatives in general use.

No brand incretin mimetic 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Insulins: AHFS 682008

Manufacturer comments on behalf of these products:

None

Dr. Bastien commented that there have been no major or clinically significant updates to the insulins since the last time this class was reviewed. None of the insulin products are available generically; however, some products are available over-the-counter.

In general, insulin is FDA-approved for use in type 1 and 2 diabetes. Essentially all insulin products act the same and have comparable efficacy among them; the primary differences between the products revolve around pharmacokinetic and pharmacodynamic properties. Insulin is the

standard of care for patients with type 1 diabetes. Treatment guidelines recommend initiation of individualized, intensive insulin therapy at the time of diagnosis in these patients, using both basal and postprandial insulin therapies. The American Diabetes Association and the American Association of Clinical Endocrinologists recommend the use of insulin analogs, as compared to human insulin products. In the management of type 2 diabetes, insulin is an option to be added to or used in combination with metformin in patients not achieving glycemic goals; however, for the most part, prescribers will maximize oral antidiabetic therapies before initiating insulin therapy in type 2 diabetics. Initiating insulin therapy in type 2 diabetics should be considered when oral therapy fails to achieve glycemic goals, or when a patient has symptomatic hyperglycemia. When insulin therapy is indicated for the management of fasting plasma glucose, use of the long-acting insulin analogs is preferred over intermediate human insulin because they are associated with less hypoglycemia. When insulin therapy is indicated for the management of postprandial glucose, use of the rapid-acting insulin analogs is preferred over short or regular human insulin because they have a more rapid onset and offset of action, and are also associated with less hypoglycemia. For type 1 and 2 diabetes, guidelines do not distinguish between the individual insulin products.

The safety and efficacy of insulin therapy in both type 1 and 2 diabetes are well established, and recently published clinical trials evaluating the insulins in the treatment of diabetes have not produced clinically different results compared to the trials included in the previous review. The insulin analogs have been shown to be at least as effective, or more efficacious, compared to human insulin. There is still a lack of conclusive evidence to support that one rapid-acting analog or long-acting analog is more efficacious than another.

All brand products within the class reviewed, with the exception of rapid- and long-acting insulin analogs, are comparable to each other and to the generics and over-the-counter products in the class, and offer no significant clinical advantage over other alternatives in general use. Rapid-acting insulin analogs offer significant clinical advantages in general use over short-acting human insulin, but are comparable to each other. Long-acting insulin analogs offer significant advantages in general use over intermediate-acting human insulin, but are comparable to each other.

No brand insulin product, with the exception of rapid- and long-acting insulin analogs, is recommended for preferred status. Alabama Medicaid should accept cost proposals to determine the most cost effective products and possibly designate one or more preferred brands. Alabama Medicaid should accept cost proposals from manufacturers so that at least one brand rapid- and long-acting insulin analog is selected as a preferred agent.

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

Meglitinides: AHFS 682016

Manufacturer comments on behalf of these products:

None

Dr. Bastien commented that there have been no major or clinically significant changes to the meglitinides since the last time this class was reviewed. Nateglinide and repaglinide are available in generic formulations.

The meglitinides are not consistently included as part of the general recommendations for the management of type 2 diabetes. While they can be viewed as a potential second-line treatment option to be added to or used in combination with metformin in patients not achieving glycemic goals, treatment guidelines note that meglitinides are associated with limited HbA_{1c} lowering ability, weight gain, and a greater risk of inducing hypoglycemia compared to other available antidiabetic agents. Among all current treatment guidelines, preference of one meglitinide over another is not stated. Meglitinides may also be used as a potential option for initial therapy in patients who have a contraindication to metformin. Meglitinides are noted as being useful when postprandial hypoglycemia is present.

Recently published clinical trials evaluating the meglitinides in the treatment of type 2 diabetes have not produced clinically different results compared to trials included in the previous review.

There is insufficient evidence to support that one brand meglitinide is safer or more efficacious than another. Since the meglitinides are not recommended as first-line therapy for the treatment of type 2 diabetes, formulations without a generic alternative should be managed through the medical justification portion of the prior authorization process.

All brand products within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class and offer no significant clinical advantage over other alternatives in general use.

No brand meglitinide 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Sodium-glucose Cotransport 1 Inhibitors: AHFS Class 682017

Manufacturer comments on behalf of these products:

None

Dr. Bastien commented that currently there are no prescription medications classified by AHFS as Sodium-glucose Cotransport 1 Inhibitors. No SGLT1 inhibitor is recommended for preferred status. Alabama Medicaid should continue to include AHFS Class 682017 in the Preferred Drug List screening process. If new prescription sodium-glucose cotransport 1 inhibitors are added, it is recommended that this class be re-reviewed.

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

Sodium-glucose Cotransport 2 Inhibitors: AHFS Class 682018

Manufacturer comments on behalf of these products:

Farxiga[®] - AstraZeneca

Dr. Bastien commented that sodium-glucose cotransport 2 (SGLT2) inhibitors are a novel class of oral antidiabetic agents recently approved by FDA. SGLT2 inhibitors improve glycemic control by producing glucosuria. This is accomplished by inhibiting SGLT2 and increasing urinary glucose excretion. The net effect is an increase excretion of glucose from the body and normalizing plasma glucose levels. Canagliflozin and dapagliflozin are oral once daily tablets, indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Canagliflozin is also formulated with metformin in a single tablet, which is given twice daily. There are no generic products available.

The American Association of Clinical Endocrinologists guidelines released in 2013 are the only guidelines to address the use of SGLT2 inhibitors. According to these recommendations, SGLT2 inhibitors may be used as a potential treatment option as an alternative to or in combination with metformin in patients not achieving glycemic goals. SGLT2 inhibitors are acceptable therapeutic alternatives that reduce glucose without weight gain or hypoglycemia. The guidelines also note that clinicians have little experience with these agents, so the utility of the SGLT2 inhibitors and their place in diabetes treatment remains undefined. The SGLT2 drugs will likely be used as add-on therapy to two or three other agents, including insulin, in patients who would benefit from weight loss.

The adverse effects associated with SGLT2 inhibitors are listed on page 796. The primary side effects are increased urinary tract and genital infections; however, an unexplained adverse effect is increased LDL-C. Cardiovascular safety studies are planned.

The clinical trials begin on page 798. Both canagliflozin and dapagliflozin reduce HbA_{1c} by approximately 0.5 to 1% when administered as monotherapy or added to metformin therapy. In general, SGLT2 inhibitors are associated with similar improvements in HbA_{1c} as other oral antidiabetic agents. Studies directly comparing SGLT2 inhibitors have not been conducted. Though clinical experience is limited, the SGLT2 inhibitors are associated with several favorable side effects compared to other antidiabetic agents such as weight loss. Compared to sulfonylureas, the risk of hypoglycemia associated with the SGLT2 inhibitors is low as it reduces plasma glucose concentrations without stimulating insulin release or inhibiting its counterregulatory response. During clinical trials, common adverse side effects associated with the SGLT2 inhibitors included increased incidence of female genital mycotic infections, urinary tract infection, and increased urination.

There is insufficient evidence to support that one brand SGLT2 inhibitor 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.

All brand products within the class reviewed are comparable to each other and offer no significant clinical advantage over other alternatives in general use.

No brand sodium-glucose cotransport 2 inhibitor 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Sulfonylureas: AHFS 682020

Manufacturer comments on behalf of these products:

None

Dr. Bastien commented that there have been no major or clinically significant updates to the sulfonylureas since the last time this class was reviewed. The sulfonylureas are FDA-approved for use as an adjunct therapy to diet and exercise to improve glycemic control in adults with type 2 diabetes. All of the sulfonylureas are available in a generic formulation, including the fixed-dose combination products.

Current treatment guidelines note that sulfonylureas are recommended as a potential second-line treatment option to be added to or used in combination with metformin in patients not achieving glycemic goals. Treatment guidelines note that sulfonylureas are associated with weight gain and a greater risk of inducing hypoglycemia compared to other available antidiabetic agents. Sulfonylureas may also be a potential treatment option for initial therapy in patients who have a contraindication to metformin. Among all current treatment guidelines, preference of one sulfonylurea over another is not stated.

The safety and efficacy of the sulfonylureas are well established and recently published clinical trials evaluating these agents in the treatment of type 2 diabetics have not produced clinically different results compared to trials included in the previous review. Evidence support the choice of these agents as both monotherapy and in combination with other antidiabetic agents, with the more aggressive treatment regimens improving glycemic parameters to a greater extent compared to less intensive regimens. In general, the efficacy among available sulfonylureas appears to be comparable.

There is insufficient evidence to support that one brand sulfonylurea 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.

All brand products within the class reviewed are comparable to each other and to the generic products in the class and offer no significant clinical advantage over other alternatives in general use.

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

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

Thiazolidinediones: AHFS 682028Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the thiazolidinediones are approved for use as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. They are selective agonists of the peroxisome proliferator-activated receptor-gamma (PPAR γ). PPAR receptors are found in tissues important for insulin action. When activated, PPAR γ regulates the transcription of insulin-responsive genes responsible for glucose production, transportation, and utilization. PPAR γ also plays a role in the regulation of fatty acid metabolism. The thiazolidinediones increase the insulin sensitivity of adipose tissue, skeletal muscle, and the liver. This results in increased glucose uptake and metabolism, suppression of hepatic glucose production, and decreased plasma free fatty acid concentrations.

Both pioglitazone and rosiglitazone are available in combination with either metformin or glimepiride. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Glimepiride improves glycemic control by stimulating the release of insulin from pancreatic beta cells.

The thiazolidinediones that are included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. Pioglitazone, pioglitazone-glimepiride, and pioglitazone-metformin are available in generic formulations. Metformin and glimepiride are also available generically in a separate formulation. Pioglitazone is also available in combination with the dipeptidyl peptidase-4 (DPP-4) inhibitor alogliptin and is included in AHFS class 682005. This class was last reviewed in November 2012.

The thiazolidinediones are approved for use as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Pioglitazone, pioglitazone-glimepiride, and pioglitazone-metformin are available in generic formulations. Metformin and glimepiride are also available generically in a separate formulation.

According to current clinical guidelines for the management of type 2 diabetes, metformin remains the cornerstone of most antidiabetic treatment regimens. Additionally, patients with a high HbA1c will likely require combination or triple therapy in order to achieve glycemic goals. At this time, uniform recommendations on the best agent to be combined with metformin cannot be made; therefore, advantages and disadvantages of specific antidiabetic agents for each patient should be considered. The thiazolidinediones are noted to be associated with weight gain, fluid retention, congestive heart failure, and fractures. The thiazolidinediones are recommended as a potential second-line treatment option to be added to or used in combination with metformin in patients not achieving glycemic goals. However, due to the mechanisms of action of the thiazolidinediones and metformin, the addition of an incretin mimetic, dipeptidyl peptidase-4 (DPP-4) inhibitor or secretagogue is preferred over a thiazolidinedione to be added to metformin. In addition, the combination of metformin and a thiazolidinedione, while efficacious, carries risks of adverse events associated with both agents. Patients who are not appropriate for initial therapy with metformin, may be initiated on another oral antidiabetic agent, such as a sulfonylurea/glinide,

pioglitazone, or a DPP-4 inhibitor, and in occasional cases where weight loss is seen as an essential aspect of therapy, initial therapy with an incretin mimetic may be useful. In general, recommendations regarding the thiazolidinediones are made for the medication class as a whole; however, more recent guidelines from the American Diabetes Association/European Association for the Study of Diabetes do not recommend rosiglitazone.

A variety of clinical trials have been conducted with the thiazolidinediones. In comparative studies, the use of pioglitazone and rosiglitazone led to similar improvements in glycemic control. Several studies evaluated the efficacy of thiazolidinediones in dual therapy regimens compared to monotherapy regimens. In these studies, the more aggressive treatment regimens improved glycemic parameters to a greater extent than the less-intensive treatment regimens. However, in studies that directly compared various dual therapy regimens, there were no differences in efficacy noted. The thiazolidinedione fixed-dose combination products have been shown to improve glycemic control in patients with type 2 diabetes. However, there were no randomized studies found in the medical literature that directly compared the efficacy of the fixed-dose combination products to the coadministration of each component as separate formulations.

Thiazolidinediones may cause weight gain and fluid retention, as well as increase the risk for congestive heart failure and fractures. The cardiovascular safety of rosiglitazone has been a controversial issue since 2007. The results of two cardiovascular outcomes studies with the thiazolidinediones have been reported (PROactive and RECORD); however, neither study directly compared pioglitazone and rosiglitazone. A variety of meta-analyses have been conducted by independent investigators to assess the link between the use of thiazolidinediones and cardiovascular events. Previously, prescribing information for pioglitazone and rosiglitazone differed with regards to myocardial ischemic events. In November 2013, the FDA announced the removal of the prescribing and dispensing restrictions for rosiglitazone medicines that were put in place in 2010. This decision was based partly on a re-evaluation of the Rosiglitazone Evaluated for Cardiovascular Outcomes and Regulation of Glycemia in Diabetes (RECORD) trial conducted by the Duke Clinical Research Institute, which determined that recent data for rosiglitazone-containing drugs do not show an increased risk of heart attack compared to the standard type 2 diabetes medicines metformin and sulfonylurea. Under these modifications, distribution of rosiglitazone-containing products is no longer restricted. Health care professionals, pharmacies, and patients will no longer be required to enroll in the rosiglitazone Risk Evaluation and Mitigation Strategy program to be able to prescribe, dispense, or receive rosiglitazone medicines.

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with the thiazolidinediones or any other antidiabetic drug. Since these agents are not recommended as first-line therapy for the treatment of type 2 diabetes mellitus, the thiazolidinediones should be managed through the medical justification portion of the prior authorization process.

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

No brand thiazolidinedione 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Antidiabetic Agents, Miscellaneous: AHFS 682092

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that Mifepristone (Korlym[®]) is classified as an antidiabetic agent, miscellaneous by the American Hospital Formulary Service. Mifepristone is a cortisol receptor blocker that the Food and Drug Administration (FDA)-approved to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes or glucose intolerance and have failed surgery or are not candidates for surgery. Mifepristone is the first and only approved medication for Cushing's syndrome patients and has been designated as an Orphan Drug by the FDA for this indication. When administered in high doses, mifepristone is a selective antagonist of the GR-II glucocorticoid receptor and blocks the effects of cortisol. Mifepristone and the three active metabolites have a greater affinity for the glucocorticoid receptor compared to dexamethasone and cortisol, and have little to no affinity for estrogen, muscarinic, histaminic, or monoamine receptors. Of note, mifepristone does not reduce cortisol levels.

The antidiabetic agents, miscellaneous that are included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. Currently Mifepristone is the only agent in the class and the class has been reviewed previously in November 2012.

There is an overall lack of guidance within published literature and clinical guidelines as to the role of mifepristone in the management of endogenous Cushing's syndrome. Following 24 weeks of treatment with mifepristone in patients with Cushing's syndrome, there were reductions in glucose area under the curve and reductions in diastolic blood pressure in adult patients with type 2 diabetes, glucose tolerance or hypertension. Patients receiving mifepristone have also demonstrated varying degrees of improvement in Cushing's syndrome manifestations; however, it is not clear as to whether these changes are a result of mifepristone treatment.

Based on the mechanism of action of mifepristone and its approved indication, the agent can only be used in certain patients with endogenous Cushing's syndrome and there is potential for it to be used in combination with other established treatments. Cushing's syndrome treatment goals include the reversal of clinical features, the normalization of biochemical changes with minimal morbidity, and long-term control without recurrence. Optimal treatment is surgical resection by selective adenomectomy, with second-line options that include repeated pituitary surgery, radiotherapy, or bilateral adrenalectomy. Medical therapy plays an essential role in patients in whom surgery has failed to control the disease to reduce or normalize hypercortisolemia. Currently, adrenolytic therapies (ketoconazole, metyrapone, aminoglutethimide [not available in the United States], mitotane, etomidate) are the most widely utilized agents, with fluconazole

considered first-line to treat hypercortisolism. The safety and efficacy of neuromodulatory therapies (somatostatin analogs, dopamine agonists, peroxisome proliferator-activated receptor- γ agonists, retinoic acid, glucocorticoid receptor antagonists) in Cushing's syndrome have not been established.

There is insufficient evidence to support that one brand antidiabetic agent; miscellaneous 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 products within the class reviewed are comparable to each other and to the generic products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand antidiabetic agent, miscellaneous 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

Multivitamin Preparations: Prenatal Vitamins: AHFS 882800

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that women of reproductive age should maintain good nutritional status prior to, during, and after pregnancy to minimize health risks to both the mother and child. This includes maintaining a healthy weight, participating in physical activity, consuming a variety of foods to meet the Dietary Reference Intake recommendations, as well as appropriate and timely supplementation with multivitamins. There are several organizations that have published dietary guidelines for the perinatal period (preconception, pregnancy, and during lactation). However, most women of childbearing age do not maintain a healthy diet and do not consume enough vitamins (A, C, B-6, and E), calcium, folic acid, iron, magnesium, or zinc.

Folic acid is important in minimizing the risk of neural tube defects, which are serious birth defects of the spine and brain. Iron deficiency during pregnancy can lead to fetal complications that include premature delivery, intrauterine growth restrictions and neonatal mortality. In addition to folic acid and iron, prenatal vitamins also contain various combinations and quantities of vitamins and minerals. Additional nutrients which may be added to a prenatal vitamin include aspartame, docusate, L-methylfolate, omega-3 fatty acids, and omega-6 fatty acids. Folic acid must be broken down to L-methylfolate to be used at the cellular level; however, some individuals are unable to convert folic acid to its active form. Some of the prenatal formulations contain L-methylfolate for women who are unable to fully metabolize folic acid. Omega-3 fatty acids include α -linolenic acid (ALA), docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA). Omega-3 and omega-6 fatty acids must be obtained from food because the human body cannot synthesize these nutrients. DHA and EPA can be synthesized de novo from ALA; however, intake of ALA has not been

shown to increase maternal, fetal, or breast milk DHA levels. Both DHA and EPA are considered essential fatty acids which are necessary for nervous tissue growth and function. Some studies suggest that they may play a role in fetal/neonatal visual and neural growth when taken during pregnancy, as well as help prevent low birth weight. There are recommended (Dietary Reference Intakes) DRIs that have been established for ALA; however, it is unclear how much DHA or EPA a pregnant woman should consume through her diet and via supplementation.

The prenatal vitamins that are included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. It should be noted that the products included in this review contain an extensive ingredient list, which can be found separately in the prescribing information. The term “prenatal vitamins” in Table 1 collectively refers to all of the active vitamin and mineral ingredients. Additional ingredients, including folic acid and iron, have been listed out separately. Many of the prenatal vitamins are available in a generic formulation, including products which contain omega-3 fatty acids. This class was last reviewed in November 2012.

It is recommended that all women planning pregnancy take a supplement containing 400 to 800 µg of folic acid on a daily basis to reduce the risk of neural tube defects. Women should receive at least 27 mg of elemental iron per day during pregnancy; however, higher amounts are necessary for pregnant women with iron deficiency anemia. There is evidence that maternal consumption of folic acid-containing multivitamins may reduce the risk of neural tube defects, cardiac defects, urinary tract defects, limb defects, as well as other birth defects. The American Dietetic Association recommends supplementation with a multivitamin for pregnant women with iron deficiency anemia, poor-quality diets, those who consume no or small amounts of animal source foods, women carrying two or more fetuses, those who smoke or abuse alcohol or drugs, and for women who are infected with human immunodeficiency virus. In addition to a well-balanced diet, supplementation with a folic acid-containing multivitamin should be encouraged in all women of reproductive age to help support healthy pregnancy outcomes.

There are many different prenatal vitamins currently available. The majority of the products contain folic acid and iron, as well as various combinations of vitamins and minerals. Additional nutrients which have been added to some of the prenatal vitamins include aspartame, docusate, L-methylfolate, omega-3 fatty acids, and omega-6 fatty acids. Many of the prenatal vitamins are available in a generic formulation, including products which contain omega-3 fatty acids.

There were no clinical trials found in the medical literature that directly compared the various prenatal vitamin preparations. Supplementation with folic acid is clearly beneficial during pregnancy, and adequate intake of iron is necessary to reduce the risk of iron deficiency anemia. There has been recent interest in the health benefits associated with the use of supplemental omega-3 fatty acids during pregnancy. Omega-3 fatty acids are necessary for nervous tissue growth and function, and dietary intake has a variety of health benefits. Some studies have suggested that omega-3 fatty acids may improve fetal/neonatal visual and neural growth and help prevent low birth weight when taken as a supplement during pregnancy. Several meta-analyses have evaluated the use of supplemental omega-3 fatty acids during pregnancy. In general, the results of these analyses have not found a significant difference in pregnancy-related outcomes. This includes assessment of maternal outcomes (blood pressure, preeclampsia, and preterm delivery) and child outcomes (neurological development, growth patterns, visual function, and cognitive

development). There is insufficient evidence regarding the supplemental use of omega-3 fatty acids and the effects on pregnancy-related maternal and child outcomes.

There is insufficient evidence to support that one brand prenatal vitamin 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 products within the class reviewed are comparable to each other and to the generic products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand prenatal vitamin 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 chairperson Cohenour asked the P&T Committee members to mark their ballots.

6. NEW DRUG REVIEW (Please refer to the website for full text reviews.)

Aerospan

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that flunisolide inhalation aerosol is a new delivery format for inhaled corticosteroid therapy used for the treatment of Asthma. Asthma is a heterogenous disease usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheezing, shortness of breath, chest tightness, and cough and by variable expiratory airflow limitation. Both clinical symptoms and airflow limitation characteristically vary over time and in intensity. These variations are often triggered by factors such as exercise, allergen or irritant exposure, change in weather, or viral respiratory infections. The diagnosis of asthma is based on both symptomatic description and objective findings, including pulmonary function tests such as forced expiratory volume in one second (FEV1) and peak expiratory flow (PEF). Asthma is a reversible disorder, and may reverse either spontaneously or with the aid of pharmacological treatment.

Pharmacological therapy for asthma is selected based upon the severity of the patient's disease. Clinical guidelines state that all patients should be prescribed a rescue inhaler such as albuterol, and that inhaled corticosteroids (ICSs) should be considered the cornerstone of long-term control therapy. Current treatment guidelines published by the National, Heart, Lung, Blood Institute (NHLBI) indicate that the ICS agents are the most potent and consistently effective long-term controller medications for asthma patients of all ages. As such, these agents are recommended as first-line therapy for long-term control of persistent asthma symptoms in all age groups. The guidelines further state that although ICS agents do reduce both impairment and risk of asthma exacerbations they do not appear to alter the progression or underlying severity of the disease. Of

note, the NHLBI guidelines do not specifically recommend one ICS agent as possessing greater clinical efficacy or as a preferred agent over the other medications within the therapeutic class. The Global Initiative for Asthma (GINA) guidelines recommend that ICSs are the most effective anti-inflammatory medications for the treatment of persistent asthma for patients of all ages. Additionally, the GINA guidelines indicate that although ICS agents differ in potency and bioavailability there have been few studies that have been able to demonstrate this difference as being of any clinical significance. The GINA guidelines also do not recommend a preferred ICS agent.

Flunisolide is an inhaled corticosteroid indicated for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients six years of age and older and asthma patients requiring oral corticosteroid therapy, where adding flunisolide inhalation aerosol may reduce or eliminate the need for oral corticosteroids. Corticosteroids have been shown to have a wide range of anti-inflammatory effects, inhibiting both inflammatory cells (e.g. mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and release of inflammatory mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in allergic and non-allergic-mediated inflammation. These anti-inflammatory actions of corticosteroids may contribute to their efficacy in asthma. The inhaled corticosteroids are considered the most effective long-term control medication for the treatment of asthma. They have been shown to reduce the severity of symptoms, improve asthma control and quality of life, improve spirometric indices, decrease airway hyperresponsiveness, prevent exacerbations, reduce the use of systemic corticosteroids, reduce hospitalizations, and decrease mortality due to asthma.

The Food and Drug Administration (FDA)-approved indications for the flunisolide aerosol inhaler are noted in Table 3. While agents within this therapeutic class may have demonstrated positive activity via in vitro trials, the clinical significance of this activity remains unknown until fully demonstrated in well-controlled, peer-reviewed in vivo clinical trials. As such, this review and the recommendations provided are based exclusively upon the results of such clinical trials.

Clinical guidelines state that inhaled corticosteroids (ICSs) should be considered the cornerstone of long-term control therapy for asthma. Flunisolide is an inhaled corticosteroid indicated for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients six years of age and older and for asthma patients requiring oral corticosteroid therapy, where adding flunisolide inhalation aerosol may reduce or eliminate the need for oral corticosteroids. The inhaled corticosteroids are the most effective long-term medications for the treatment of mild, moderate or severe persistent asthma; therefore, they are consistently recommended as first-line maintenance therapy. Guidelines do not give preference to one inhaled corticosteroid over another for the treatment of asthma.

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 (e.g., leukotriene modifiers, long-acting β 2-agonists, cromolyn, or theophylline). 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.

Specific inhalation techniques are necessary for the proper use of each of the available types of inhaler devices. According to the American College of Chest Physicians/ American College of Asthma, Allergy, and Immunology guidelines, devices used for the delivery of bronchodilators and steroids are equally effective; therefore, efficacy should not be the basis for selecting one device over another. However, it should be noted that devices studied are only equally effective in patients who can use them appropriately. When selecting an inhalation delivery device for patients with asthma, health care providers should consider the following: device/drug availability, clinical setting, patient age and the ability to use the selected device correctly, device use with multiple medications, drug administration time, convenience in both outpatient and inpatient settings, as well as physician and patient preference.

At this time, there is insufficient data to conclude that flunisolide inhalation aerosol is safer or more efficacious than other brand or generic products within this class, and that it offers a significant clinical advantage over other alternatives in general use.

No brand flunisolide product 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 chairperson Cohenour 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. NEXT MEETING DATE

The next P&T Committee Meeting is scheduled for May 20, 2015 at the Medicaid Building in the Commissioner's Board Room.

9. ADJOURN

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

Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
February 11, 2015

- A. **Recommendation:** No brand first generation antihistamine 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. Rouz MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie G Approve Approve as amended Disapprove No action
Commissioner

- B. **Recommendation:** No brand estrogen 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. Rouz MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie G Approve Approve as amended Disapprove No action
Commissioner

C. **Recommendation:** No brand alpha glucosidase inhibitor 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. Rouze, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie H Approve Approve as amended Disapprove No action
Commissioner

D. **Recommendation:** No brand amylinomimetic 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. Rouze, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie H Approve Approve as amended Disapprove No action
Commissioner

E. **Recommendation:** No brand biguanide 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. Rouze, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

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

F. Recommendation: No brand dipeptidyl peptidase-4 inhibitor 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. Poyms Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

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

G. Recommendation: No brand incretin mimetic 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. Poyms Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

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

H. Recommendation: No brand insulin, with the exception of rapid-acting and long-acting insulin analogs, 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.

Alabama Medicaid should work with manufacturers on cost proposals so that at least one brand rapid-acting insulin analog is selected as a preferred agent.

Alabama Medicaid should work with manufacturers on cost proposals so that at least one brand long acting insulin analog is selected as a preferred agent.

Amendment: None

Vote: Unanimous to approve as recommended

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

Kathy Kelly Approve Approve as amended Disapprove No action
Deputy Commissioner

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

- I. **Recommendation:** No brand meglitinide 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. Pomey MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Kelly Approve Approve as amended Disapprove No action
Deputy Commissioner

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

- J. **Recommendation:** No sodium-glucose cotransport 1 inhibitor is recommended for preferred status. Alabama Medicaid should continue to include AHFS Class 682017 in the Preferred Drug List screening process. If new prescription sodium-glucose cotransport 1 inhibitors are added, it is recommended that this class be re-reviewed.

Amendment: None

Vote: Unanimous to approve as recommended

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

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

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

K. Recommendation: No brand sodium-glucose cotransport 2 inhibitor 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. Rouzma Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

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

L. Recommendation: No brand sulfonylurea 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. Rouzma Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner


Commissioner

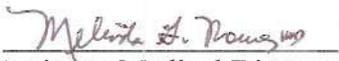
Approve Approve as amended Disapprove No action

M. Recommendation: No brand thiazolidinedione 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.

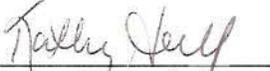
Rosiglitazone-containing products should not be placed in preferred status regardless of cost.

Amendment: None

Vote: Unanimous to approve as recommended


Assistant Medical Director

Approve Approve as amended Disapprove No action


Deputy Commissioner

Approve Approve as amended Disapprove No action

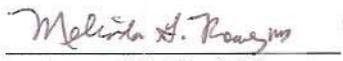

Commissioner

Approve Approve as amended Disapprove No action

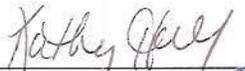
N. Recommendation: No brand antidiabetic agent, miscellaneous is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended


Assistant Medical Director

Approve Approve as amended Disapprove No action


Deputy Commissioner

Approve Approve as amended Disapprove No action


Commissioner

Approve Approve as amended Disapprove No action

O. Recommendation: No brand prenatal vitamin 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. Rowan Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie Fox Approve Approve as amended Disapprove No action
Commissioner

P. Recommendation: No brand flunisolide product 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. Rowan Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hull Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie Fox Approve Approve as amended Disapprove No action
Commissioner

Respectfully submitted,

Rachel Bastien

February 17, 2015

Rachel Bastien, Pharm.D.

Date

Amy Levy

February 17, 2015

Amy Levy, R.Ph., MHP

Date