

Minutes of Meeting

Alabama Medicaid Agency Pharmacy and Therapeutics Committee

February 13, 2013

Members Present: Vice chair-Ms. Janet Allen, Dr. Julia Boothe, Dr. Frances Cohenour, Dr. Kelli Littlejohn, Dr. Melinda Rowe, and Dr. Chivers Woodruff

Members Absent: Chair-Dr. Gerard Ferris, Dr. Donald Marks, and Ms. LaTonage Porter

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

Presenters: Dr. James Gagnon and Dr. Andrea Lewtas

Presenters Present via teleconference: None

1. OPENING REMARKS

Vice chairperson Allen called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 9:05 a.m.

2. APPROVAL OF MINUTES

Vice chairperson Allen asked if there were any corrections to the minutes from the November 14, 2012 P&T Committee Meeting.

There were no objections. Dr. Woodruff made a motion to approve the minutes as presented and Dr. Boothe 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.

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 nine 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 9:10 a.m. There were a total of 23 drug class re-reviews. The first generation antihistamines; estrogens; alpha glucosidase inhibitors; amylinomimetics; biguanides; dipeptidyl peptidase-4 inhibitors; incretin mimetics; insulins; meglitinides; sulfonylureas; thiazolidinediones and antidiabetic agents, miscellaneous were all last reviewed in May 2010. The prenatal vitamins were last reviewed in November 2009. The platelet aggregation inhibitors; antiarrhythmics; cardiotoxic agents; cardiac drugs, miscellaneous; bile acid sequestrants; cholesterol absorption inhibitors; fibric acid derivatives; HMG-CoA reductase inhibitors; antilipemic agents, miscellaneous and nitrates and nitrites were all last reviewed in August 2010.

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

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that the first generation antihistamines are available as single-entity agents, as well as fixed-dose combination products with another first generation antihistamine and/or an oral decongestant. This is a highly generic class and several agents are available over-the-counter. The first generation antihistamines are available in a wide variety of formulations including chewable tablet, drop, injection, liquids and tablet. 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.

There have been no major clinical changes in the prescribing information of the first generation antihistamines, treatment guideline recommendations regarding the use of these agents, and clinical trials demonstrating the safety and efficacy of these agents since the last time this class was reviewed.

There is overall insufficient evidence to support that one first generation antihistamine 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.

No brand first generation antihistamine 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.

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

Estrogens: AHFS 681604Manufacturer comments on behalf of these products:

Premarin[®] vaginal cream - Pfizer

Dr. Lewtas commented that estrogens are approved for a variety of conditions including abnormal uterine bleeding, hypoestrogenism, palliative treatment of prostate and breast cancer, and prevention of postmenopausal osteoporosis. However, as a class, estrogens are primarily utilized in the management of vasomotor symptoms and vulvar and vaginal atrophy associated with menopause.

Estrogen monotherapy is appropriate for women who have had a hysterectomy; while combination estrogen and progestin therapy is recommended for patients with an intact uterus, as progestin provides endometrial protection and reduces the risk of endometrial cancer. Results from the Women's Health Initiative and Heart and Estrogen/Progestin Replacement Studies, demonstrated no beneficial effects of long term hormone therapy on the prevention of chronic disease, including primary and secondary prevention of cardiovascular disease. As such, it is now recommended that women receiving hormone therapy for the management of symptoms related to menopause do so for the shortest duration possible and at the lowest effective dose.

Estrogens are available in a variety of dosage forms including injectable, oral, topical, transdermal, and vaginal preparations. Certain estrogens are also available as fixed-dose combination products with a progestin. Currently there are single-entity estrogen tablets, transdermal patches and injections, as well as fixed-dose combination tablets, available generically. Since the last time this class was reviewed Ogen[®], generic estropipate vaginal cream, has been discontinued.

Updated treatment guidelines recommend hormone therapy for the management of moderate to severe menopausal symptoms in select postmenopausal women, on the basis of individually determined benefit-to-risk profile. Hormone therapy is associated with several safety concerns, including cardiovascular, cerebrovascular and oncologic events and may not be appropriate for every patient based on age, contraindications and/or past or current health. Overall, there are no significant differences between the effects of the different types of estrogens and research is inadequate at this time to endorse one specific dosage regimen over another. With regards to the various preparations, when hormone therapy is considered solely for urogenital atrophy, local vaginal estrogen therapy is generally preferred. In addition, transdermal formulations of hormone therapy should be considered in order to avoid the hepatic "first-pass effect" of oral estrogen, this is due to a reduction in the risk of venous thromboembolism compared to oral preparations. Based on data from randomized-controlled trials, hormone therapy reduces postmenopausal osteoporotic fractures. While none of the estrogens have FDA-approval for the treatment osteoporosis, several have approval for the prevention of postmenopausal osteoporosis. Estrogens can be utilized for this indication; however, they should typically be reserved for patients in which nonhormonal therapies are not appropriate and/or cannot be utilized.

Recently published clinical trials evaluating the estrogens in FDA-approved indications have not produced clinically different results compared to trials included in the previous review. A variety

of clinical trials have been conducted with the estrogens and numerous trials have demonstrated a similar improvement in menopausal symptoms with the various preparations.

There is overall insufficient to support that one estrogen 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.

No brand estrogen 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.

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

Alpha Glucosidase Inhibitors: AHFS 682002

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that there have been no major or clinically significant changes to the alpha glucosidase inhibitors since the last time this class was reviewed. The alpha glucosidase inhibitors are approved for use as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. The alpha glucosidase inhibitors included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. Currently, acarbose is available generically.

According to current treatment guidelines, metformin remains the cornerstone of most type 2 diabetic treatment regimens. Additionally, patients with a high glycosylated hemoglobin (HbA_{1c}) 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. Guidelines note that the alpha glucosidase inhibitors are less commonly utilized in the management of type 2 diabetes, and they are not recommended for use in patients with a high HbA_{1c}, mainly due to the limited HbA_{1c} lowering potential associated with the medication class compared to other available antidiabetic medications. The alpha glucosidase inhibitors may be considered for use as monotherapy in the management of patients with a low HbA_{1c}; however, metformin remains the most appropriate initial choice for monotherapy in all patients. Among all current treatment guidelines, preference of one alpha glucosidase inhibitors over another is not stated.

Recently published clinical trials evaluating the alpha glucosidase inhibitors 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 alpha glucosidase inhibitor 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 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.

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

Amylinomimetics: AHFS 682003

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that there have been no major or clinically significant changes to the amylinomimetics since the last time this class was reviewed. Pramlintide remains the only amylinomimetic agent in the class. It is FDA-approved for use as an adjunctive treatment in patients with type 1 and type 2 diabetes who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy. Pramlintide is available for subcutaneous injection as either a vial or a multidose pen. Currently there are no amylinomimetics available generically.

According to a position statement released by the American Diabetes Association/European Association for the Study of Diabetes regarding the management of type 2 diabetes, pramlintide is typically reserved for patients treated with intensive insulin therapy, usually in type 1 diabetes. Furthermore, the agent is not included in the recommended treatment algorithm; however, it may be used in selected patients when modest efficacy is appropriate and/or adverse events are not a concern. For the management of type 1 diabetes, current treatment guidelines recommend the initiation of individualized insulin therapy at the time of diagnosis. Among type 1 diabetics, the addition of pramlintide to insulin therapy may be considered to enhance systemic control and to assist with weight management.

Pramlintide is associated with a boxed warning regarding increased risk of insulin-induced severe hypoglycemia, particularly in patients with type 1 diabetes. Pramlintide does not cause hypoglycemia when used alone; however, as indicated by the FDA-approved indication, as well as recommendations from treatment guidelines, pramlintide is to be used in patients receiving insulin, and in this setting, the risk of insulin induced severe hypoglycemia is increased.

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

There is insufficient evidence to support that one brand amylinomimetic is safer or more efficacious than another. Since pramlintide is only approved for use as an adjunctive treatment in patients with type 1 and type 2 diabetes, it should be managed through the existing 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 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 Allen asked the P&T Committee members to mark their ballots.

Biguanides: AHFS 682004

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that metformin remains the only biguanide that is currently available and that 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 formulation. 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 and triple therapy regimens. Among all 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 Allen 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:

Januvia[®] - Merck Global Medical Information

Janumet[®] - Merck Global Medical Information

Janumet XR[®] - Merck Global Medical Information

Juvisync[®] - Merck Global Medical Information

Dr. Gagnon commented that since the last time the DPP-4 inhibitors were reviewed, several new agents 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 simvastatin 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. In one trial conducted by Scheen et al, saxagliptin was found to be noninferior to sitagliptin with regards to HbA_{1c} lowering ability in type 2 diabetic patients not adequately controlled on metformin monotherapy. 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 Allen asked the P&T Committee members to mark their ballots.

Incretin Mimetics: AHFS 682006

Manufacturer comments on behalf of these products:

Victoza[®] - Novo Nordisk

Dr. Gagnon commented that there are three incretin mimetics currently available. Byetta[®] was the only agent included in the last review of this class. At the time, Victoza[®] had been approved by the FDA, but had not been available for the minimum of 180 days for inclusion in the therapeutic class review. 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. The difference between the two agents is that Bydureon[®] is a new long-acting formulation of exenatide. There are no incretin mimetics available generically.

Current treatment guidelines recommend as a potential second-line treatment option to be added to or 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 all current treatment guidelines, preference of one incretin mimetic over another is not stated.

Both extended-release exenatide 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, and Victoza[®] is administered once daily 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 another clinical trial, 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.

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 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 Allen asked the P&T Committee members to mark their ballots.

Insulins: AHFS 682008

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that there have been no major or clinically significant updates to the insulins since the last time this class was reviewed. Two new prefilled syringe pens have become available since the last time this class was reviewed and include the Apidra Solostar[®] and the Lantus Solostar[®]. 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 Allen asked the P&T Committee members to mark their ballots.

Meglitinides: AHFS 682016

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that there have been no major or clinically significant changes to the meglitinides since the last time this class was reviewed. Nateglinide remains the only generic meglitinide available.

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 initially 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 Allen asked the P&T Committee members to mark their ballots.

Sulfonylureas: AHFS 682020

Manufacturer comments on behalf of these products:

None

Dr. Gagnon 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. Since the last review branded MetaGlip[®], generic glipizide and metformin, has been discontinued; however, the fixed-dose combination product is available generically. 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 generics and over-the-counter 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 Allen asked the P&T Committee members to mark their ballots.

Thiazolidinediones: AHFS 682028

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that there are two thiazolidinediones available, pioglitazone and rosiglitazone. Both agents are available as single-entity agents, as well as fixed-dose combination products with metformin or a sulfonylurea. Since the last time this class was reviewed, pioglitazone has become available generically both as a single-entity agent and as a fixed-dose combination product with metformin. No other thiazolidinediones are available generically. In addition, a new fixed-dose combination products with pioglitazone and extended-release metformin has been approved by the FDA as the branded product Actoplus Met XR[®]. In general, the thiazolidinediones are approved for use as an adjunct therapy to diet and exercise to improve glycemic control in adults with type 2 diabetes. The thiazolidinediones fixed-dose combination products are available for use when treatment with both drug components is appropriate. Due to the observed adverse cardiovascular outcomes associated with rosiglitazone, all rosiglitazone-containing products are specifically FDA-approved for patients who are already receiving rosiglitazone or those who are not already receiving rosiglitazone and are unable to achieve glycemic control on other diabetes medications and in consultation with their healthcare provider have decided not to take pioglitazone for medical reasons.

Thiazolidinediones are recommended in the treatment guidelines as a potential second-line treatment option to be added to or used in combination with metformin in patients not achieving glycemic goals. Due to the mechanism of action of the thiazolidinediones and metformin, the addition of an incretin mimetic, DPP-4 inhibitor, or secretagogue is preferred over a thiazolidinedione to be added to metformin. The combination of metformin and a thiazolidinedione, while efficacious, carries risks of adverse events for both agents. Treatment guidelines note that thiazolidinediones are associated with weight gain, fluid retention, congestive

heart failure and fractures. The thiazolidinediones may also be a potential treatment option for initial therapy in patients who have a contraindication to metformin. 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 of the Study for Diabetes do not recommend rosiglitazone.

The thiazolidinediones are associated with a boxed warning regarding the risk of development or exacerbation of congestive heart failure. Rosiglitazone is associated with an additional boxed warning regarding an increased risk of myocardial infarction. As a result of this warning, rosiglitazone and rosiglitazone-containing products are available only through a restricted distribution program called the AVANDIA-Rosiglitazone Medicines Access Program. Both prescribers and patients need to enroll in the program.

The efficacy of the thiazolidinediones in the treatment of type 2 diabetes is well established and recently published clinical trials evaluating these agents have not produced clinically different results compared to trials included in the previous review. Evidence supports the use of the thiazolidinediones as both monotherapy and in combination with other antidiabetic agents with more aggressive treatment regimens improving glycemic parameters to a greater extent compared to less intensive regimens. In addition, results from several head-to-head trials comparing pioglitazone to rosiglitazone do not consistently demonstrate that one agent is more efficacious than another in terms of HbA_{1c} lowering ability.

All brand pioglitazone-containing 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. Based on available evidence, rosiglitazone-containing products within the class reviewed have a clinical disadvantage compared to the other branded and generic products. In addition, thiazolidinedione formulations without a generic equivalent should be managed through the medical justification portion of the prior authorization process.

No brand pioglitazone-containing 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.

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

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

Antidiabetic Agents, Miscellaneous: AHFS 682092

Manufacturer comments on behalf of these products:

None

Dr. Gagnon commented that mifepristone, or brand only Korlym[®], is the only miscellaneous antidiabetic agent and while this class has been reviewed previously, this is the first review of Korlym[®]. Mifepristone is a cortisol receptor blocker 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 medication approved for Cushing's Syndrome.

Excess cortisol production, the biochemical hallmark of endogenous Cushing's Syndrome, may be caused by either excess adrenocorticotropic hormone secretion or independent adrenal overproduction of cortisol. Patients with Cushing's Syndrome typically develop weight gain, severe fatigue and muscle weakness, high blood pressure, depression, cognitive impairment, easy bruising, loss of libido, diabetes, acne and mental disorders as a result of prolonged exposure to glucocorticoids. The condition is ultimately associated with an increase in cardiovascular mortality. Cushing's Syndrome is typically managed through surgery; however, in patients in whom surgery has failed or is not appropriate, medical therapies play an essential role in reducing or normalizing hypercortisolemia.

With regards to mifepristone, when administered at high doses, the agent is a selective antagonist of the GR-II glucocorticoid receptor and blocks the effects of cortisol. Therefore, mifepristone does not reduce cortisol levels; it just blocks the effects of the cortisol. At lower doses, mifepristone is a selective antagonist of the progesterone receptor. Mifeprex[®], another formulation of mifepristone is approved for the medical termination of intrauterine pregnancy through 49 days of pregnancy.

No treatment guidelines regarding the treatment of Cushing's Syndrome were identified, and current treatment guidelines for the management of type 2 diabetes do not address the role of mifepristone.

Mifepristone is associated with a variety of adverse events including gastrointestinal, musculoskeletal and central nervous system related. The agent is also associated with a boxed warning regarding its effects on the progesterone receptor and its ability to terminate pregnancy.

Mifepristone is available as a 300 mg tablet and is to be administered at that dose once daily initially. Patients may receive up to a maximum of 1,200 mg/day or 20 mg/kg/day.

Clinical trial data demonstrating the safety and efficacy of mifepristone in Cushing's Syndrome is limited. In a single arm, open-label trial, it was concluded that treatment with mifepristone produced significant clinical and metabolic improvements in patients with Cushing's Syndrome during six months of treatment. Patients in this trial had Cushing's Syndrome and either type 2 diabetes, glucose intolerance, or hypertension. In addition, patients had to be experiencing at least two signs or symptoms of Cushing's Syndrome. After receiving mifepristone at doses between 300 and 1,200 mg/day for six months, patients with Cushing's Syndrome and type 2 diabetes demonstrated a significant baseline reduction in area under the curve for glucose on oral glucose tolerance test, with a median decrease of 36%. Patients also achieved comparable reductions in plasma glucose levels. Other glucose-related endpoints were significant baseline reductions in fasting plasma glucose and HbA_{1c} and several patients were able to reduce their antidiabetic medications. Among all patients improvements were observed in depression, cognition and quality of life scores.

At this time, there is insufficient evidence to support that one brand miscellaneous antidiabetic 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.

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 miscellaneous antidiabetic 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 chairperson Allen asked the P&T Committee members to mark their ballots.

Multivitamin Preparations: Prenatal Vitamins: AHFS 882800

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that there have been no major or clinically significant updates to the prenatal vitamins since the last time this class was reviewed. Prenatal vitamins are FDA-approved to provide nutritional supplement for use prior to conception, throughout pregnancy and during the postnatal period. The prenatal vitamins remain available in a wide variety and most of them contain folic acid and iron. 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. Many prenatal vitamins are available generically.

Current treatment guidelines recommend that women of reproductive age consume folic acid on a daily basis and that women who are planning on becoming pregnant should take a supplement containing 400 to 800 µg of folic acid daily. Pregnant women should consume 27 mg of elemental iron per day, and those with a diagnosis of iron deficiency anemia should receive 60 to 120 mg of elemental iron per day.

Recently published clinical trials evaluating the prenatal vitamins have not produced clinically different results compared to trials included in the previous review. The benefits of prenatal vitamins are well established and they are viewed as standard of care.

Due to the wide variety of prenatal vitamins available and the manner in which these agents work, through supplementation, there is insufficient evidence to support that one prenatal vitamin 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.

No brand prenatal vitamin 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.

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

Platelet Aggregation Inhibitors: AHFS 201218

Manufacturer comments on behalf of these products:

Brilinta[®] - AstraZeneca LP

Dr. Lewtas commented that the platelet-aggregation inhibitors included in this review are listed in Table 1. Branded Effient[®] was approved by the FDA since the last time this class was reviewed in August 2010. As a class, the platelet-aggregation inhibitors play a major role in the management of cardiovascular, cerebrovascular and peripheral vascular disease. They are approved for the treatment and/or prevention of acute coronary syndromes (ACS), angina, intermittent claudication, myocardial infarction, stroke, and transient ischemic attack. They are also approved for the prevention of thrombosis in patients undergoing cardiovascular procedures and/or surgery. Currently, there are several generic platelet-aggregation inhibitors available including the newest agent to go generic in the class, clopidogrel, or what was branded Plavix[®].

There are numerous guidelines that incorporate the use of the platelet-aggregation inhibitors, and not much has changed since the last time this class has been reviewed, with the exception of the incorporation of the newer agents in the class, branded Effient[®] and Brilinta[®], and where they fit into therapy. Aspirin remains the most recommended platelet-aggregation inhibitor as first-line therapy for general use. Other platelet-aggregation inhibitors are usually reserved for patients with contraindications to aspirin or for use in high-risk patients when dual antiplatelet therapy is recommended. Dual antiplatelet therapy, with aspirin plus clopidogrel, prasugrel or ticagrelor is recommended for patients with non-ST segment elevation ACS, ST-segment elevation myocardial infarction, and in those undergoing percutaneous coronary intervention (PCI). Clopidogrel, prasugrel, and ticagrelor all share the indication for reducing the risk of thrombotic cardiovascular events in patients with ACS, respectively, and within the United States, all three agents are recommended as potential antithrombotic therapy options in ACS patients scheduled to undergo PCI with stent placement. Clopidogrel and ticagrelor are also recommended as potential options in ACS patients who did not undergo PCI. Overall, recommendations from all organizations are in line with available clinical trial data and specific FDA-approved indications. The updated 2012 CHEST guidelines, is the only American guideline to give preference to one platelet-aggregation inhibitor over another. Their guideline states ticagrelor is suggested over clopidogrel for choice of antithrombotic therapy following ACS. According to the CHEST grading system this is a weak recommendation.

A variety of clinical trials have assessed the effects of the platelet-aggregation inhibitors on cardiovascular, cerebrovascular and peripheral artery disease outcomes. With the exception of prasugrel and ticagrelor, recently published clinical trials evaluating the platelet-aggregation inhibitors have not demonstrated clinically different results compared to the trials included in the previous review. The pivotal PLATO trial was a large international prospective double-blind

randomized-controlled trial that compared ticagrelor to clopidogrel in hospitalized adult patient with documented ACS, with or without ST-segment elevation. After 12 months, ticagrelor significantly reduced the primary composite endpoint of cardiovascular death, myocardial infarction, or stroke compared to clopidogrel, which was driven mainly by a reduction in cardiovascular death and myocardial infarction. Ticagrelor also significantly reduced the risk of several secondary endpoints including all-cause mortality. While the rates of major bleeding were similar between ticagrelor and clopidogrel, ticagrelor was associated with a higher rate of major bleeding not related to coronary artery bypass grafting surgery, including more fatal intracranial bleeding and less fatal and other bleeding. A subgroup analyses of the PLATO trial also demonstrated that in patients receiving PCI, ticagrelor significantly reduced the rate of stent thrombosis compared to clopidogrel.

Overall, the newer platelet-aggregation inhibitors prasugrel and ticagrelor have demonstrated increased potency and a faster onset of action compared to clopidogrel, respectively. While clopidogrel and prasugrel are irreversible inhibitors that require enzymatic conversion to become pharmacologically active, ticagrelor is a reversible inhibitor that is orally active. Overall, concerns with drug-drug interactions and genetic variations in cytochrome P450 isoenzymes are not as strong with prasugrel and ticagrelor compared to clopidogrel.

All brand platelet-aggregation inhibitors 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. The fixed-dose combination of aspirin and extended-release dipyridamole should remain available as first-line therapy through the medical justification portion of the prior authorization process for patients who have experienced an ischemic stroke or transient ischemic attack. Prasugrel and ticagrelor should be available as first-line therapy through the medical justification portion of the prior authorization process for patients who have experienced an ACS who are going to be managed medically or with PCI.

No brand platelet-aggregation inhibitor 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.

Dr. Woodruff commented that he disagreed with the use of the word “potency” in Dr. Lewtas’ presentation of the platelet-aggregation inhibitors. A network pharmacist via teleconference commented that a subgroup analysis of the PLATO trial demonstrated that the beneficial effects of ticagrelor were not observed in North American patients compared to the entire international patient population. Dr. Lewtas added that the authors of this subanalysis believed that the loss of effect observed among the North American patients receiving ticagrelor in the PLATO trial was due to the specific dose of aspirin that was administered; they believed it to be too high. As such the FDA-approved dosing of ticagrelor recommends that after the initial loading dose of aspirin at a dose of 325 mg, a daily maintenance dose of aspirin of 75 to 100 mg should be used.

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

Antiarrhythmics: AHFS 240404

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that antiarrhythmics are effective for the treatment of atrial fibrillation/flutter and ventricular arrhythmias. Agents included in this review are listed in Table 1 and since the last time the antiarrhythmics were reviewed branded Nexterone[®], a new injectable formulation of amiodarone was approved by the FDA. The antiarrhythmics are a highly generic class, with all of the antiarrhythmics available generically, with the exception of dofetilide and dronedarone.

Overall, there have been no major changes in treatment guidelines since the last time this class was reviewed. Choice of antiarrhythmic agent for the treatment of atrial fibrillation remains patient specific and is based on comorbidities and cardiac history. The goals of therapy are to reduce symptoms and prevent recurrent atrial fibrillation, while minimizing the incidence of toxicity. Dronedarone, or branded Multaq[®], was approved by the FDA in July 2009 to reduce the risk of hospitalization for atrial fibrillation and a 2011 focused update on the management of atrial fibrillation released by the American Academy of Cardiology Foundation states that dronedarone is a reasonable option for this indication. Overall, the antiarrhythmics are generally not recommended for the initial treatment of ventricular arrhythmias, but may be utilized as adjunctive therapy in certain clinical situations.

As a class, the antiarrhythmics are associated with significant safety concerns. There are structural differences between amiodarone and dronedarone which were made to decrease the risk of thyroid and pulmonary toxicity with dronedarone. Overall, clinical trials have demonstrated this to be true. However, dronedarone is associated with safety concerns of its own. Early clinical trials demonstrated that in patients with symptomatic heart failure with recent decompensation requiring hospitalization or New York Heart Association Class IV heart failure, dronedarone increased the risk of death. In 2011, the FDA completed a safety review of dronedarone and concluded that dronedarone should not be used in patients with permanent atrial fibrillation due to an increased risk of death, stroke and hospitalization for heart failure.

The safety and efficacy of antiarrhythmics for the treatment of arrhythmias are well established. Recently published clinical trials evaluating the antiarrhythmics have not produced clinically different results compared to trials included in the previous class review.

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

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

No brand antiarrhythmic 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.

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

Cardiotonic Agents: AHFS 240408

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that digoxin is the only cardiotonic agent in the class and is available generically as an injection, solution and tablet. There have been no major clinical changes in the prescribing information, treatment guideline recommendations for the use, or clinical trials demonstrating the safety and efficacy of digoxin in the management of atrial fibrillation or heart failure since the last time this class was reviewed.

All brand products within the class 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 cardiotonic agent 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.

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

Cardiac Drugs, Miscellaneous: AHFS 240492

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that ranolazine, or branded Ranexa[®], is the only miscellaneous cardiac drug in the class and is available only as a brand extended-release tablet. Ranolazine is approved for the treatment of chronic angina. The mechanism of action of ranolazine is not completely understood. Per the approved package insert, the anti-ischemic and anti-anginal effects of ranolazine appear to not depend upon reductions in heart rate or blood pressure. In the 2011 European Cardiology Society guidelines, ranolazine exerts antianginal effects by inhibiting the late sodium current. Ranolazine is ultimately used to help reduce the number of angina attacks and has also been shown to decrease nitroglycerin use and increase walking time. It should not be used as a rescue medication as it will not stop an angina attack once it has started. Ranolazine can be used in combination with other cardiac drugs such as nitrates, antiplatelet therapies, antihypertensives and antilipemics.

Beta-blockers are still considered first-line therapy for reducing symptoms of angina in patients with coronary artery disease, with long-acting calcium channel blockers or nitrates appropriate for add-on therapy or for initial use when beta-blockers are contraindicated. There are few available guidelines that address the role of ranolazine for the treatment of chronic angina. The 2011 Institute for Clinical Systems Improvement guidelines on stable coronary artery disease state that

ranolazine is not a first-line drug and should be used in conjunction with a cardiologist. With regards to American guidelines, in 2007 the American College of Cardiology/American Heart Association stated that ranolazine may be safely administered for symptom relief after unstable angina/non-ST-segment myocardial infarction, but it does not appear to significantly improve the underlying disease.

The majority of clinical evidence supporting the use of ranolazine for the treatment of chronic angina is based on results from placebo-controlled trials and recently published clinical trials evaluating ranolazine have not produced clinically different results compared to trials included in the previous class review.

There is insufficient evidence to support that ranolazine is safer or more effective compared to other agents commonly used, and recommended, for the treatment of chronic angina. Due to the fact that ranolazine is not recommended as first-line therapy, it should be managed through the medical justification portion of the prior authorization process.

All brand products within the class 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 miscellaneous cardiac drug 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.

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

Bile Acid Sequestrants: AHFS 240604

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that the bile acid sequestrants included in this review are listed in Table 1. This class is approved as adjunct therapy to diet and exercise to reduce total and low-density lipoprotein (LDL) cholesterol. In addition, colestevlam is approved for the treatment of heterozygous familial hypercholesterolemia, as well as adjunct treatment to diet and exercise for the treatment of type 2 diabetes in adults. Cholestyramine also has an additional indication for relief of pruritus associated with partial biliary obstruction. Currently cholestyramine and colestipol are available generically. With regards to treatment of hypercholesterolemia, the bile acid sequestrants are associated with an approximate decrease in LDL cholesterol of 15 to 30% and increase in high-density lipoprotein (HDL) cholesterol of 3 to 5%.

Lowering LDL cholesterol is the primary target of cholesterol lowering therapy and for this, the HMG-CoA reductase inhibitors, or statins, are generally considered first-line therapy, in addition to life style changes. If after six weeks of therapy, lipid goals have not been achieved, an increase in statin dose or an addition of a bile acid sequestrant, niacin, or ezetimibe can be considered.

Statins are also considered first line for the treatment of heterozygous familial hypercholesterolemia; however, if required a bile acid sequestrant may be added to therapy. Pruritus is a complication of primary biliary cirrhosis and bile acid sequestrants are the drug of choice for the treatment of this complication. With regards to their use in the management of type 2 diabetes, colesevelam has been shown to reduce blood glucose levels in patients not adequately controlled on standard antidiabetics. For any disease state or indication, guidelines do not give preference to one bile acid sequestrant over another.

The safety and efficacy of the bile acid sequestrants for the treatment of lipid disorders are well established and recently published clinical trials evaluating the bile acid sequestrants have not produced clinically different results compared to trials included in the previous class review.

There is insufficient evidence to support that one brand bile acid sequestrant is safer or more effective than another. Formulations without a generic alternative should be managed through the medication justification portion of the prior authorization process.

All brand products within the class 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 bile acid sequestrant 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.

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

Cholesterol Absorption Inhibitors: AHFS 240605

Manufacturer comments on behalf of these products:

Zetia[®] - Merck & Co., Inc.

Dr. Lewtas commented that ezetimibe, or branded Zetia[®], is the only cholesterol absorption inhibitor in the class and is available as a brand only tablet. Ezetimibe is approved for several lipid conditions included primary hypercholesterolemia, mixed hyperlipidemia, homozygous familial hypercholesterolemia, and homozygous familial sitosterolemia. Ezetimibe is associated with an approximate decrease in LDL cholesterol of 18%.

In general, ezetimibe is recommended as a potential option to be added to statin therapy if lipid goals have not been met or as a potential initial treatment option if statins, bile acid sequestrants, and/or niacin are not appropriate. Guidelines also note that the long-term effects of ezetimibe on cardiovascular morbidity and mortality remain unknown.

Recently published clinical trials evaluating the cholesterol absorption inhibitors have not produced clinically different results compared to trials included in the previous class review. The majority of clinical trials evaluate ezetimibe as combination therapy with standard antilipemics and results consistently demonstrate its complementary effects on various lipid/lipoprotein parameters.

The effects of ezetimibe, administered as monotherapy or combination therapy, on cardiovascular morbidity and mortality have not been established.

There is insufficient evidence to support that ezetimibe is safer or more effective compared to other agents commonly used, and recommended, for the treatment of lipid disorders. Due to the fact that ezetimibe is not recommended as first-line therapy, it should be managed through the medical justification portion of the prior authorization process.

All brand products within the class 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 cholesterol absorption inhibitor 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.

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

Fibric Acid Derivatives: AHFS 240606

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that the fibric acid derivatives that are included in this review are listed in Table 1. The fibric acid derivatives are approved for the treatment of hypertriglyceridemia, primary hypercholesterolemia and mixed dyslipidemia. All of the agents are available in generic formulation in at least one dosage form and/or strength. Fibric acid derivatives are associated with an approximate decrease in triglycerides of 20 to 50% and increase in HDL cholesterol of 10 to 35%. They are also associated with an approximate decrease in LDL cholesterol of 5 to 20%.

Fibric acid derivatives are considered an option for lipid lowering in patients who are unable to take a statin but they are typically reserved for the treatment of hypertriglyceridemia to reduce the risk of pancreatitis or for use in patients with isolated low HDL cholesterol levels. Guidelines do not give preference to one fibric acid derivative over another.

Recently published clinical trials evaluating the fibric acid derivatives have not produced clinically different results compared to trials included in the previous class review. Overall, because of chemical, pharmacological and clinical similarities between the various fibric acid derivatives, findings from clinical trials and recommendations from treatment guidelines apply to all of the agents in the class.

There is insufficient evidence to support that one brand fibric acid derivative 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 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 fibric acid derivative 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.

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

HMG-CoA Reductase Inhibitors: AHFS 240608

Manufacturer comments on behalf of these products:

Vytorin[®] - Merck & Co., Inc.

Dr. Lewtas commented that the HMG-CoA reductase inhibitors, or statins, that are included in this review are listed in Table 1. Agents include single entity statins, as well as fixed-dose combination products with other cardiovascular drugs such as calcium channel blockers, cholesterol absorption inhibitors, and niacin. Generic pitavastatin, or branded Livalo[®], was not eligible for inclusion in the last review of this class because it had not been on the market for at least 180 days. Pitavastatin has only been evaluated compared to placebo for the treatment of primary hypercholesterolemia and mixed dyslipidemia. As a class, the statins are approved for the treatment of a variety of lipid disorders, including primary hypercholesterolemia, mixed dyslipidemia, and hypertriglyceridemia. Atorvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin all have additional indications related to the prevention of cardiovascular disease. All fixed-dose combination statin products are approved for use when dual therapy is appropriate. The statins are associated with an approximate decrease in LDL cholesterol of 18 to 60% and triglycerides of 7 to 30%. Statins are also associated with an approximate increase in HDL cholesterol of 5 to 15%. Currently, atorvastatin, fluvastatin, lovastatin, pravastatin, simvastatin and the fixed-dose combination product amlodipine and atorvastatin are all available generically.

Statins are generally considered first line when LDL cholesterol lowering therapy is required. If after six weeks of therapy lipid goals are not achieved, the dose of a statin can be doubled or a second lipid lowering agent can be added to the treatment regimen. The statins have also been shown to have beneficial effect on coronary heart disease and therefore, they are recommended in patients with established coronary heart disease or coronary heart disease equivalents. Guidelines do not give preference to one statin over another and choice is often dictated by the amount of lipid lowering required for a specific agent.

Numerous clinical trials have demonstrated the beneficial effects of the statins on lipids and cardiovascular disease and recently published clinical trials evaluating the statins have not produced clinically different results compared to trials included in the previous class review. In general, the fixed-dose combination products do not offer any significant clinical advantage over coadministration of their individual components.

In June 2011 the FDA issued a safety warning regarding the highest dose of simvastatin. Specifically, the FDA has recommended that simvastatin 80 mg be restricted due to an increased risk of muscle damage. Patients who have been receiving simvastatin 80 mg for at least 12 months without evidence of myopathy may continue therapy; however, this strength should not be initiated in new patients.

There is insufficient evidence to support that one brand statin 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 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 statin 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.

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

Antilipemic Agents, Miscellaneous: AHFS 240692

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that niacin and omega-3 acid ethyl esters are the only miscellaneous antilipemic agents included in the review and these agents are approved for the treatment of hypertriglyceridemia. Niacin is also approved for the treatment of primary hypercholesterolemia and mixed dyslipidemia. Currently, niacin is available generically and over-the-counter. The over-the-counter products are considered dietary supplements and because of this their manufacturer is not regulated by the FDA. Omega-3 acid ethyl ester agents are only available as branded Lovaza[®].

The miscellaneous antilipemic agents are approved for the treatment of hypertriglyceridemia. A fibric acid derivative or niacin should be initiated in patients with elevated triglycerides and omega-3 acid ethyl esters represent an alternative option.

Recently published clinical trials evaluating the miscellaneous antilipemic agents have not produced clinically different results compared to trials included in the previous class review. There are limited head-to-head trials comparing the efficacy and safety of the different niacin formulations. Flushing is more common with the immediate-release formulations; however, it still can occur with sustained- and extended-release formulations. In addition, cases of severe hepatotoxicity have been reported in patients switching to sustained-release niacin formulations. Due to these safety concerns, the American Heart Association stresses that dietary supplement niacin should not be used for cholesterol lowering.

Therefore, prescription niacin products offer significant clinical advantage in general use over the over-the-counter product, but are comparable to other prescription niacin products. In addition, due

to its limited FDA-approved indications, prescription omega-3-acid ethyl esters should be available through the medical justification portion of the prior authorization process for adults with severe hypertriglyceridemia, defined as a triglyceride level of at least 500 mg/dL.

Prescription niacin is recommended for preferred status. Alabama Medicaid should accept cost proposals so that at least one brand prescription niacin product is selected for preferred status. No brand omega-3-acid ethyl ester 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.

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

Nitrates and Nitrites: AHFS 241208

Manufacturer comments on behalf of these products:

None

Dr. Lewtas commented that the nitrates and nitrites that are included in this review are listed in Table 1 and all of the products are available in generic formulation. There have been no major changes in prescribing information, treatment guidelines or clinical trials since the last time this class was reviewed.

All brand products within the class 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 nitrate or nitrite 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.

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

6. 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.

7. NEXT MEETING DATE

The next P&T Committee Meeting is scheduled for May 15, 2013 at the Medicaid Building in the Commissioner's Board Room.

8. ADJOURN

There being no further business, Dr. Woodruff moved to adjourn and Dr. Boothe seconded. The meeting adjourned at 11:25 a.m.

Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
February 13, 2013

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. Paug MD Approve Approve as amended Disapprove No action
Assistant Medical Director
Kathy Hill Approve Approve as amended Disapprove No action
Deputy Commissioner
Stephanie K... 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.

No brand monoamine oxidase inhibitor is recommended for preferred status, regardless of cost.

Amendment: None

Vote: Unanimous to approve as recommended

Melinda S. Paug MD Approve Approve as amended Disapprove No action
Assistant Medical Director
Kathy Hill Approve Approve as amended Disapprove No action
Deputy Commissioner
Stephanie K... 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 H. Rougemont Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Kelly Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. ... 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 H. Rougemont Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Kelly Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. ... 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 H. Rougemont Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Kelly Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie A. ... 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 H. Ponce, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Bell Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie H. 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 H. Ponce, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Bell Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie H. 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. Young Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephano 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. Young Approve Approve as amended Disapprove No action
Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephano Approve Approve as amended Disapprove No action
Commissioner

J. 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 S. Ponce Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie R. Approve Approve as amended Disapprove No action

Commissioner

K. Recommendation: No brand pioglitazone-containing 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.

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

Amendment: None

Vote: Unanimous to approve as recommended

Melinda S. Ponce Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie R. Approve Approve as amended Disapprove No action

Commissioner

L. 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

Melinda S. Ponce Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Hall Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie R. Approve Approve as amended Disapprove No action

Commissioner

M. 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. Rouss Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Hill Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action

Commissioner

N. Recommendation: No brand platelet aggregation 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. Rouss Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Hill Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action

Commissioner

O. Recommendation: No brand antiarrhythmic 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. Rouss Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Hill Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action

Commissioner

P. Recommendation: No brand cardiotoxic 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 A. Rouzas Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Kelly Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action

Commissioner

Q. Recommendation: No brand cardiac drugs, 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

Melinda A. Rouzas Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Kelly Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action

Commissioner

R. Recommendation: No brand bile acid sequestrant 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. Rouzas Approve Approve as amended Disapprove No action

Assistant Medical Director

Kathy Kelly Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action

Commissioner

S. Recommendation: No brand cholesterol absorption 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 S. Rowan Approve Approve as amended Disapprove No action
Assistant Medical Director

Nathy Kelly Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action
Commissioner

T. Recommendation: No brand fibric acid derivative 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

Nathy Kelly Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action
Commissioner

U. Recommendation: No brand HMG-CoA reductase 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 S. Rowan Approve Approve as amended Disapprove No action
Assistant Medical Director

Nathy Kelly Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie B. Approve Approve as amended Disapprove No action
Commissioner

V. **Recommendation:** Prescription niacin is recommended for preferred status. Alabama Medicaid should work with manufacturers on cost proposals so that at least one brand prescription niacin product is selected as a preferred agent.

No brand omega-3 acid ethyl ester 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. Proulx Approve Approve as amended Disapprove No action

Assistant Medical Director

Jathy Hall Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie Approve Approve as amended Disapprove No action

Commissioner

W. No brand nitrate and nitrite 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. Proulx Approve Approve as amended Disapprove No action

Assistant Medical Director

Jathy Hall Approve Approve as amended Disapprove No action

Deputy Commissioner

Stephanie Approve Approve as amended Disapprove No action

Commissioner

Respectfully submitted,



February 27, 2013

James Gagnon, Pharm.D., BCPS

Date