

**Minutes of Meeting**  
**Alabama Medicaid Agency**  
**Pharmacy and Therapeutics Committee**

**May 20, 2015**

**Members Present:** Dr. Lee Carter, Dr. Frances Cohenour (Vice-chair), Dr. David Harwood (Chair), Dr. Kelli Littlejohn Newman, Dr. Pilar Murphy, Dr. Melinda Rowe, and Dr. Robert Smith

**Members Absent:** Ms. Janet Allen, Dr. Elizabeth Jacobson

**Patient Care Networks of Alabama (PCNA) Staff Present:** Dr. Lydia Rather, Dr. Kristian Testerman, Dr. Lauren Ward

**Presenters:** Dr. Rachel Bastien and Ms. Amy Levy

**Presenters Present via teleconference:** None

**1. OPENING REMARKS**

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

**2. APPROVAL OF MINUTES**

Chairperson Harwood asked if there were any corrections to the minutes from the February 11, 2015 P&T Committee Meeting.

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

**3. PHARMACY PROGRAM UPDATE**

Dr. Littlejohn Newman commented that in March, the Agency held a series of ICD-10 classes for providers throughout the state. [http://medicaid.alabama.gov/news\\_detail.aspx?ID=9525](http://medicaid.alabama.gov/news_detail.aspx?ID=9525)

In April, the Agency disseminated clarification language regarding the use of a physician designee when signing medical documentation (referral forms).  
[http://medicaid.alabama.gov/news\\_detail.aspx?ID=9593](http://medicaid.alabama.gov/news_detail.aspx?ID=9593)

In April, the Agency applied the routine, quarterly PDL update.  
[http://medicaid.alabama.gov/news\\_detail.aspx?ID=9507](http://medicaid.alabama.gov/news_detail.aspx?ID=9507)

The Agency continues to work internally, and with stakeholders, on RCO development and implementation. A kick-off Medical Management meeting will be held this week with all Probationary RCO Medical Directors, Executive Directors, Network Pharmacists, and other key staff. More information on the state RCOs can be found on the Agency website at: [http://medicaid.alabama.gov/CONTENT/2.0\\_newsroom/2.7.3\\_Regional\\_Care\\_Organizations.aspx](http://medicaid.alabama.gov/CONTENT/2.0_newsroom/2.7.3_Regional_Care_Organizations.aspx)

The Agency continues to work very closely with the legislature and the Governor's office on several key pieces of legislation, and the state budgetary process. The routine legislative session will come to a close during the first part of June.

#### **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 two manufacturer verbal presentations at the meeting.

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

The pharmacotherapy class reviews began at approximately 9:06 a.m. There was one initial class review, the oral anticoagulants. There were a total of 10 drug class re-reviews. 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 February 2013.

##### **Oral Anticoagulants: AHFS 201204**

##### Manufacturer comments on behalf of these products:

Eliquis<sup>®</sup> - Bristol-Myers Squibb

Xarelto<sup>®</sup> - Janssen

Dr. Bastien commented that the oral anticoagulants included in this review are listed in Table 1 on page 8. This review encompasses only oral dosage forms and strengths within the AHFS class. Warfarin is the only product available in a generic formulation. This is the first review of the oral anticoagulants.

Warfarin has been the principle oral anticoagulant for more than 60 years and has extensive, well established data demonstrating its safety and efficacy in all of its FDA-approved indications. Apixaban and rivaroxaban are selective factor Xa inhibitors while dabigatran is a direct thrombin inhibitor. All are approved to reduce the risk of stroke and systemic embolism in patients with

nonvalvular atrial fibrillation and for treatment and reduction in the risk of recurrence of deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients who have previously been treated. Rivaroxaban and apixaban are also indicated for the prophylaxis of DVT which may lead to PE in patients undergoing knee or hip replacement surgery. Detailed indications are listed on page 38 in Table 3.

Current treatment guidelines that incorporate the use of the oral anticoagulants are summarized in Table 2. In 2014, the American Heart Association, the American College of Cardiology, and the Heart Rhythm Society jointly released an updated guideline on the management of AF. The guidelines state that antithrombotic therapy should be individualized based on shared decision-making after discussion of the absolute and relative risks of stroke, bleeding, and the patient's values and preferences. Dietary limitations and the need for repeated International Normalized Ratio (INR) testing are eliminated with the new agents. If patients are stable, their condition is easily controlled, and they are satisfied with warfarin therapy, it is not necessary to change to a new agent. Notably, patients with mechanical heart valves or hemodynamically significant mitral stenosis were excluded from all three major trials (RE-LY, ROCKET AF, and ARISTOTLE); therefore, these patients should be managed with warfarin. The 2012 American College of Chest Physicians guidelines regarding antithrombotic therapy and prevention of thrombosis state that oral anticoagulation is recommended in patients with AF at intermediate to high risk of stroke, with dabigatran suggested over adjusted-dose VKA therapy; however, this is a weak recommendation and treatment decisions should be individualized. A Science Advisory by the American Heart Association and American Stroke Association states that apixaban, dabigatran, and rivaroxaban are recommended as alternatives to warfarin in patients with AF who have at least one additional risk factor for stroke. All of the oral anticoagulants are recommended as potential options for thromboprophylaxis of total hip and knee arthroplasty, with LMWH suggested in preference to other recommended options. The American Heart Association/American Stroke Association Guidelines for the Prevention of Stroke in Patients with Stroke or Transient Ischemic Attack from 2014 offer recommendations consistent with other published guidelines.

Turning to page 39, the significant drug interactions are listed in Table 5. Because warfarin is metabolized by Cytochrome P450 (CYP) enzymes, many drug interactions may occur. Close monitoring should be utilized when inhibitors and inducers of CYP2C9, 1A2, and 3A4 are coadministered with warfarin. The evidence demonstrating the efficacy of warfarin for FDA-approved indications, including reducing the risk of stroke and systemic embolism in patients with AF, is well established, and warfarin has been considered the standard of care in high-risk patients with AF. Warfarin therapy is associated with challenges including a slow onset and offset of action, unpredictable inter-patient variability in pharmacologic response, a narrow therapeutic window necessitating frequent monitoring, and numerous food and drug interactions. Moreover, maintenance of a therapeutic level of anticoagulation may be difficult for some patients and requires a good understanding of the pharmacokinetic and pharmacodynamic properties of warfarin. In comparison to warfarin, treatment with apixaban, dabigatran etexilate mesylate, or rivaroxaban does not require routine monitoring, but clinicians may find it difficult to objectively assess a patient's adherence to therapy and to verify if a fixed-dose regimen can be universally applied to all patients. Additionally, compliance with these new oral anticoagulants is critical. Missing even one dose could result in a period without protection from thromboembolism; As a result, the FDA issued boxed warnings that discontinuation of these new agents can increase the

risk of thromboembolism and that coverage with another anticoagulant may be needed. Warfarin has a boxed warning for the risk of major bleeding. These warnings can be found on pages 43 and 44. Warfarin does not require a dosage adjustment in patients with renal impairment, while a lower dose of apixaban, dabigatran, and rivaroxaban (in AF only) is recommended. Moreover, apixaban requires a dosage adjustment when two or more of the following factors are present: age  $\geq 80$  years, weight  $\leq 60$  kg or serum creatinine  $\geq 1.5$  mg/dL.

In situations where a major bleed occurs, no specific antidote is currently available for the new oral anticoagulants. Reversal of warfarin anticoagulation may be obtained by discontinuing warfarin therapy and administering vitamin K. The overall bleeding risk appears to be comparable overall between apixaban and aspirin. Clinical trials comparing apixaban to warfarin have demonstrated a lower incidence of major intracranial bleeding and major bleeding at other locations with apixaban, with a similar incidence of gastrointestinal bleeding. In clinical trials, warfarin was associated with more intracranial bleeding, while dabigatran was associated with more gastrointestinal bleeding.

In the clinical trial that was the basis for FDA-approval of dabigatran, the incidence of myocardial infarction was higher with dabigatran compared to warfarin. Whether or not this is a true risk associated with the agent is unclear; however, a subanalysis of the trial did not demonstrate an increase in MI with either dose of dabigatran compared to warfarin. In the trial that was the basis for FDA-approval of rivaroxaban for use in AF, there was no difference in major and clinically relevant nonmajor bleeding between rivaroxaban and warfarin, but like dabigatran, rivaroxaban and apixaban were associated with a lower risk of intracranial bleeding. Rivaroxaban had a higher incidence of gastrointestinal bleeding compared to warfarin.

Due to the lack of unanimous recommendations from guidelines preferring one of the newer agents over another, the reports of significant adverse drug reactions reported to the FDA, and the lack of long-term safety data, it is recommended that apixaban, rivaroxaban, and dabigatran be managed via the prior authorization process.

Therefore, all brand warfarin-containing 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. The other available agents in the class, apixaban, dabigatran, and rivaroxaban, currently have no therapeutic advantage compared to the other brand and generic products in the class (if applicable).

No brand oral anticoagulant 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.

Dr. Carter inquired about the basis of the prior authorization criteria and how a therapeutic failure is defined. He pointed out that in rural practice settings not all patients can come in every two weeks for INR testing. Dr. Littlejohn Newman stated that the Agency is aware of these concerns and remarks that the committee is welcome to discuss other options. The current criteria follows the standard process of appropriate diagnosis, failure with two preferred agents (which would just be one agent, warfarin, in this case), contraindications/allergies, and sufficient medical justification. She commented that if the committee feels more discussion is necessary to please

make other recommendations. Dr. Carter added that certain circumstances like patient compliance can impact the choice of anticoagulant agent. Dr. Harwood responded that a newer oral anticoagulant versus unmonitored warfarin therapy is a valuable real-life comparison to make. Dr. Carter commented that he practices in a rural setting and has substantial concerns with monitoring of therapy. Dr. Littlejohn Newman responded that Dr. Carter will be affected by this, and notes that it can be rediscussed if prior authorizations become an issue.

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

**Platelet Aggregation Inhibitors: AHFS 201218**

Manufacturer comments on behalf of these products:

None

Dr. Bastien commented that the platelet-aggregation inhibitors included in this review are listed in Table 1 on page 103. The newest platelet inhibitor to be approved by the Food and Drug Administration, vorapaxar (Zontivity<sup>®</sup>), is a reversible antagonist of protease-activated receptor 1 (PAR-1). Blocking PAR-1 results in potent inhibition of thrombin-induced platelet aggregation. Due to vorapaxar's long half-life, it acts as an irreversible inhibitor. Unlike other platelet inhibitors, vorapaxar does not inhibit platelet aggregation induced by ADP, collagen, or a thromboxane mimetic. Cilostazol, clopidogrel, dipyridamole, and ticlopidine are the platelet-aggregation inhibitors that are available generically.

Treatment guidelines for these agents are summarized in Table 2. Although there have been updates to the existing guidelines, there have been no major or clinically significant updates. Vorapaxar is yet to be incorporated into the guidelines.

With the exception of newly approved vorapaxar, recently published clinical trials evaluating the platelet-aggregation inhibitors have not demonstrated clinically different results compared to the trials included in the previous review. Vorapaxar is indicated for the reduction of thrombotic cardiovascular events in patients with a history of MI or with peripheral arterial disease (PAD). The TRACER study was a randomized, double-blind, placebo-controlled trial evaluating the efficacy of vorapaxar in addition to standard therapy in 12,944 patients who had acute coronary syndromes without ST-segment elevation. This trial was stopped early due to a significant increase in the risk of major bleeding, including intracranial hemorrhage, in vorapaxar-treated patients. The preliminary clinical outcomes data showed no significant advantage of vorapaxar over placebo in preventing the primary composite endpoint of death from cardiovascular causes, MI, stroke, recurrent ischemia with rehospitalization, or urgent coronary revascularization. Vorapaxar increased the rate of moderate or severe bleeding, as compared with placebo. FDA approval of vorapaxar was based on the TRA2P-TIMI 50 trial. A population of 26,449 patients with peripheral arterial disease or a history of MI or ischemic stroke was randomized to receive either vorapaxar or placebo, in addition to standard care. After two years, the data and safety monitoring board recommended that patients with a history of stroke stop taking vorapaxar because of an increased risk of intracranial hemorrhage; the trial was continued in all other patients. At three years, the composite efficacy endpoint of cardiovascular death, MI, or stroke had occurred in less patients treated with vorapaxar compared to placebo. Due to the increased risk of bleeding events with

vorapaxar, it is contraindicated in patients with a history of stroke, transient ischemic attack, intracranial hemorrhage, or active pathologic bleeding, as indicated in the boxed warning.

All brand platelet-aggregation inhibitors 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. The fixed-dose combination of aspirin and extended-release dipyridamole should be available as first-line therapy through the medical justification portion of the prior authorization process for patients who have experienced an ischemic stroke or TIA. Prasugrel and ticagrelor should be available as first-line therapy (in combination with aspirin) 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.

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

**Antiarrhythmics: AHFS 240404**

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the antiarrhythmic agents included in the review are listed in Table 1. There have been no changes to the medications included in this class since it was last reviewed in February 2013. Treatment guidelines for these agents are summarized in Table 2. Although there have been updates to the existing guidelines, there have been no major or clinically significant updates to the treatment of arrhythmias.

The antiarrhythmic agents are effective for the treatment of atrial fibrillation/flutter and ventricular arrhythmias. These agents differ in regards to their Food and Drug Administration approved indications, mechanism of action, pharmacokinetic properties, drug interactions, and adverse events. All of the antiarrhythmic agents are available in a generic formulation with the exception of dofetilide and dronedarone.

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

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

No brand antiarrhythmic 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. Chairperson Harwood asked the P&T Committee members to mark their ballots.

**Cardiotonic Agents: AHFS 240408**

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the cardiotonic agents included in this review are listed in Table 1. There have been no changes to the medication included in this class since it was last reviewed in February 2013. Treatment guidelines for this agent are summarized in Table 2. Although there have been updates to the existing guidelines, there have been no major or clinically significant updates to the treatment guidelines with cardiotonic agents. The effectiveness of these agents is discussed in Table 8. Recently published clinical trials evaluating the cardiotonic class in the treatment of atrial fibrillation and heart failure have not produced clinically different results compared to effectiveness trials included in previous reviews.

Therefore, all brand cardiotonic agents 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 cardiotonic 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. Chairperson Harwood asked the P&T Committee members to mark their ballots.

**Cardiac Drugs, Miscellaneous: AHFS 240492**

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the miscellaneous cardiac drugs included in this review are listed in Table 1. There have been no changes to the medication included in this class since it was last reviewed in February 2013. Ranolazine is the only miscellaneous cardiac drug currently available and it is approved for the treatment of chronic angina. Ranolazine is not available in a generic formulation.

Available guidelines recommend ranolazine as an alternative agent when  $\beta$ -blockers, calcium channel blockers, and nitrates are not adequately effective or are not tolerated. The American College of Cardiology/American Heart Association Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes states that ranolazine may also improve outcomes in NSTEMI-ACS patients due to a reduction in recurrent ischemia.

Four trials have evaluated the efficacy and safety of ranolazine SR in patients with chronic angina. Ranolazine (administered either as monotherapy or in combination with other anti-anginal drugs)

was more effective compared to placebo with regards to exercise duration, time to onset of angina, frequency of angina, and nitroglycerin use.

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

Therefore, all brand miscellaneous cardiac drugs 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 miscellaneous cardiac drug 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. Chairperson Harwood asked the P&T Committee members to mark their ballots.

**Bile Acid Sequestrants: AHFS 240604**

Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the bile acid sequestrants included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. Cholestyramine (regular and light) and colestipol are available in a generic formulation. This class was last reviewed in February 2013 and there have been no changes to the medications included in this class.

Treatment guidelines for this agent are summarized in Table 2. Although there have been updates to the existing guidelines, there have been no major or clinically significant updates to the treatment guidelines with bile acid sequestrants.

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

Therefore, all brand bile acid sequestrants 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 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.

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

### **Cholesterol Absorption Inhibitors: AHFS 240605**

#### Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the cholesterol absorption inhibitors that are included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. Ezetimibe is not available in a generic formulation. There have been no changes to the medications included in this class since it was last reviewed in February 2013.

Treatment guidelines for this agent are summarized in Table 2. Although there have been updates to the existing guidelines, there have been no major or clinically significant updates to the treatment guidelines with cholesterol absorption inhibitors.

The majority of available clinical trials evaluate ezetimibe as combination therapy with colesvelam, fenofibrates, niacin, and statins, and results demonstrate that complementary effects on various lipid/lipoprotein parameters are achieved. The effects of ezetimibe given either alone or in addition to a statin or fenofibrate on cardiovascular morbidity and mortality have not been established. Ezetimibe should be available as adjunctive therapy through the medical justification portion of the prior authorization process.

Therefore, all brand cholesterol absorption inhibitors 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 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.

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

### **Fibric Acid Derivatives: AHFS 240606**

#### Manufacturer comments on behalf of these products:

None

Ms. Levy commented that the fibric acid derivatives that are included in this review are listed in Table 1. This review encompasses all dosage forms and strengths. This class was last reviewed in February 2013. All fibric acid derivatives are available in a generic formulation.

Treatment guidelines for this agent are summarized in Table 2. Although there have been updates to the existing guidelines, there have been no major or clinically significant updates to the treatment guidelines with fibric acid derivatives.

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.

Therefore, all brand fibric acid derivatives 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 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.

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

### **HMG-CoA Reductase Inhibitors: AHFS 240608**

#### Manufacturer comments on behalf of these products:

None

Dr. Bastien commented that the HMG-CoA reductase inhibitors, or statins, included in this review are listed in Table 1 on page 566. 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. 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. Liptruzet<sup>®</sup>, a fixed-dose combination of ezetimibe and atorvastatin, has been approved since the last review. 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.

The American College of Cardiology/American Heart Association and Institute for Clinical Systems Improvement both released updated guidelines in 2013 which support initiating a statin in patients with established atherosclerotic cardiovascular disease (ASCVD). According to these recommendations, percent reduction in LDL-C is an indicator of response and adherence to therapy, but treating to a targeted level is not a primary goal. Combination therapy can be considered on an individual basis, but studies of combination therapy have generally not shown benefit beyond statin monotherapy. Additionally, if patients are unable to take a statin, then bile acid sequestrants, niacin, fibric acid derivatives or fibrates, and ezetimibe are available. High-intensity statin therapy should be initiated or continued as first-line therapy in women and men  $\leq 75$  years of age that have clinical ASCVD, unless contraindicated. When high-intensity statin therapy is contraindicated or when characteristics predisposing to statin-associated adverse effects are present, moderate-intensity statin should be used as the second option if tolerated. Adults  $\geq 21$  years of age with LDL-C  $\geq 190$  mg/dL should be treated with statin therapy even with no 10-year

ASCVD risk estimation required. The ACC/AHA guidelines note that there is no differentiation between the specific statins and doses used in primary- and secondary-prevention trials and that statins reduce ASCVD risk similarly in both populations.

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.

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.

Therefore, all brand HMG-CoA reductase inhibitors 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 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.

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

**Antilipemic Agents, Miscellaneous: AHFS 240692**  
Manufacturer comments on behalf of these products:

Dr. Bastien commented that the miscellaneous antilipemic agents included in this review are listed in Table 1 on page 807. Since the last review in February 2013, icosapent ethyl, lomitapide, and mipomersen have been added to the review. Niacin and omega-3 acid ethyl esters are available in a generic formulation. Prescription niacin, icosapent ethyl, and omega-3 acid ethyl esters are approved by the FDA for the treatment of hypertriglyceridemia. Lomitapide and mipomersen are approved for adjunctive treatment of homozygous familial hypercholesterolemia (HoFH).

Each omega-3 acid ethyl esters capsule contains at least 900 mg of ethyl esters of omega-3 fatty acids sourced from fish oil, which are predominantly EPA (approximately 465 mg) and DHA (approximately 375 mg). The total EPA and DHA dose recommended for TG-lowering is approximately 2 to 4 grams per day. Vascepa<sup>®</sup> is a new omega-3 fatty acid formulation. It also contains EPA obtained from fish oil; however, it contains at least 96% EPA and does not contain DHA. Studies suggest that this formulation may not cause significant increases in LDL-C, unlike the traditional mixtures of EPA and DHA.

Since the last review, two new drugs have been approved as adjuncts to diet and other lipid-lowering treatments to improve lipid parameters in patients with homozygous familial hypercholesterolemia (HoFH). HoFH is a genetic condition usually leading to loss-of-function

mutations in the LDL receptor and is associated with substantially elevated LDL-C (>400 mg/dL) and premature atherosclerotic cardiovascular disease. Lomitapide is a microsomal triglyceride transfer protein inhibitor: This inhibition prevents the assembly of apolipoprotein (apo) B-containing lipoproteins, which inhibits the synthesis of VLDL, leading to reduced levels of plasma LDL-C. Mipomersen is an oligonucleotide inhibitor of apo B-100 synthesis. Apo B-100 is an essential component of VLDL and LDL-C.

Icosapent ethyl, lomitapide, and mipomersen are all recently approved medications which are not yet addressed in clinical guidelines. Two placebo-controlled icosapent ethyl trials (MARINE and ANCHOR) suggest that the drug significantly decreases triglyceride levels without increasing LDL-C levels. Studies of lomitapide in combination with other lipid-lowering therapies have shown a reduction in LDL-C from baseline of 35 to 50%. Mipomersen, which is administered as a weekly subcutaneous injection, has shown a mean percent change in LDL-C from baseline ranging from 25 to 47% in patients on maximally tolerated lipid-lowering therapy across five clinical trials. Both lomitapide and mipomersen have boxed warnings regarding the risk of hepatotoxicity and are only available through Risk Evaluation and Mitigation Strategy (REMS) programs and are only used as adjunctive therapy in patients with HoFH.

Recent guidelines discourage use of niacin in combination with statins, as trials have shown increased side effects without any reduction in cardiovascular outcomes. Clinical trials have demonstrated that niacin positively impacts a variety of lipid/lipoprotein parameters. However, the 3-year AIM-HIGH trial found no difference in the primary composite cardiovascular outcome end point between the niacin group (16.4%) and placebo group (16.2%). There are limited head-to-head studies comparing the efficacy and safety of the different niacin formulations. Due to significant safety concerns, the American Heart Association stresses that dietary supplement niacin must not be used as a substitute for prescription niacin, and should not be used for cholesterol lowering due to the potential for serious side effects.

Therefore, prescription niacin products offer significant clinical advantages in general use over the other brand, generic, and OTC niacin products in the same class (if applicable), but are comparable to each other. Extended-release niacin is available in a generic formulation. Due to their limited FDA-approved indications, prescription omega-3 acid ethyl esters and icosapent ethyl should be available through the medical justification portion of the prior authorization process for adults with severe hypertriglyceridemia ( $\geq 500$  mg/dL). Also due to their limited FDA-approved indications, lomitapide and mipomersen should be available through the medical justification portion of the prior authorization process for adjunctive use to diet and other lipid-lowering treatments in patients with HoFH.

No brand miscellaneous antilipemic 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. Chairperson Harwood asked the P&T Committee members to mark their ballots.

**Nitrates and Nitrites: AHFS 241208**

Manufacturer comments on behalf of these products:

None

Dr. Bastien 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 review in February 2013.

All brand products within the class 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 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. Chairperson Harwood 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 August 19, 2015 at the Medicaid Building in the Commissioner's Board Room.

**8. ADJOURN**

There being no further business, Dr. Carter moved to adjourn and Dr. Smith seconded. The meeting adjourned at 10:00 a.m.

Appendix

RESULTS OF THE BALLOTING  
Alabama Medicaid Agency  
Pharmacy and Therapeutics Committee  
May 20, 2015

A. **Recommendation:** No brand oral anticoagulant 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

M. Spivey, MD  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

Kathy Spill  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

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

B. **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

M. Spivey, MD  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

Kathy Spill  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

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

C. **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

*M. P. Rowe, MD*  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

*Kathy Steel*  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

*Stephen D.*  Approve  Approve as amended  Disapprove  No action  
Commissioner

D. **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

*M. P. Rowe, MD*  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

*Kathy Steel*  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

*Stephen D.*  Approve  Approve as amended  Disapprove  No action  
Commissioner

E. **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

*M. P. Rowe, MD*  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

Kathy Hull  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

Stephanie A  Approve  Approve as amended  Disapprove  No action  
Commissioner

**F. 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

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

Kathy Hull  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

Stephanie A  Approve  Approve as amended  Disapprove  No action  
Commissioner

**G. 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

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

Kathy Hull  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

Stephanie A  Approve  Approve as amended  Disapprove  No action  
Commissioner

**H. 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

*M. Malone, MD*  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

*Talley Shell*  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

*Stephanie Fox*  Approve  Approve as amended  Disapprove  No action  
Commissioner

**I. 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

*M. Malone, MD*  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

*Talley Shell*  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

*Stephanie Fox*  Approve  Approve as amended  Disapprove  No action  
Commissioner

**J. 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

*M. Brown, MD*  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

*Kathy Hill*  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

*Stephen H*  Approve  Approve as amended  Disapprove  No action  
Commissioner

K. 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

*M. Brown, MD*  Approve  Approve as amended  Disapprove  No action  
Assistant Medical Director

*Kathy Hill*  Approve  Approve as amended  Disapprove  No action  
Deputy Commissioner

*Stephen H*  Approve  Approve as amended  Disapprove  No action  
Commissioner

Respectfully submitted,

*Rachel Bastien*

Rachel Bastien, Pharm.D.

May 27, 2015

Date

*Amy Levy*

Amy Levy, R.Ph., MHP

May 27, 2015

Date

Date