

Minutes of Meeting

Alabama Medicaid Agency Pharmacy and Therapeutics Committee

May 15, 2013

Members Present: Chair-Dr. Gerard Ferris, Dr. Julia Boothe, Dr. Frances Cohenour, Dr. Kelli Littlejohn, Ms. LaTouge Porter, Dr. Melinda Rowe, and Dr. Chivers Woodruff

Members Absent: Vice chair-Ms. Janet Allen, and Dr. Donald Marks

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

Presenters: Dr. James Gagnon and Dr. Mark Kohn

Presenters Present via teleconference: None

1. OPENING REMARKS

Chair-Dr. Ferris called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 9:06 a.m.

2. APPROVAL OF MINUTES

Chair-Dr. Ferris asked if there were any corrections to the minutes from the February 13, 2013 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. She noted that the last legislative day is approaching and the general fund bill is awaiting the Governor's signature. Dr. Littlejohn noted that Alabama Medicaid will work with stakeholders to determine the next stages as it relates to the pharmacy program and any program modifications will be noticed to the public.

4. ORAL PRESENTATIONS BY MANUFACTURERS/MANUFACTURERS' REPRESENTATIVES

There were no verbal presentations made on behalf of pharmaceutical manufacturers 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 18 drug class re-reviews. The central alpha-agonists; direct vasodilators; peripheral adrenergic inhibitors; hypotensive agents, miscellaneous; alpha-adrenergic blocking agents; beta-adrenergic blocking agents; dihydropyridines; calcium-channel blocking agents, miscellaneous; angiotensin-converting enzyme inhibitors; angiotensin II receptor antagonists; mineralocorticoid (aldosterone) receptor antagonists; renin inhibitors; loop diuretics; potassium-sparing diuretics; thiazide diuretics; thiazide-like diuretics; vasopressin antagonists; and diuretics, miscellaneous were last reviewed in November 2010.

Central alpha-agonists, AHFS 240816

Manufacturer comments on behalf of these products:

None

Dr. Gagnon stated that the central alpha-agonists that are included in the review are listed in Table 1. They are approved for the treatment of hypertension and all of the agents are available in a generic formulation. There have been no major changes in the prescribing information, treatment guidelines or clinical studies since this class was last reviewed.

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

No brand central alpha-agonist 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 Ferris asked the P&T Committee members to mark their ballots.

Direct vasodilators: AHFS 240820

Manufacturer comments on behalf of these products:

None

Dr. Gagnon stated that the direct vasodilators are approved for the treatment of heart failure and hypertension, as well as for the treatment of hypoglycemia due to hyperinsulinism. He noted that the direct vasodilators that are included in the review are listed in Table 1 and hydralazine and minoxidil are available in a generic formulation. Dr. Gagnon highlighted current treatment guidelines that incorporate the use of the direct vasodilators. He noted that hydralazine and isosorbide dinitrate have been used off label for many years to treat heart failure. Guidelines currently recommend the use of hydralazine and an oral nitrate in patients who do not tolerate an angiotensin converting enzyme inhibitor or an angiotensin receptor blocker. Concerning hydralazine and minoxidil, no specific recommendation is made in the identified hypertension guidelines regarding their use. Although no treatment guidelines were identified for diazoxide it is considered a first line treatment option for the treatment of hypoglycemia due to hyperinsulinism.

Therefore, all brand direct vasodilators within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use. The fixed-dose combination of isosorbide dinitrate and hydralazine (BiDil[®]) should be available through the medical justification portion of the prior authorization process as an adjunct to standard heart failure therapy in self-identified black patients. Due to its limited FDA-approved indications, diazoxide (Proglycem[®]) should be managed through the existing medical justification portion of the prior authorization process.

No brand direct vasodilator 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 Ferris asked the P&T Committee members to mark their ballots.

Peripheral adrenergic inhibitors: AHFS 240832

Manufacturer comments on behalf of these products:

None

Dr. Gagnon stated that the peripheral adrenergic inhibitors that are included in the review are listed in Table 1. Reserpine is the only agent in the class and it is available in a generic formulation. There have been no major changes in the prescribing information, treatment guidelines or clinical studies since this class was last reviewed.

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

No brand peripheral adrenergic 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 Ferris asked the P&T Committee members to mark their ballots.

Hypotensive agents, miscellaneous: AHFS 240892

Manufacturer comments on behalf of these products:

None

There are currently no covered outpatient drugs available in the miscellaneous hypotensive agents class.

No brand miscellaneous hypotensive agent is recommended for preferred status. Alabama Medicaid should continue to include AHFS Class 240892 in the PDL screening process. If new outpatient miscellaneous hypotensive agents are added, it is recommended that this class be re-reviewed at that time.

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

Alpha-adrenergic blocking agents: AHFS 2420000

Manufacturer comments on behalf of these products:

None

Dr. Gagnon stated that the alpha-adrenergic blocking agents are approved for the treatment of benign prostatic hyperplasia and hypertension. He noted that all agents in the class are available in a generic dosage form and Cardura XL[®] is only available as a branded agent. Although hypertension and benign prostatic obstruction guidelines have been updated since the last review, there have been no major changes regarding the utilization of the alpha-adrenergic blocking agents. Additionally, there have been no significant changes in the prescribing information of these agents since the last review. Overall there have been no changes in the clinical trial outcomes reported since the last review of these agents. Clinical trials demonstrating no clinical difference between doxazosin and doxazosin SR in the treatment of benign prostate hyperplasia and hypertension were presented.

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

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

No brand alpha-adrenergic blocking 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 Ferris asked the P&T Committee members to mark their ballots.

Beta-adrenergic blocking agents: AHFS 2424000

Manufacturer comments on behalf of these products:

None

Dr. Gagnon stated that the beta-adrenergic blocking agents that are included in the review are listed in Table 1. All of the agents are available in a generic formulation, with the exception of nebivolol and penbutolol. Since the last review Dutoprol[®] an extended release combination product formulation of metoprolol and hydrochlorothiazide was approved. Due to improvements in morbidity and mortality, guidelines recommend the use of a beta-adrenergic blocking agent in patients with acute coronary syndromes, angina, arrhythmias, coronary artery disease, heart failure, hypertension, left ventricular dysfunction, and post myocardial infarction. They are also recommended as one of the several initial options for the prevention of migraine headaches, as well as for the treatment of essential tremors. In general comparative studies have demonstrated similar efficacy among the beta-adrenergic blocking agent.

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

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

No brand beta-adrenergic blocking 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.

Dr. Ferris stated that for patients with hypertension and heart failure carvedilol, bisoprolol or extended release metoprolol are the recommended beta-adrenergic blocking agents and this is supported by clinical trials; also for hypertension any beta-adrenergic blocking agent could be used.

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

Dihydropyridines: AHFS 242808

Manufacturer comments on behalf of these products:

None

Dr. Gagnon noted that the dihydropyridines are approved for the treatment of angina and hypertension. Amlodipine is also indicated to reduce the risk of hospitalization due to angina and to reduce the risk of a coronary revascularization procedure in patients with recently documented coronary artery disease. The dihydropyridines are available in a variety of single entity formulations. Amlodipine is also available in combination with benazepril, olmesartan, valsartan, or valsartan/hydrochlorothiazide. As noted in Table 1 all of the single entity products are available in a generic formulation, as well as the amlodipine and benazepril fixed-dose combination. Dr. Gagnon noted that the amlodipine and telmisartan fixed dose combination product is classified by American Hospital Formulary Service (AHFS) as an angiotensin II receptor antagonist; therefore it is included in that class review. This also holds true for the amlodipine, olmesartan and hydrochlorothiazide fixed dose combination product which has been approved since the last time the classes were reviewed. Additionally, since the last time the classes were reviewed aliskiren and amlodipine and aliskiren, amlodipine and hydrochlorothiazide fixed dose combination products were approved. Since these products are classified by AHFS as renin inhibitors, they are included in that review. There have been no major changes in the prescribing information or treatment guidelines relative to the dihydropyridines since the last time the class was reviewed.

The dihydropyridines have been shown to favorably affect cardiovascular morbidity and mortality. Numerous clinical trials have shown that the dihydropyridines can effectively lower systolic and diastolic blood pressure when administered alone or in combination with other agents. In studies comparing combination therapy to monotherapy, the more aggressive treatment regimens lowered blood pressure to a greater extent than the less-intensive treatment regimens. Some comparative trials have demonstrated slight differences in blood pressure effects among the various dihydropyridines; however, the clinical significance of these differences remains to be established. Most patients will require more than one antihypertensive

agent to achieve blood pressure goals. The use of a fixed-dose combination product may simplify the treatment regimen and improve adherence. However, no prospective randomized trial that demonstrated better clinical outcomes with a fixed-dose combination product compared to the coadministration of the individual components as separate formulations was identified.

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

No brand dihydropyridine 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 Ferris asked the P&T Committee members to mark their ballots.

Calcium-channel blocking agents, miscellaneous: AHFS 242892

Manufacturer comments on behalf of these products:

None

Dr. Gagnon stated that the miscellaneous calcium-channel blocking agents include diltiazem and verapamil which are approved for the treatment of angina, arrhythmias and hypertension. Both diltiazem and verapamil are available in a variety of modified-release delivery systems that alter their pharmacokinetic properties, including onset and duration of action. Diltiazem and verapamil are available in a generic formulation and since the last review Matzim LA[®] has been approved. It should be noted that the trandolapril and verapamil fixed dose combination product is classified by AHFS as an angiotensin converting enzyme inhibitor; therefore it is included in that class review. There have been no major changes in the prescribing information, treatment guidelines or clinical trials since the last time the class was reviewed.

Therefore, all brand miscellaneous calcium-channel blocking agents within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand miscellaneous calcium-channel blocking 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 Ferris asked the P&T Committee members to mark their ballots.

Angiotensin-converting enzyme inhibitors: AHFS 243204

Manufacturer comments on behalf of these products:

None

Dr. Kohn noted that the angiotensin converting enzyme inhibitors included within this review are listed in Table 1. This class was last reviewed in November 2010 and there have been no major or clinically significant changes to the medication class since the last time it was reviewed. All of the angiotensin converting enzyme inhibitors are approved for the treatment of hypertension. Some of the products are also approved for the treatment of diabetic nephropathy, heart failure and post-myocardial infarction. The angiotensin converting enzyme inhibitors are available as single entity products, as well as in combination with hydrochlorothiazide or verapamil. All of the products are available in a generic formulation.

Several national and international guidelines recommend the use of angiotensin converting enzyme inhibitors in patients with acute coronary syndrome, cerebrovascular disease, coronary artery disease, diabetes, diabetic nephropathy, heart failure, hypertension, left ventricular dysfunction, left ventricular hypertrophy, previous myocardial infarction and renal disease. In general, guidelines do not give preference to one angiotensin converting enzyme inhibitor over another.

In clinical trials, the angiotensin converting enzyme inhibitors have been shown to reduce cardiovascular morbidity and mortality, preserve renal function in patients with nephropathy, and effectively lower blood pressure when administered as monotherapy or in combination with other antihypertensive agents. There are no prospective randomized trials that have demonstrated better clinical outcomes with a fixed-dose combination product compared to the coadministration of the individual components as separate formulations; however, fixed-dose combination products may simplify the treatment regimen and improve adherence.

At this time, there is insufficient evidence to support that one angiotensin converting enzyme 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.

Therefore, all brand angiotensin-converting enzyme inhibitors within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand angiotensin-converting enzyme 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 Ferris asked the P&T Committee members to mark their ballots.

Angiotensin II receptor antagonists: AHFS 243208

Manufacturer comments on behalf of these products:

None

Dr. Kohn stated that the angiotensin II receptor antagonists included within this review are listed in Table 1. This class was last reviewed in November 2010 and since that time azilsartan has been approved and is available in combination with chlorthalidone, telmisartan is available in combination with amlodipine, and olmesartan is available in combination with amlodipine and hydrochlorothiazide (triple therapy). Generic formulations have become available for single entity eprosartan, irbesartan and fixed-dose combination products candesartan and hydrochlorothiazide, irbesartan and hydrochlorothiazide, and valsartan and hydrochlorothiazide. Single entity losartan and in combination with hydrochlorothiazide are also available generically. All of the angiotensin II receptor antagonists are approved for the treatment of hypertension. Some of the products are also approved for the treatment of diabetic nephropathy (irbesartan and losartan), heart failure (candesartan and valsartan), post-myocardial infarction (valsartan), as well as cardiovascular and cerebrovascular risk reduction (telmisartan and losartan, respectively). The angiotensin II receptor antagonists are available as single entity products, as well as in combination with hydrochlorothiazide.

National and international guidelines recommend the use of angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists in patients with cerebrovascular disease, coronary artery disease, heart failure, hypertension, left ventricular dysfunction, left ventricular hypertrophy, diabetes, diabetic nephropathy, previous myocardial infarction and renal disease. In general, guidelines do not give preference to one angiotensin II receptor antagonist over another. Some guidelines recommend the use of angiotensin converting enzyme inhibitors as initial therapy, with the subsequent use of angiotensin II receptor antagonists in patients who do not tolerate angiotensin converting enzyme inhibitors.

Some comparative trials have demonstrated slight differences in blood pressure effects among the various angiotensin II receptor antagonists; however, the clinical significance of these differences remains to be established. Guidelines do not give preference to one angiotensin II receptor antagonist over another for the treatment of hypertension. Most patients will require more than one antihypertensive agent to achieve blood pressure goals. No published prospective randomized trials were identified that have demonstrated better clinical outcomes with a fixed-dose combination product compared to the coadministration of the individual components as separate formulations.

Angiotensin II receptor antagonists have been shown to reduce cardiovascular morbidity and mortality, as well as preserve renal function. The use of losartan also decreases the risk of stroke in patients with hypertension and left ventricular hypertrophy. It should be noted that the angiotensin converting enzyme inhibitors have also been shown to positively impact these endpoints. Several studies comparing angiotensin II receptor antagonists and angiotensin converting enzyme inhibitors have demonstrated similar efficacy with regards to cardiovascular events, heart failure and the rate of progression of nephropathy.

In April 2011, the Food and Drug Administration (FDA) determined that the benefits of olmesartan outweigh its potential risks when used for the treatment of patients with high blood pressure according to the approved drug label. Olmesartan is not recommended as a treatment to delay or prevent protein in the urine in diabetic patients. In June of 2011, the FDA also concluded that a review of a meta-analysis of 31 randomized-controlled trials comparing angiotensin II receptor antagonists to other treatments found no

evidence of an increased risk of incident (new) cancer, cancer-related death, breast cancer, lung cancer, or prostate cancer in patients receiving angiotensin II receptor antagonists.

At this time, there is insufficient evidence to conclude that the angiotensin II receptor antagonists offer a significant clinical advantage over other alternatives in general use. Therefore, all brand angiotensin II receptor antagonists within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand angiotensin II receptor antagonist 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 Ferris asked the P&T Committee members to mark their ballots.

Mineralocorticoid (aldosterone) receptor antagonists: AHFS 243220

Manufacturer comments on behalf of these products:

None

Dr. Kohn stated that the mineralocorticoid (aldosterone) receptor antagonists included within this review are listed in Table 1. This class was last reviewed in November 2010 and there have been no major or clinically significant changes to the medication class since the last time it was reviewed. The mineralocorticoid (aldosterone) receptor antagonists are approved for the treatment of hypertension. Eplerenone is also indicated to improve survival in patients with left ventricular systolic dysfunction and clinical evidence of congestive heart failure after an acute myocardial infarction. Spironolactone is approved for the management of hyperaldosteronism, hypokalemia, and edema associated with congestive heart failure, cirrhosis or the nephrotic syndrome. It is also indicated for patients with severe heart failure to increase survival and to reduce the need for hospitalization for heart failure when used in addition to standard therapy. Spironolactone is available as a single entity agent, as well as in combination with hydrochlorothiazide as a fixed-dose combination product. All of the mineralocorticoid (aldosterone) receptor antagonist products are available in a generic formulation.

Several national and international guidelines provide recommendations regarding the use of the mineralocorticoid (aldosterone) receptor antagonists. For the treatment of heart failure, a mineralocorticoid (aldosterone) receptor antagonist is recommended in addition to standard therapy in patients with symptoms and a left ventricular ejection fraction (LVEF) $\leq 35\%$. A mineralocorticoid (aldosterone) receptor antagonist is also recommended following a myocardial infarction in patients with an LVEF $\leq 40\%$ who also have either diabetes or heart failure. Most guidelines for the treatment of hypertension do not address the use of the mineralocorticoid (aldosterone) receptor antagonists. For the treatment of cirrhosis and ascites, spironolactone is recommended as first line therapy in addition to sodium restriction. Spironolactone is also recommended for the treatment of patients with unilateral primary aldosteronism (in lieu of surgery) and in those with bilateral adrenal disease. Eplerenone is considered an alternative treatment option, especially in men who experience erectile dysfunction and gynecomastia with spironolactone therapy.

Eplerenone and spironolactone have been shown to reduce cardiovascular morbidity and mortality in patients with heart failure when added to standard therapy. Adverse events are similar with the mineralocorticoid (aldosterone) receptor antagonists and both agents can increase serum potassium levels. Eplerenone is a selective aldosterone receptor antagonist, while spironolactone may also antagonize glucocorticoid, progesterone and androgen receptors, increasing the risk of steroid-related adverse effects.

There is insufficient evidence to support that one brand mineralocorticoid (aldosterone) receptor antagonist 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 mineralocorticoid (aldosterone) receptor antagonists within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand mineralocorticoid (aldosterone) receptor antagonist 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 Ferris asked the P&T Committee members to mark their ballots.

Renin inhibitors: AHFS 243240

Manufacturer comments on behalf of these products:

None

Dr. Kohn stated that the renin inhibitors included within this review are listed in Table 1. Aliskiren is the only renin inhibitor in this class and it is approved for the treatment of hypertension. It is available as a single entity product, as well as in combination with amlodipine, amlodipine and hydrochlorothiazide, hydrochlorothiazide, or valsartan. This class was last reviewed in November 2010 and since then, the fixed combination products aliskiren and amlodipine and aliskiren, amlodipine and hydrochlorothiazide were approved. There are no generic renin inhibitor products currently available; however, amlodipine and hydrochlorothiazide are available generically.

The majority of the guidelines published for the management of hypertension do not address the use of the renin inhibitors, with the exception of the European Society of Hypertension and European Society of Cardiology which state that evidence is available to justify the use of aliskiren for the management of hypertension, particularly in combination with other antihypertensive agents. According to the National Heart, Lung, and Blood Institute's Seventh Report of The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), thiazide-type diuretics should be utilized first-line for most patients with hypertension, either alone or in combination with another antihypertensive from a different medication class. Several guidelines consistently recommend that the selection of an antihypertensive agent be based on compelling indications for use.

Several clinical trials have demonstrated that renin inhibitors effectively lower blood pressure. The reduction in blood pressure with aliskiren monotherapy was similar to monotherapy with angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, beta-adrenergic blocking agent and

dihydropyridines. In clinical trials comparing combination therapy to monotherapy, the more aggressive treatment regimen lowered blood pressure to a greater extent than the less-intensive treatment regimen. No prospective randomized trials were indentified that have demonstrated better clinical outcomes with a fixed-dose combination product compared to the coadministration of the individual components as separate formulations. Aliskiren has been shown to have positive effects on surrogate markers of cardiovascular and renal damage in patients with type 2 diabetes and nephropathy, heart failure and left ventricular hypertrophy; however, the effects of aliskiren on hard cardiovascular and renal endpoints have not been established.

At this time, there is insufficient evidence to conclude that the renin inhibitors offer a significant clinical advantage over other alternatives in general use. Therefore, all brand renin inhibitors within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand renin 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 Ferris asked the P&T Committee members to mark their ballots.

Loop diuretics: AHFS 402808

Manufacturer comments on behalf of these products:

None

Dr. Kohn stated that the loop diuretics included within this review are listed in Table 1. This class was last reviewed in November 2010 and there have been no major or clinically significant changes to the medication class since the last time it was reviewed. Although guidelines for the treatment of heart failure have been updated since the previous review, the role of the loop diuretics within the guidelines has not changed. All of the loop diuretics are approved for the treatment of edema associated with congestive heart failure, hepatic disease or renal disease. Furosemide and torsemide are also approved for the treatment of hypertension. Bumetanide, furosemide, and torsemide are available in a generic formulation.

Guidelines recommend the use of diuretics and sodium restriction for the management of ascites due to cirrhosis. Spironolactone is recommended as first-line therapy, either as monotherapy or in combination with furosemide. Several studies have compared furosemide and torsemide in cirrhotic patients with ascites. Although torsemide significantly increased natriuresis and diuresis compared to furosemide, these effects were not consistently demonstrated across the studies and there was no difference in plasma renin or aldosterone concentrations between treatment groups. Diuretics are recommended in all chronic heart failure patients with evidence of volume overload. Loop diuretics are recommended as initial therapy in patients with left ventricular dysfunction. For those with persistent fluid retention despite treatment with a loop diuretic, a thiazide diuretic or metolazone may be added. In patients with normal left ventricular function, either a thiazide diuretic or loop diuretic may be used as initial therapy to manage fluid overload. Few studies have directly compared the loop diuretics for the treatment of chronic heart failure. Torsemide decreased mortality, hospitalizations and improved New York Heart Association functional class compared

to treatment with furosemide; however, due to the open-label study designs, it is difficult to draw firm conclusions about the results.

According to the JNC 7, thiazide-type diuretics should be utilized first-line for most patients with hypertension, either alone or in combination with another hypertensive from a different medication class. Several guidelines consistently recommend that the selection of an antihypertensive agent be based on compelling indications for use.

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

No brand loop diuretic 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 Ferris asked the P&T Committee members to mark their ballots.

Potassium-sparing diuretics: AHFS 402816

Manufacturer comments on behalf of these products:

None

Dr. Kohn stated that the potassium-sparing diuretics included within this review are listed in Table 1. This class was last reviewed in November 2010 and there have been no major or clinically significant changes to the medication class since the last time it was reviewed. Although guidelines for the treatment of heart failure have been updated since the previous review, the role of the potassium-sparing diuretics within the guidelines has not changed. The potassium-sparing diuretics are approved for the treatment of congestive heart failure, edema and hypertension. The potassium-sparing diuretics are generally used in combination with other diuretics to help restore normal serum potassium levels or to prevent the development of hypokalemia. Amiloride and triamterene are available as a fixed-dose combination with hydrochlorothiazide.

For the treatment of chronic heart failure, guidelines recommend the use of diuretics in all patients who have evidence of volume overload. The loop diuretics are generally recommended as initial therapy in patients with left ventricular dysfunction. For those with persistent fluid retention despite treatment with a loop diuretic, a thiazide diuretic or metolazone may be added to the regimen. In patients with normal left ventricular function, either a thiazide diuretic or loop diuretic may be used as initial therapy to manage fluid overload. The potassium-sparing diuretics are typically used as adjunctive therapy in patients receiving thiazide diuretics to prevent hypokalemia or to restore normal serum potassium levels.

According to the JNC 7, thiazide-type diuretics should be utilized first-line for most patients with hypertension, either alone or in combination with another antihypertensive from a different medication. Several guidelines consistently recommend that the selection of an antihypertensive agent be based on compelling indications for use. Amiloride has been shown to be effective for the treatment of edema, hypertension, as well as for the prevention of serum potassium loss in patients taking a thiazide or loop diuretic. Clinical trials have also demonstrated comparable efficacy with the fixed-dose combination of amiloride and hydrochlorothiazide and triamterene and hydrochlorothiazide in patients with hypertension and heart failure.

There is insufficient evidence to support that one brand potassium-sparing diuretic 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 potassium-sparing diuretics within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand potassium-sparing diuretic 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 Ferris asked the P&T Committee members to mark their ballots.

Thiazide diuretics: AHFS 402820

Manufacturer comments on behalf of these products:

None

Dr. Kohn stated that the thiazide diuretics included within this review are listed in Table 1. This class was last reviewed in November 2010 and there have been no major or clinically significant changes to the medication class since the last time it was reviewed. Although guidelines for the treatment of heart failure have been updated since the previous review, the role of the thiazide diuretics within the guidelines has not changed. The thiazide diuretics are approved for the treatment of hypertension and edema due to renal dysfunction. They are also approved as adjunctive therapy for the management of edema associated with congestive heart failure, hepatic cirrhosis, as well as corticosteroid and estrogen therapy. All of the agents are available in a generic formulation.

Guidelines recommend the use of diuretics and sodium restriction for the management of ascites due to cirrhosis. Spironolactone is recommended as first-line therapy, either as monotherapy or in combination with furosemide. Triamterene, metolazone and hydrochlorothiazide have also been used to treat ascites. For the treatment of chronic heart failure, guidelines recommend the use of diuretics in all patients who have evidence of volume overload. Loop diuretics are generally recommended as initial therapy in patients with left ventricular dysfunction. For those with persistent fluid retention despite treatment with a loop diuretic, a thiazide diuretic or metolazone may be added to the regimen. In patients with normal left ventricular function, either a thiazide diuretic or loop diuretic may be used as initial therapy to manage fluid overload.

According to the JNC 7, thiazide-type diuretics should be utilized first-line for most patients with hypertension, either alone or in combination with another hypertensive from a different medication class. Several guidelines consistently recommend that the selection of an antihypertensive agent be based on compelling indications for use.

In clinical trials, the thiazide diuretics have been shown to effectively lower blood pressure. There were no studies found in the medical literature that directly compared the efficacy and safety of the thiazide diuretics for the treatment of hypertension.

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

No brand thiazide diuretic 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 Ferris asked the P&T Committee members to mark their ballots.

Thiazide-like diuretics: AHFS 402824

Manufacturer comments on behalf of these products:

None

Dr. Kohn stated that the thiazide-like diuretics included within this review are listed in Table 1. This class was last reviewed in November 2010 and there have been no major or clinically significant changes to the medication class since the last time it was reviewed. Although guidelines for the treatment of heart failure have been updated since the previous review, the role of the thiazide-like diuretics within the guidelines has not changed. The thiazide-like diuretics are approved for the treatment of hypertension and edema associated with congestive heart failure. All of the agents are available in a generic formulation.

Guidelines recommend the use of diuretics and sodium restriction for the management of ascites due to cirrhosis. Spironolactone is recommended as first-line therapy, either as monotherapy or in combination with furosemide. Triamterene, metolazone, and hydrochlorothiazide have also been used to treat ascites. For the treatment of chronic heart failure, guidelines recommend the use of diuretics in all patients who have evidence of volume overload. Loop diuretics are generally recommended as initial therapy in patients with left ventricular dysfunction. For those with persistent fluid retention despite treatment with a loop diuretic, a thiazide diuretic or metolazone may be added. In patients with normal left ventricular function, either a thiazide diuretic or loop diuretic may be used as initial therapy to manage fluid overload.

According to the JNC 7, thiazide-type diuretics should be utilized first-line for most patients with hypertension, either alone or in combination with another hypertensive from a different medication. Several

guidelines consistently recommend that the selection of an antihypertensive agent be based on compelling indications for use.

In clinical trials, the thiazide-like diuretics have been shown to effectively lower blood pressure. There were no studies found in the medical literature that directly compared the efficacy and safety of the thiazide-like diuretics for the treatment of hypertension.

There is insufficient evidence to support that one brand thiazide-like diuretic 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 thiazide-like diuretics within the class reviewed are comparable to each other and to the generics and over-the-counter products in the class (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand thiazide-like diuretic 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 Ferris asked the P&T Committee members to mark their ballots.

Vasopressin antagonists: AHFS 402828

Manufacturer comments on behalf of these products:

None

Dr. Kohn noted that the vasopressin antagonists included within this review are listed in Table 1. Tolvaptan, the only oral vasopressin antagonist, is FDA-approved for the treatment of clinically significant euvolemic and hypervolemic hyponatremia, including patients with heart failure, cirrhosis, and Syndrome of Inappropriate Antidiuretic Hormone Secretion. This class was last reviewed in November 2010 and there have been no major or clinically significant changes to the medication class since the last time it was reviewed. The management of hyponatremia depends on the clinical presentation and duration of the disease.

There are limited guidelines available that discuss the management of hyponatremia. An expert panel provided treatment recommendations in 2007, which includes fluid restriction, sodium chloride administration, and diuresis. The panel concluded that the optimal use of the vasopressin receptor antagonists has not been determined and further studies are needed.

Three short-term studies evaluated the safety and efficacy of tolvaptan in a relatively small number of patients with euvolemic or hypervolemic hyponatremia demonstrated significant improvements in serum sodium concentrations compared to fluid restriction or placebo. Evidence suggests that hyponatremia recurs after discontinuation of tolvaptan. Several other studies have evaluated the use of tolvaptan in patients with congestive heart failure as an add-on to conventional treatments. Significant changes in body weight have been observed; however, the long-term use of tolvaptan failed to improve mortality or hospitalizations for worsening heart failure. A meta-analysis also failed to demonstrate a benefit in mortality with vaptan

therapy compared to control in patients with cirrhosis and hyponatremia or ascites. Hospitalization is required for initiation and reinitiation of tolvaptan therapy so that serum sodium can be monitored closely.

There is insufficient evidence to conclude that tolvaptan offers a significant clinical advantage over other alternatives in general use. Since tolvaptan is not indicated as first-line therapy for the management of hyponatremia, it should be managed through the medical justification portion of the prior authorization process.

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

No brand vasopressin antagonist 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 Ferris asked the P&T Committee members to mark their ballots.

Diuretics, miscellaneous: AHFS 402892

Manufacturer comments on behalf of these products:

None

There are no drugs available in the miscellaneous diuretics class.

No brand miscellaneous diuretic is recommended for preferred status. Alabama Medicaid should continue to include AHFS Class 402892 in the PDL screening process. If new outpatient miscellaneous diuretics are added, it is recommended that this class be re-reviewed at that time.

There were no further discussions on the agents in this class. Chairperson Ferris 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 14, 2013 at the Medicaid Building in the Commissioner's Board Room.

8. ADJOURN

There being no further business, Dr. Boothe moved to adjourn and Dr. Woodruff seconded. The meeting adjourned at 9:55 a.m.

Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
May 15, 2013

A. **Recommendation:** No brand central alpha-agonist 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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie B Approve Approve as amended Disapprove No action
Acting Commissioner

B. **Recommendation:** No brand direct vasodilator 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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie B Approve Approve as amended Disapprove No action
Acting Commissioner

C. Recommendation: No brand peripheral adrenergic 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. R. Powe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie B. Cox Approve Approve as amended Disapprove No action
Acting Commissioner

D. Recommendation: No brand miscellaneous hypotensive agent is recommended for preferred status. Alabama Medicaid should continue to include AHFS Class 240892 in the PDL screening process. If new outpatient miscellaneous hypotensive agents are added, it is recommended that this class be re-reviewed at that time.

Amendment: None

Vote: Unanimous to approve as recommended

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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie B. Cox Approve Approve as amended Disapprove No action
Acting Commissioner

E. Recommendation: No brand alpha-adrenergic blocking 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

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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie Byrd Approve Approve as amended Disapprove No action
Acting Commissioner

F. Recommendation: No brand beta-adrenergic blocking 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

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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

Stephanie Byrd Approve Approve as amended Disapprove No action
Acting Commissioner

G. Recommendation: No brand dihydropyridine 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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

H. Recommendation: No brand miscellaneous calcium-channel blocking 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. Rowe, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

I. Recommendation: No brand angiotensin-converting enzyme 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. Skow, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

J. Recommendation: No brand angiotensin II receptor antagonist 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. Skow, MD Approve Approve as amended Disapprove No action
Assistant Medical Director

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

K. Recommendation: No brand mineralocorticoid (aldosterone) receptor antagonist 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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

L. Recommendation: No brand renin 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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

M. Recommendation: No brand loop diuretic 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. [Signature] Approve Approve as amended Disapprove No action
Assistant Medical Director

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

N. Recommendation: No brand potassium-sparing diuretic 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. [Signature] Approve Approve as amended Disapprove No action
Assistant Medical Director

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

O. Recommendation: No brand thiazide diuretic 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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

P. Recommendation: No brand thiazide-like diuretic 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

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

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

Q. Recommendation: No brand vasopressin antagonist 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

 Approve Approve as amended Disapprove No action
Assistant Medical Director

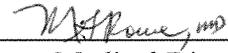
_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

 Approve Approve as amended Disapprove No action
Acting Commissioner

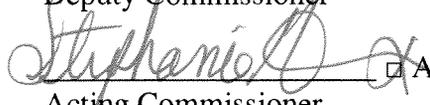
R. Recommendation: No brand miscellaneous diuretic is recommended for preferred status. Alabama Medicaid should continue to include AHFS Class 402892 in the PDL screening process. If new outpatient miscellaneous diuretics are added, it is recommended that this class be re-reviewed at that time.

Amendment: None

Vote: Unanimous to approve as recommended

 Approve Approve as amended Disapprove No action
Assistant Medical Director

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner

 Approve Approve as amended Disapprove No action
Acting Commissioner

Respectfully submitted,



May 23, 2013

James Gagnon, Pharm.D., BCPS

Date