

Minutes of Meeting

Alabama Medicaid Agency Pharmacy and Therapeutics Committee

May 4, 2022

Members Present: Dr. Frances Heinze (Chairperson), Dr. Lee Carter, Dr. Charles Nevels, Dr. Kelli Littlejohn Newman, Dr. Tiffany Lyght, and Dr. Christopher Stanley

Members Absent: Dr. Albert Holloway and Dr. Peter Hughes

Presenters: Dr. Thomas Pomfret and Dr. Wilson Haong

1. OPENING REMARKS

Chairperson Heinze called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 1:04 p.m. CST

2. APPROVAL OF MINUTES

Chairperson Heinze asked if there were any corrections to the minutes from the February 9, 2022 P&T Committee Meeting.

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

3. PHARMACY PROGRAM UPDATE

Recent ALERTs are included in the member's packets. A yellow card campaign is beginning as the unwinding process starts from the COVID-19 pandemic allowances. The yellow card campaign is geared towards recipients as eligibility is verified.

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 was a total of one (1) manufacturer verbal presentation at the meeting.

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

The pharmacotherapy class reviews began at approximately 1:09 p.m. CST. There were a total of 19 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; diuretics, miscellaneous were last reviewed in February 2020. The Alzheimer's Agents class review was last presented in November 2020.

Mineralocorticoid (aldosterone) receptor antagonists: AHFS 243220

Manufacturer comments on behalf of these products:

Kerendia[®] - (Bayer U.S., LLC)

Dr. Haong noted that the mineralocorticoid (aldosterone) receptor antagonist agents included in this review are listed in Table 1 on page 827. Agents in this class include eplerenone, spironolactone, and spironolactone/hydrochlorothiazide combination products, which are all available in a generic formulation. Kerendia[®] (finerenone) has been added since the last review.

Finerenone is a non-steroidal, selective mineralocorticoid receptor antagonist indicated to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end stage renal disease (ESRD), cardiovascular (CV) death, non-fatal myocardial infarction (MI), and hospitalization for heart failure (HF) in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D). Finerenone is available as oral tablets and is administered once daily. When compared in a placebo-controlled trial among adult patients with CKD associated with T2D who were previously treated with an angiotensin-converting enzyme (ACE) inhibitor and/or angiotensin receptor blocker (ARB), treatment with finerenone reduced the incidence of the primary composite endpoint consisting of a sustained decline in eGFR of $\geq 40\%$, kidney disease, or renal death; and the secondary composite endpoint of CV death, non-fatal MI, non-fatal stroke, or hospitalization from HF. The most common adverse events reported in clinical trials include hyperkalemia, hypotension, and hyponatremia.

The 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America guideline recommends use of a sodium-glucose cotransporter-2 (SGLT2) inhibitor among patients with Stage C heart failure with mildly or preserved EF in decreasing HF hospitalizations and CV mortality. For patients with Stage C with mildly reduced EF and current or previous symptomatic HF as well as Stage C with preserved ejection fraction, the use of mineralocorticoid receptor antagonists may be considered to reduce the risk of HF hospitalizations and CV mortality. The 2022 American Diabetes Association guideline recommends finerenone to reduce CKD progression and CV events among at-risk patients with CKD who are unable to use an SGLT2 inhibitor.

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 generic products in the class 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 Heinze asked the P&T Committee members to mark their ballots.

Central alpha-agonists, AHFS 240816

Manufacturer comments on behalf of these products:

None

Dr. Haong noted that the central alpha-agonist agents included in this review are listed in Table 1 on page 7. Agents in this class include clonidine, guanfacine, methyldopa, and methyldopate, which are all available in a generic formulation. No agents have been added since the last review. There have been no major changes in the prescribing information, clinical studies, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

There is insufficient evidence to support that one brand central alpha-agonist 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 central alpha-agonists 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 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 Heinze asked the P&T Committee members to mark their ballots.

Direct vasodilators: AHFS 240820

Manufacturer comments on behalf of these products:

None

Dr. Haong noted that the direct vasodilator agents included in this review are listed in Table 1 on page 43. Agents in this class include hydralazine, minoxidil, nitroprusside, and isosorbide dinitrate/hydralazine combination products. Hydralazine and minoxidil are available in a generic formulation. No agents have been added since the last review.

The 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America guideline recommends a combination of hydralazine and isosorbide dinitrate to improve symptoms and reduce morbidity and mortality for patients self-identified as African Americans with New York Heart Association (NYHA) Class III to IV Stage C heart failure (HF) with reduced ejection fraction who were receiving optimal therapy. For patients with current or previous symptomatic Stage C HF with reduced

ejection fraction who cannot be given first-line agents due to drug intolerance or renal insufficiency, a combination of hydralazine and isosorbide dinitrate might be considered to reduce morbidity and mortality.

All brand direct vasodilators 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 isosorbide dinitrate and hydralazine (BiDil®) should continue to be made available through the medical justification portion of the prior authorization process as an adjunct to standard heart failure therapy in self-identified black patients.

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

Peripheral adrenergic inhibitors: AHFS 240832

Manufacturer comments on behalf of these products:

None

Dr. Haong noted that the review of peripheral adrenergic inhibitors is on page 90. Currently, there are no drugs classified by AHFS as peripheral adrenergic inhibitors.

No brand peripheral adrenergic inhibitor is recommended for preferred status. Alabama Medicaid should continue to include this AHFS Class in the PDL screening process. If new outpatient peripheral adrenergic inhibitors 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 Heinze asked the P&T Committee members to mark their ballots.

Hypotensive agents, miscellaneous: AHFS 240892

Manufacturer comments on behalf of these products:

None

Dr. Haong noted that the miscellaneous hypotensive agents included in this review are listed in Table 1 on page 91. Mecamylamine is the only agent in this class. No drugs have been added since the last review.

Although the clinical literature reports that mecamylamine is effective for the management of moderate-to-severe hypertension, its clinical utility is minimal due to its adverse events profile and the availability of newer and more effective agents. Current hypertension treatment guidelines do not mention mecamylamine as a first-line or alternative agent for the treatment of hypertension. Therefore, all brand miscellaneous hypotensive 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 miscellaneous hypotensive agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine cost effective products and possibly designate one or more preferred brands.

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

Alpha-adrenergic blocking agents: AHFS 242000

Manufacturer comments on behalf of these products:

None

Dr. Haong noted that the alpha-adrenergic blocking agents included in this review are listed in Table 1 on page 96. Agents in this class include doxazosin, prazosin, and terazosin, which are all available in a standard-release generic formulation. Cardura XL[®] is only available as a branded agent. No drugs have been added since the last review. There have been no major changes in the prescribing information, clinical studies, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

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

Beta-adrenergic blocking agents: AHFS 242400

Manufacturer comments on behalf of these products:

None

Dr. Haong noted that the beta-adrenergic blocking agents included in this review are listed in Table 1 on page 165. All currently available oral products in this class are available generically, as generic nebivolol (Bystolic[®]) has been launched since this class was last reviewed.

The 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America guideline recommends use of a sodium-glucose cotransporter-2 (SGLT2) inhibitor in patients with Stage C heart failure (HF) with modified or preserved ejection fraction in decreasing HF hospitalizations and cardiovascular mortality. Evidence-based beta-adrenergic blocking agents should be used to prevent symptomatic HF in patients with Stage B HF with reduced ejection fraction and to reduce mortality in such

patients with a recent or remote history of myocardial infarction or acute coronary syndrome. Bisoprolol, carvedilol, or sustained-release metoprolol succinate are recommended to reduce mortality and hospitalizations in patients with Stage C HF with reduced ejection fraction and current or previous symptoms. For patients with Stage C HF with mildly reduced ejection fraction and current or previous symptoms, the use of evidence-based beta-blockers may be considered to reduce the risk of HF hospitalizations and cardiovascular mortality.

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 generic 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.

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

Dihydropyridines: AHFS 242808

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that the dihydropyridines included in this review are listed in Table 1 on page 336. All agents are available generically in at least one dosage form or strength. There have been no major changes in the prescribing information, clinical studies, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

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 generic 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 Heinze 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. Pomfret noted that the miscellaneous calcium-channel blocking agents included in this review are listed in Table 1 on page 468. These agents include immediate- and extended-release formulations of diltiazem and verapamil, which are approved for the treatment of angina, arrhythmias, and hypertension. There have been no major changes in the prescribing information, clinical trials, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

Therefore, all brand miscellaneous calcium-channel blocking 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 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 Heinze 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. Pomfret noted that the ACE (angiotensin-converting enzyme) inhibitors included in this review are listed in Table 1 on page 542 and are indicated for a wide range of indications, including cardiovascular risk reduction, diabetic nephropathy, heart failure, hypertension, left ventricular dysfunction, and myocardial infarction. All of the products are available in a generic formulation, including the combination products with hydrochlorothiazide. There have been no major changes in the prescribing information, clinical studies, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

There is insufficient evidence to support that one brand 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 generic 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 Heinze 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. Pomfret noted that the angiotensin II receptor antagonists (ARBs) included in this review are listed in Table 1 on page 677. All single entity products with the exception of azilsartan are available generically. Fixed-dose combination products are available in a generic formulation with the exception of azilsartan-chlorthalidone (Edarbyclor[®]). Valsartan is now approved for the treatment of hypertension in children over one year of age, an expansion upon the previous approval of six to 16 years of age. There have been no major changes in the other prescribing information, clinical studies, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

There is insufficient evidence to conclude that one brand angiotensin II 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 angiotensin II receptor antagonists 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 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 Heinze asked the P&T Committee members to mark their ballots.

Renin inhibitors: AHFS 243240

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that the renin inhibitors that are included in this review are listed in Table 1 on page 922. Aliskiren, which is indicated for the treatment of hypertension, is available in a generic formulation; whereas the combination agent, aliskiren with hydrochlorothiazide, is available only as a branded product. There have been no major changes in the prescribing information, clinical trials, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

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

Loop diuretics: AHFS 402808

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that the loop diuretics included in this review are listed in Table 1 on page 983. All agents are available in a generic formulation. There have been no major changes in the prescribing information, clinical trials, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

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

Potassium-sparing diuretics: AHFS 402816

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that the potassium-sparing diuretics included in this review are listed in Table 1 on page 1036. All of the products are available in a generic formulation. Generic triamterene is commercially available again and has been included in the class review. There have been no other major changes in the prescribing information, clinical trials, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

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

Thiazide diuretics: AHFS 402820

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that the thiazide diuretics included in this review are listed in Table 1 on page 1083, and include chlorothiazide and hydrochlorothiazide products, which are all available in a generic formulation. There have been no major changes in the prescribing information, clinical trials, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

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

Thiazide-like diuretics: AHFS 402824

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that the thiazide-like diuretics included in this review are listed in Table 1 on page 1158. All of the agents are available in a generic formulation. There have been no major changes in the prescribing information, clinical trials, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

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

Vasopressin antagonists: AHFS 402828

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that the vasopressin antagonists that are included in this review are listed in Table 1 on page 1208. Since the last review of this class, a generic formulation of Samsca[®] (tolvaptan) has been approved. There have been no major changes in the prescribing information, clinical trials, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

There is insufficient evidence to support that one vasopressin antagonist is safer or more efficacious than another for its associated indications. Formulations without a generic alternative 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 generic 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 Heinze asked the P&T Committee members to mark their ballots.

Diuretics, miscellaneous: AHFS 402892

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that there are currently no drugs classified by AHFS as miscellaneous diuretics.

No brand miscellaneous diuretic is recommended for preferred status. Alabama Medicaid should continue to include this AHFS Class 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 Heinze asked the P&T Committee members to mark their ballots.

**Alzheimer's Agents [Parasympathomimetic (Cholinergic) Agents, AHFS Class 120400;
Central Nervous System Agents, Miscellaneous, AHFS Class 289200]**

Manufacturer comments on behalf of these products:

None

Dr. Pomfret noted that the Alzheimer's agents that are included in this review are listed in Table 1 on page 1235. Donepezil, galantamine, rivastigmine, and memantine agents are all available generically, while the extended-release combination product, memantine and donepezil (Namzaric[®]), is only available in a branded formulation. Since the last review of this class, Aduhelm[®] (aducanumab-avwa) has been approved. With the exception of the availability of aducanumab, there have been no changes in the prescribing information, clinical trials, or treatment guidelines that impact the management of this therapeutic category since the class was last reviewed.

Aducanumab is the first disease-modifying amyloid beta-directed antibody therapy approved for the treatment of Alzheimer's disease (AD) in patients with mild cognitive impairment or mild dementia stage of the disease. There are no safety or efficacy data for initiating treatment with aducanumab at earlier or later stages of the disease. This product is available in single-use vials, is administered as a slow intravenous infusion, and dosing is weight-based (up to 10 mg/kg) every four weeks with titration occurring over seven months of dosing.

Aducanumab-avwa was evaluated in the EMERGE and ENGAGE trials, two double-blind, randomized, parallel group studies that compared low-dose (target dose of 3 mg/kg or 6 mg/kg) or high-dose (6 mg/kg or 10 mg/kg) aducanumab to placebo. Included patients were 50 to 85 years of age with mild cognitive impairment due to AD or mild AD dementia with confirmed presence of amyloid pathology based on visual assessment of positron emission tomography (PET) scan. The patient population was consistent with Stage 3 and Stage 4 AD based upon Clinical Dementia Rating [CDR]-Global scores, Mini-Mental State Exam [MMSE] score, and Repeatable Battery for Assessment of Neuropsychological Status (RBANS) delayed memory index score. Patients were allowed to utilize symptomatic treatments, but doses were required to be stable for at least eight weeks prior to screening. There were at least nineteen exclusionary criteria for trial enrollment, which limited a diverse study population and subsequent generalizability to the larger population. Of note, approximately half of patients were utilizing another AD medication and the majority of patients had a diagnosis of mild cognitive impairment due to AD (80 to 83%) compared with mild Alzheimer's dementia. The primary endpoint for both studies was the change from baseline to week-78 in Clinical Dementia Rating-Sum of Boxes (CDR-SB) Scale score.

This trial and the subsequent FDA review process drew national attention based upon the FDA advisory committee recommendations and the final FDA decision. In March 2019, an independent data monitoring committee reviewed the unblinded results of the interim analysis for futility and made the recommendation to the sponsor to terminate the studies. Following this futility announcement, all dosing stopped at the study

sites, and data collection and review continued. The prespecified futility methodology used pooled data from EMERGE and ENGAGE to predict the future unobserved treatment effect. The individual study results using the prespecified primary efficacy analysis methods on the futility data set showed a -18% treatment difference on the CDR-SB (primary endpoint), favoring high-dose aducanumab in EMERGE, and a 15% treatment difference on CDR-SB, favoring placebo in ENGAGE. This refuted an assumption of conditional power (i.e., that the treatment effect in the two studies would be similar), so conditional power was then recalculated using the data from each of the two studies to predict the future unobserved treatment effect, and this non-pooled analysis yielded estimates of 59% and 0% on the primary endpoint for the high-dose groups in EMERGE and ENGAGE, respectively.

High-dose aducanumab in EMERGE demonstrated a difference of -0.39 compared to placebo in the mean change from baseline in CDR-SB score at week 78 ($P=0.012$), a 22% reduction in decline. Results from the low-dose aducanumab arm were not statistically significant compared to placebo on the primary endpoint. In ENGAGE, the difference in mean change from baseline in CDR-SB scores at week 78 was 0.03 with high-dose aducanumab compared to placebo ($P=0.833$), an increase of 2%. Results from the low-dose aducanumab arm were not statistically significant compared to placebo on the primary endpoint. Ultimately, results from the EMERGE trial showed statistically significant differences from placebo, but the clinical significance of the difference remains unclear; and the ENGAGE trial did not show a statistically significant difference in clinical endpoints. Amyloid PET substudies showed a dose- and time-dependent reduction in amyloid PET standardized uptake value ratio in both studies.

There is the potential for significant adverse events and close monitoring with advanced imaging studies is warranted, given the extensive exclusionary parameters of the trials in a controlled environment. The incidence of adverse events was similar in both trials. Adverse events occurring with an incidence $>10\%$ among any dose group included, amyloid-related imaging abnormalities (ARIA edema, brain microhemorrhages and superficial siderosis), headache, nasopharyngitis, falls, and dizziness. The incidence of ARIA-E was higher in the high-dose groups compared with low-dose groups (35% vs. 26%, respectively, in EMERGE and 36% vs. 26%, respectively, in ENGAGE).

Aduhelm[®] (aducanumab-avwa) received accelerated approval based on surrogate endpoints and continued approval for the indication may be contingent upon verification of clinical benefit in required confirmatory trial(s).

The Centers for Medicare & Medicaid Services (CMS) completed further evaluation of aducanumab-avwa (Aduhelm[®]), including stakeholder input. After extensive evaluation and review due to the limited clinical efficacy outcomes data beyond that seen with surrogate marker evaluation compared to placebo in clinical trials and the significant safety concerns, CMS published the final National Coverage Determination (NCD) for aducanumab-avwa (Aduhelm[®]) on April 7, 2022. The final Medicare NCD indicates coverage of FDA-approved monoclonal antibody therapies directed against amyloid for the treatment of AD when provided in accordance with the extensive coverage criteria outlined for coverage with evidence development for patients who have a clinical diagnosis of mild cognitive impairment due to AD or mild AD dementia, both with confirmed presence of amyloid-beta pathology consistent with AD. The guidance indicates that monoclonal antibodies directed against amyloid that are approved by the FDA for the treatment of AD based upon evidence of efficacy from a change in a surrogate endpoint considered as reasonably likely to predict clinical benefit (e.g., amyloid reduction), may be covered in a randomized controlled trial conducted under an investigational new drug application. Additionally, monoclonal antibodies directed against amyloid that are

approved by FDA for the treatment of AD based upon evidence of efficacy from a direct measure of clinical benefit may be covered in CMS-approved prospective comparative studies, that meet specific protocol and analysis requirements outlined by CMS.

There is insufficient evidence to support that one brand Alzheimer's 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 Alzheimer's 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 Alzheimer's 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. Aducanumab-avwa should not be placed in preferred status regardless of cost.

The committee noted that there is another drug in the pipeline with a similar mechanism of action to aducanumab. Chairperson Heinze 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. NEW BUSINESS

There was no new business.

8. NEXT MEETING DATE

The next P&T Committee Meeting is scheduled for August 10, 2022 at the Medicaid Building in the Commissioner's Board Room.

9. ADJOURN

There being no further business, Dr. Carter moved to adjourn and Dr. Nevels seconded. The meeting adjourned at 2:03 p.m. CST

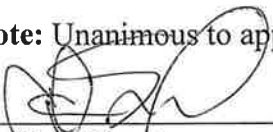
Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
May 4, 2022

- 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


_____ Approve Approve as amended Disapprove No action
Medical Director

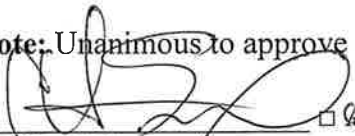

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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


_____ Approve Approve as amended Disapprove No action
Medical Director



_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
Commissioner

C. Recommendation: No brand peripheral adrenergic inhibitor is recommended for preferred status. Alabama Medicaid should continue to include AHFS Class 240832 in the PDL screening process. If new outpatient peripheral adrenergic inhibitors are added, it is recommended that this class be re-reviewed at that time.

Amendment: None

Vote: Unanimous to approve as recommended



Medical Director Approve Approve as amended Disapprove No action



Deputy Commissioner Approve Approve as amended Disapprove No action

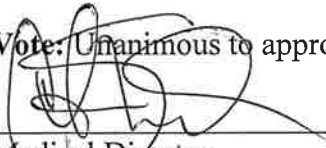


Commissioner Approve Approve as amended Disapprove No action

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

Amendment: None

Vote: Unanimous to approve as recommended



Medical Director Approve Approve as amended Disapprove No action



Deputy Commissioner Approve Approve as amended Disapprove No action



Commissioner Approve Approve as amended Disapprove No action

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


_____ Approve Approve as amended Disapprove No action
Medical Director


_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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


_____ Approve Approve as amended Disapprove No action
Medical Director


_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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


_____ Approve Approve as amended Disapprove No action
Medical Director


_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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


_____ Approve Approve as amended Disapprove No action
Medical Director


_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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


_____ ~~Approve~~ Approve as amended Disapprove No action
Medical Director


_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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


_____ ~~Approve~~ Approve as amended Disapprove No action
Medical Director



_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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


_____ Approve Approve as amended Disapprove No action
Medical Director


_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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


_____ Approve Approve as amended Disapprove No action
Medical Director


_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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

 Approve Approve as amended Disapprove No action
Medical Director

 Approve Approve as amended Disapprove No action
Deputy Commissioner

 Approve Approve as amended Disapprove No action
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

 Approve Approve as amended Disapprove No action
Medical Director

 Approve Approve as amended Disapprove No action
Deputy Commissioner

 Approve Approve as amended Disapprove No action
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

 Approve Approve as amended Disapprove No action
Medical Director


 Approve Approve as amended Disapprove No action
Deputy Commissioner

 Approve Approve as amended Disapprove No action
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

 Approve Approve as amended Disapprove No action
Medical Director

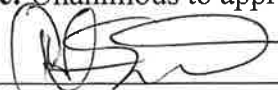
 Approve Approve as amended Disapprove No action
Deputy Commissioner

 Approve Approve as amended Disapprove No action
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
Medical Director


_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
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
Medical Director

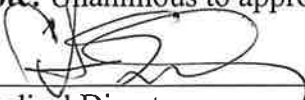

_____ Approve Approve as amended Disapprove No action
Deputy Commissioner


_____ Approve Approve as amended Disapprove No action
Commissioner

S. **Recommendation:** No brand Alzheimer's 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. Aducanumab-avwa should not be placed in preferred status regardless of cost.

Amendment: None

Vote: Unanimous to approve as recommended



Medical Director Approve Approve as amended Disapprove No action

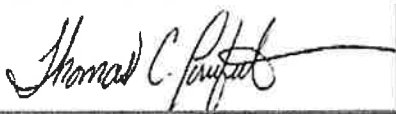


Deputy Commissioner Approve Approve as amended Disapprove No action



Commissioner Approve Approve as amended Disapprove No action

Respectfully submitted,



05/05/2022

Thomas Pomfret, PharmD, MPH, BCPS

Date



05/05/2022

Rachel Bacon, PharmD, MPH

Date