Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Pharmacy Advisory Committee Meeting

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Agenda Topics

- Overview of Disease State
- Indications
- Dosage & Formulations
- Guideline Updates

Immunomodulators, Asthma

Magellan Medicaid Administration

Overview of Disease State - Asthma

- Prevalence of asthma in the United States (U.S.) continues to rise. An estimated 7.8% (24.6 million) Americans have asthma with approximately 10% to 20% in poor control
- The National Asthma Education and Prevention Program (NAEPP) has defined asthma as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role
- Asthma phenotypes have been identified by clinical and/or pathophysiological characteristics
- It has been established that eosinophils play a role in the inflammatory process of asthma and eosinophilic asthma is identified as a phenotype of asthma
- Generally, patients with eosinophilic asthma have severe disease with high eosinophil levels in the blood and sputum despite treatment with a glucocorticoid. Persistent levels of eosinophils in sputum may also be an indicator of disease severity

Overview of Disease State - Urticaria

- The prevalence of chronic urticaria (CU) is estimated to be 0.5% to 5% of the general population
- Typically, CU presents as pruritic edematous red wheals of variable size and shape with surrounding erythema
- Chronic urticaria is defined as episodic or daily hives lasting for 6 weeks or more that impairs quality of life
- The majority of cases of CU have an undetermined cause (idiopathic); however, infectious and autoimmune conditions can be associated with CU
- Chronic urticaria may be associated with presence of mononuclear cells (CD4+ Th1 and Th2 lymphocytes), eosinophils, neutrophils, basophils, mast cells, and activated macrophages

Immunomodulators, Asthma – Indications

Drugs	Indications
Interleukin-5 (IL-5) Antagonists	
benralizumab (Fasenra)	▪ Add-on maintenance treatment of patients with severe asthma aged ≥ 12 years, and with an eosinophilic phenotype
mepolizumab (Nucala)	▪ Add-on maintenance treatment of patients with severe asthma aged ≥ 12 years, and with an eosinophilic phenotype
reslizumab (Cinqair)	▪ Add-on maintenance treatment of patients with severe asthma aged ≥ 18 years, and with an eosinophilic phenotype
Anti-Immune Globulin E (IgE) Antibody	
omalizumab (Xolair)	• Moderate to severe persistent asthma in patients ≥ 6 years of age with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids • Chronic idiopathic urticaria in adults and adolescents ≥ 12 years of age who remain symptomatic despite H1 antihistamine treatment

Immunomodulators, Asthma – Dosing and Availability

Drugs	Dose	Dosage/Administration Comments	Dosage Forms
Interleukin-5 (IL-5) Antagonists			
benralizumab (Fasenra)	30 mg subcutaneously (SC) every 4 weeks for 3 doses, followed by 30 mg once every 8 weeks thereafter	For SC use only (upper arm, thigh, abdomen) Should only be administered by an HCP	30 mg/mL solution in a single-dose prefilled syringe
mepolizumab (Nucala)	100 mg SC every 4 weeks	For SC use only (upper arm, thigh, abdomen) Should only be administered by an HCP	100 mg lyophilized powder for injection in a single-dose vial
reslizumab (Cinqair)	3 mg/kg every 4 weeks by intravenous (IV) infusion over 20 to 50 minutes	For IV infusion only; do not administer vial IV push or bolus. Should only be administered in a healthcare setting by an HCP who can manage anaphylaxis Discontinue infusion immediately if anaphylaxis occurs	100 mg/10 mL solution in single-use vial
Anti-Immune Globulin E (IgE) Antibody			
omalizumab (Xolair)	**Asthma:** 75 mg to 375 mg SC every 2 or 4 weeks Dose and frequency is determined by serum total IgE level before the start of treatment, and body weight, as instructed in the package insert **CIU:** 150 mg to 300 mg SC every 4 weeks Dosing is not dependent on serum IgE or body weight	Should only be administered in a healthcare setting by an HCP who can manage anaphylaxis Injection may take 5 to 10 seconds to administer due to the solution viscosity Doses > 150 mg should be divided among more than one injection site; do not administered > 150 mg per site	150 mg lyophilized powder for injection in a single-dose vial

Immunomodulators, Asthma – Guidelines

- American Thoracic Society (ATS) and European Respiratory Society (ERS) Task Forces
  - Severe asthma defined as asthma that requires treatment with high-dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming uncontrolled or that remains uncontrolled despite this therapy
  - The guidelines suggest a trial of omalizumab (Xolair) in adults and children aged 6 years and older with a confirmed IgE-dependent allergic asthma despite optimal drug and non-drug therapy
  - If there is no response within 4 months of beginning omalizumab, it is unlikely that continued treatment will be of benefit
  - Benralizumab (Fasenra), mepolizumab (Nucala), and reslizumab (Cinqair) were not available at the time that these guidelines were published

Immunomodulators, Asthma – Guidelines

- Global Initiative for Asthma (GINA), 2017

Adults and Children 6 Years of Age And Older	
Step 1	As-needed reliever medication ▪ Recommended: SABA ▪ Alternative Controller: consider low dose ICS
Step 2	One controller AND an as-needed reliever medication ▪ Preferred controller: low-dose ICS + SABA ▪ Alternative controllers: leukotriene modifier or low dose theophylline*
Step 3	One or 2 controllers and an as-needed reliever medication ▪ Preferred for adolescents and adults: low-dose ICS AND a LABA as maintenance plus as-needed SABA OR ICS/formoterol maintenance and reliever therapy ▪ Preferred for children 6 to 11 years of age: medium dose ICS + as-needed SABA ▪ Alternative controllers: medium- or high-dose ICS, OR low-dose ICS + leukotriene modifier, OR ▪ Sublingual immunotherapy (SLIT) may be considered in adults with allergic rhinitis or house dust mite sensitivity and exacerbations despite ICS use
Step 4	Two or more controllers AND an as-needed reliever medication ▪ Preferred for adolescents and adults: low-dose ICS/formoterol as maintenance + reliever treatment; **OR** medium-dose ICS + LABA plus as-needed SABA ▪ Preferred for children 6 to 11 years of age: referral to expert for assessment and advice ▪ Alternative controllers: For adults and adolescents: medium- or high-dose ICS, OR low-dose ICS + leukotriene modifier, **OR** low-dose ICS + sustained release theophylline*, **OR** tiotropium ▪ Sublingual immunotherapy (SLIT) may be considered in adults with allergic rhinitis or house dust mite sensitivity and exacerbations despite ICS use
Step 5	Higher level of care and/or add-on treatment ▪ In addition to Step 4 treatment, refer for add-on treatment: tiotropium, monoclonal antibody treatment (omalizumab [anti-IgE therapy], mepolizumab or reslizumab [anti-IL-5 therapy]), low-dose oral corticosteroids, bronchial thermoplasty, or sputum guided therapy

* For children 6 to 11 years of age, theophylline is not recommended.
ICS = inhaled corticosteroid; LABA = long acting beta$_2$-agonist; SABA = short acting beta$_2$-agonist

Immunomodulators, Urticaria – Guidelines

- The AAAAI/ACAAI/JCAAI recommend a stepwise approach to care is recommended for chronic urticaria
- Treatment should begin based on the patient's level of severity and previous treatment history
- At each level, medications should be evaluated for efficacy and patient tolerance and step-down should be considered when consistent control is achieved
- Step 1:
  - Monotherapy with second-generation antihistamines is considered first-line for CU in addition to avoidance of triggers (e.g., nonsteroidal anti-inflammatory drugs, food allergens) and relevant physical factors
- Step 2:
  - If CU is not controlled, the antihistamine dose can be increased (if appropriate for the particular agent)
  - One of the following can be added: another second-generation or a first-generation antihistamine, a histamine-2 antagonist, or an LTRA
- Step 3
  - If control is still not achieved, dose advancement of a potent antihistamine (e.g. hydroxyzine or doxepin) may be considered, as tolerated
- Step 4:
  - CU that is refractory to maximal antihistamine therapy in step 3, alternative agents such as Xolair (omalizumab) can be used; other anti-inflammatory, immunosuppressant, or biologic agents may be considered, but have a lower level of supporting evidence

Antiasthmatic – Monoclonal Antibodies

- **Recommendation:**
  - All products are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of HCA.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Antiasthmatic – Monoclonal Antibodies

- Motion: "I move that the Apple Health Medicaid Program implement the limitations for the antiasthmatic – monoclonal antibody drug class listed on slide #11 as recommended."

Motion: Flatebo

2nd: Storhaug

Lipotropic, Statins

Magellan Medicaid Administration

Overview of Disease State

- Cardiovascular disease (CVD) is one of the leading causes of death and disability in the Western world, and has been estimated to be the cause of one out of every three deaths in the United States
- Hypercholesterolemia constitutes a major risk factor for the development of atherosclerosis and consequently atherosclerotic cardiovascular disease (ASCVD), especially coronary heart disease (CHD)
- Approximately 15.5 million Americans have CHD, defined as a history of myocardial infarction, angina pectoris, heart failure, stroke, or congenital cardiovascular defects
- The National Health and Nutrition Examination Survey (NHANES) reported that in 2015 to 2016 approximately 12.4% of adults had high total cholesterol (≥ 240 mg/dL) and 18.4% had low HDL-C (< 40 mg/dL)
  - Higher in women (13.7%) compared to men (11.2%)
- Many clinical trials have demonstrated that a high serum concentration of low-density lipoprotein cholesterol (LDL-C) and low levels of high-density lipoprotein cholesterol (HDL-C) are major risk factors for coronary heart disease (CHD)
- High level of evidence supporting the use of statins for secondary prevention and moderate to high level of evidence for their use for primary prevention
  - As a class, they can lower LDL-C by up to 60% in a dose-related fashion
  - Statins typically have relatively minor effects on triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C), reducing TG by 6% to 30% and increasing HDL-C by 2% to 16%

Lipotropic, Statins - Availability

Drugs	Generic
amlodipine / atorvastatin (Caduet)	X
atorvastatin (Lipitor)	X
ezetimibe / simvastatin (Vytorin)	X
fluvastatin	X
fluvastatin ER (Lescol XL)	X
lovastatin	X
lovastatin ER (Altoprev)	
pitavastatin (Livalo)	
pravastatin (Pravachol)	X
rosuvastatin (Crestor)	X
simvastatin (Flolipid)	
simvastatin (Zocor)	X

Lipotropic, Statins - Indications

Indications	atorvastatin (Lipitor), amlodipine/ atorvastatin* (Caduet),	ezetimibe/ simvastatin (Vytorin)	fluvastatin, fluvastatin ER (Lescol XL),	lovastatin	lovastatin ER (Altoprev)
Primary hypercholesterolemia ▪ **Heterozygous familial and nonfamilial** **Reduce: Total-C, LDL-C, TG and ApoB** **Increase: HDL-C**	X	X	X	X	X
Heterozygous familial hypercholesterolemia ▪ **pediatric**	X 10–17 years (Lipitor only)	--	X 10–16 years	X 10–17 years	--
Mixed dyslipidemia **Fredrickson Type** ▪ **II_a and II_b** **Reduce: Total-C, LDL-C, TG and ApoB**	X	X	X	X To reduce total-C, LDL-C	X
Increase HDL-C	X	X	X	--	X
Hypertriglyceridemia **Fredrickson Type IV**	X	--	--	--	--
Primary dysbetalipoproteinemia **Fredrickson Type III**	X	--	--	--	--
Homozygous familial hypercholesterolemia	X	X	--	--	--
Atherosclerosis ▪ **slow progression**	--	--	X	X	X
CVD ▪ **primary prevention of coronary events**	Reduces risk of MI, stroke, revascularization, angina	--	--	Reduces risk of MI, unstable angina, and need for coronary revascularization	Reduces risk of MI, unstable angina, coronary revascularization
CHD ▪ **secondary prevention of coronary events**	Reduces risk of MI, stroke in Type 2 diabetics without CHD; Reduces risk of MI, stroke, CHF hospitalization, angina, and revascularization in CHD patients	--	Reduces risk of coronary revascularization	--	--

Lipotropic, Statins - Indications

Indications	pitavastatin (Livalo)	pravastatin (Pravachol)	rosuvastatin (Crestor)	simvastatin (Flolipid, Zocor)
Primary hypercholesterolemia ▪ **Heterozygous familial and nonfamilial** **Reduce: Total-C, LDL-C, TG and ApoB**	X	X	X	X
Heterozygous familial hypercholesterolemia ▪ **pediatric**	--	X 8 years and older	X 8–17 years	X 10–17 years
Mixed dyslipidemia **Fredrickson Type** ▪ **II_a and II_b** **Reduce: Total-C, LDL-C, TG and ApoB**	--	X	X	X
Increase HDL-C	X	X	X	X
Hypertriglyceridemia - Fredrickson Type IV	--	X	X	X
Primary dysbetalipoproteinemia - Fredrickson Type III	--	X	X	X
Homozygous familial hypercholesterolemia	--	--	X 7–17 years	X
Atherosclerosis ▪ **slow progression**	--	X	X	--
CVD ▪ **primary prevention of coronary events**	--	Reduces risk of MI, myocardial revascularization, CV mortality	Reduces risk of MI, stroke, revascularization, in patients without clinically evident CHD, but with multiple risk factors	Reduces total mortality risk by reducing CHD death, MI, stroke, and need for revascularization in high risk patients
CHD ▪ **secondary prevention of coronary events**	--	Reduces risk of MI, myocardial revascularization, CV mortality, stroke/TIA	--	Reduces total mortality risk by reducing CHD death, MI, stroke, and need for revascularization

Lipotropic, Statins - Guideline

- U.S Preventive Task Force (USPSTF), 2016
  - Final recommendations on the use of statins for primary prevention of CVD in adults
  - Recommends a low- to moderate-dose statin for the prevention of CVD events and mortality in adults ages 40 to 75 years with *no* history of CVD, 1 or more CVD risk factor, and a 10-year calculated CVD event risk of 10% or greater (Grade B)
  - Since the likelihood of benefit is smaller, USPSTF states that clinicians may consider a low- to moderate-dose statin in adults ages 40 to 75 years with *no* history of CVD, at least 1 CVD risk factor, and a 10-year calculated CVD event risk of 7.5% to 10% (Grade C)
  - There is insufficient evidence to assess adequately the risk versus benefits of statin use in older adults (≥ 76 years) without CVD history (Grade I)
- American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE), 2017
  - Recommends aggressive lipid-modifying therapy to lower LDL-C with statins as the drugs of choice for LDL-C reduction
  - They recommend LDL goals of < 55 mg/dL, < 70 mg/dL, < 100 mg/dL, and < 130 mg/dL for individuals at extreme, very high, high/moderate, and low risk for cardiovascular events, respectively
  - AACE supports the use of apolipoprotein B (apo B) in evaluating lipid status
  - These guidelines address the unique challenges associated with atherosclerosis and heart disease in women and recommend pharmacotherapy, preferably with a statin, for all women at high risk regardless of LDL-C level and for those at intermediate risk with LDL-C > 130 mg/dL

Statins

- **Recommendation:**
  - All statin products are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of HCA.
  - All non-preferred products require a trial of two preferred products with the same indication and different active ingredients before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

Statins

- Motion: “I move that the Apple Health Medicaid Program implement the limitations for the statin drug class listed on slide #19 as recommended.”

Motion: Lee

2nd: Park

PCSK9 Inhibitors

Magellan Medicaid Administration

Overview of Disease State

- While hypercholesterolemia is common among the general population, it is even more prevalent in patients with Familial Hypercholesterolemia (FH), a genetic disorder that leads to accumulation of LDL-C particles in plasma and premature CV disease
- The more severe form, homozygous familial hypercholesterolemia (HoFH), is rare, occurring in about 1 out of a million people in the U.S.
  - In HoFH, LDL receptor activity is nearly absent and LDL-C levels commonly range between 400 mg/dL to 1,000 mg/dL
  - Severe and widespread atherosclerosis affects all major arteries and children are at risk for early coronary events and valve abnormalities, particularly aortic stenosis
  - Historically, treating patients with HoFH has been very difficult since it is resistant to diet modifications and most medications indicated for lowering cholesterol
- The less serious heterozygous familial hypercholesterolemia (HeFH) occurs in 1 in 500 persons in the U.S.
  - CAD symptoms begin to manifest in the fourth and fifth decades of life, in men and women, respectively
  - Additional risk factors (e.g., genetic, metabolic, and environmental) can lead to variations in the clinical manifestations and severity of atherosclerotic disease of HeFH
  - Accumulation of cholesterol in nonvascular tissue (cornea, skin, tendons, and joints) also commonly occurs in children with HoFH, and in adults with HeFH

Lipotropics, Other (PCSK9 Inhibitors) - Indications

Drug	Generic	Indications
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors		
alirocumab (Praluent)		Treatment of adults with HeFH or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of LDL-C as an adjunct to diet and maximally-tolerated statin therapy
evolocumab (Repatha)		• Treatment of adults with HeFH or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of LDL-C as an adjunct to diet and maximally-tolerated statin therapy • Treatment of patients with HoFH who require additional lowering of LDL-C as an adjunct to diet and other LDL-lowering therapies

Lipotropics, Other (PCSK9 Inhibitors) - Dosage and Availability

Drug	Dose	Availability
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors		
alirocumab (Praluent)	75 mg or 150 mg subcutaneously once every 2 weeks; may be increased to a maximum of 150 mg administered every 2 weeks; and alternative starting dose is 300 mg (2 x 150 mg SC injections) may be given once monthly	75 mg/1 mL and 150 mg/1 mL single-use prefilled pen
evolocumab (Repatha)	HeFH or with primary hyperlipidemia: 140 mg subcutaneously once every 2 weeks or 420 mg once monthly; HoFH: 420 mg once monthly	140 mg/1 mL prefilled autoinjector or syringe; 420 mg/3.5 mL single-use Pushtronex system (on-body infusor with prefilled cartridge)

Lipotropics, Other (PCSK9 Inhibitors) - Guidelines

- American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE), 2017
  - Guidelines for the management of dyslipidemia and prevention of cardiovascular disease
    - Adults ≥ 20 years of age should be assessed annually for dyslipidemia
    - Children should be screened who are at risk for familial hypercholesterolemia
    - Recommend fibrates for treatment of TG > 500 mg/dL
    - Omega-3 fish oil (2 g to 4 g) can be used, as adjunct to fibrates or niacin, to achieve satisfactory TG levels
    - Recommends bile acid sequestrants for reducing LDL-C and apo B and modestly increasing HDL-C
    - Ezetimibe is effective monotherapy in reducing LDL-C and apo B (particularly in statin-intolerant patients)
    - Maintain statins as primary therapy and recommend ezetimibe in addition to statins for addition LDL-C reduction
    - PCSK9 inhibitors may be considered in patients with clinical CVD who are not at goal with maximally tolerated statin or in those with familial hypercholesterolemia
- American Diabetes Association (ADA), 2017
  - Recommends moderate- or high-intensity statin therapy in patients with diabetes bases on patient age and presence of ASCVD or ASCVD risk factors
  - Recommend ezetimibe as add-on to moderate-intensity statin therapy in patients with ACS and LDL-C ≥ 50 mg/dL or in patients with history of ASCVD who cannot tolerate high-dose statins
  - PCSK9 inhibitor to maximally tolerated statin doses may be considered in those at high risk for ASCVD events who require additional LDL-C reduction or who are intolerant to high-intensity statin therapy
  - The ADA does not recommend niacin therapy added onto statin therapy in diabetic patients

PCSK9

- **Recommendation:**
  - All PCSK9 products are considered safe and efficacious and are eligible for preferred status and grandfathering at the discretion of HCA.
  - All non-preferred products require a trial of two preferred products with the same indication before a non-preferred drug will be authorized unless contraindicated, not clinically appropriate, or only one product is preferred.

PCSK9

- Motion: “I move that the Apple Health Medicaid Program implement the limitations for the PCSK9 drug class listed on slide #26 as recommended.”

Motion: Schwilke

2nd: Brown