Pharmacy Policy Bulletin: J-1336 Lodoco (colchicine) – Commercial and Healthcare Reform	
Number: J-1336	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** 1. Other Managed Prior Authorization = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1336-002	**Original Date:** 08/02/2023
Effective Date: 08/23/2024	**Review Date:** 08/07/2024

Drugs Product(s):	• Lodoco (colchicine)
FDA-Approved Indication(s):	• To reduce the risk of myocardial infarction (MI), stroke, coronary revascularization, and cardiovascular (CV) death in adult patients with established atherosclerotic disease or with multiple risk factors for cardiovascular disease (CVD).

Background:	• Lodoco is an alkaloid that prevents the activation, degranulation, and migration of neutrophils and mediates the activation of interleukin-1β. These anti-inflammatory effects are consistent with clinical data demonstrating that colchicine reduces high sensitivity C-reactive protein (hs-CRP). However, the mechanism of action of Lodoco in the prevention of major CV events is not understood. • Colchicine 0.6 mg is indicated for gout +/- Familial Mediterranean fever, while Lodoco is supplied as a 0.5 mg strength and is only indicated to reduce CV events. • Heart disease is the leading cause of death across genders and most racial and ethnic groups in the United States (US). Atherosclerosis is the hardening of arteries due to gradual plaque buildup. Risk factors for atherosclerosis include high cholesterol, high blood pressure (BP), obesity, diabetes, and smoking. Complications of atherosclerotic disease include coronary artery disease (CAD), cerebrovascular disease, and peripheral artery disease. • Clinical atherosclerotic cardiovascular disease (ASCVD) includes acute coronary syndromes, a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin. • The 2019 American College of Cardiology (ACC)/American Heart Association (AHA) Guideline on the Primary Prevention of Cardiovascular Disease recommends the following: o A healthy lifestyle throughout life including diet and exercise.

	○ Statin therapy is the first-line treatment for primary prevention of atherosclerotic cardiovascular disease (ASCVD) in patients with elevated low-density lipoprotein cholesterol levels (≥190 mg/dL), those with diabetes mellitus, who are 40 to 75 years of age, and those determined to be at sufficient ASCVD risk after a clinician–patient risk discussion. ○ Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit. ○ Nonpharmacological interventions are recommended for all adults with elevated BP or hypertension. For those requiring pharmacological therapy, the target BP should generally be < 130/80 mm Hg. • The 2018 AHA/ACC Multisociety Guideline Cholesterol Guideline recommends the following for secondary prevention of ASCVD: ○ A healthy lifestyle throughout life including diet and exercise. ○ High-intensity statin as first-line treatment for ASCVD in patients < 75 years of age with clinical ASCVD. For patients at very high risk, if LDL-C remains ≥ 70 mg/dL on maximally tolerated statin, first consider adding ezetimibe; if LDL-C remains ≥ 70 mg/dL, consider adding PCSK9 inhibitor. ○ In patients > 75 years of age with ASCVD, initiate moderate- or high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, drug–drug interactions, patient frailty, and patient preferences. • ICD-10 Code Information: ○ ICD-10: I10 “Essential (primary) hypertension”, E78: “Disorders of lipoprotein metabolism and other lipidemias”, E66: “Overweight and obesity” (except E66.3: “Overweight”), E08-E13: “Diabetes mellitus”, or F17: “Nicotine dependence” may apply to Lodoco; however, the prescriber must confirm that the member has multiple risk factors. • Prescribing Considerations: ○ Maximally tolerated statin therapy is defined as the highest tolerated intensity and frequency of a statin. If statin tolerance is zero, the member meets the statin intolerance definition in the criteria. ○ Lodoco is contraindicated in patients with a creatinine clearance < 15 mL/minute, pre-existing blood dyscrasias, severe hepatic dysfunction. ○ Use with a moderate to strong CYP3A4 inhibitor or P-glycoprotein inhibitors can cause fatal colchicine toxicity and is not recommended. ○ Concomitant use of Lodoco and HMG CoA reductase inhibitors, gemfibrozil, fenofibric acid, cyclosporine may increase the risk of muscle weakness and fatigue.

Approval Criteria

I. Approval Criteria

When a benefit, coverage of Lodoco may be approved when all of the following criteria are met **(A. through E.)**:

A. The member is 18 years of age or older.

B. The member has a diagnosis of one (1) of the following **(1. or 2.)**:

1. Established atherosclerotic disease (ICD-10: I70) supported by one (1) of the following **(a. through g.)**:

a. Acute coronary syndrome

b. Coronary or other arterial revascularization

c. History of MI

d. History of stroke

e. History of transient ischemic attack

f. Peripheral arterial disease presumed to be of atherosclerotic origin
g. Stable or unstable angina

2. Multiple risk factors for cardiovascular disease (e.g., high cholesterol, high blood pressure, obesity, diabetes, smoking; no ICD-10 code).

C. The member is using Lodoco to reduce the risk of MI, stroke, coronary revascularization, or cardiovascular death.

D. The member meets one (1) of the following criteria **(1. or 2.)**:

1. The member has experienced therapeutic failure to a maximally tolerated statin.

2. The member is statin intolerant defined as one (1) of the following **(a. or b.)**:

a. While receiving at least two (2) separate trials of different statins, the member experienced one (1) of the following **(i. or ii.)**:

i. Statin related rhabdomyolysis, which resolved upon discontinuation of the statins.
ii. Skeletal-related muscle symptoms, which resolved upon discontinuation of the statins.

b. The member experienced one (1) of the following during any course of statin therapy **(i., ii., or iii.)**:

i. Creatinine kinase (CK) increase to 10 times upper limit of normal (ULN).
ii. Liver function tests (LFTs) increase to 3 times ULN.
iii. Hospitalization due to severe statin-related adverse event (e.g., rhabdomyolysis).

E. The member has experienced therapeutic failure, contraindication, or intolerance to plan-preferred Repatha.

II. Reauthorization

When a benefit, reauthorization of Lodoco may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced positive clinical response to therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Lodoco [package insert]. Parsippany, NJ: Agepha Pharma USA, LLC; June 2023.
2. Centers for Disease Control and Prevention. Heart Disease Facts. Available at: https://www.cdc.gov/heart-disease/data-research/facts-stats/index.html. Accessed June 13, 2024.
3. WebMD. Atherosclerosis. Available at: https://www.webmd.com/heart-disease/what-is-atherosclerosis. Accessed June 13, 2024.
4. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2023.

5. Deftereos SG, Beerkens FJ, Shah B, et al. Colchicine in Cardiovascular Disease: In-Depth Review. *Circulation*. 2022;145(1):61-78.
6. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140(11):e596-e646.
7. Virani SS, Smith Jr SC, Stone NJ, MGrundy SM. Secondary Prevention for Atherosclerotic Cardiovascular Disease: Comparing Recent US and European Guidelines on Dyslipidemia. *Circulation*. 2020;141(14):1121-1123.
8. Pasternak RC, Smith SC Jr, Bairey-Merz CN, et al; American College of Cardiology; American Heart Association; National Heart, Lung and Blood Institute. ACC/AHA/NHLBI Clinical Advisory on the Use and Safety of Statins. *Circulation*. 2002 Aug 20;106(8):1024-8.