Lodoco® (colchicine)

Policy # 00861
Original Effective Date: 01/08/2024
Current Effective Date: 01/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Lodoco®‡ (colchicine) to be **eligible for coverage**** when the below patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Lodoco (colchicine) will be considered when the following criteria are met:

- Patient is greater than or equal to 18 years of age; AND
- Patient has had one of the following conditions or diagnoses:
    - A previous myocardial infarction or a history of acute coronary syndrome; OR
    - Angina (stable or unstable); OR
    - A history of stroke or transient ischemic attack; OR
    - Coronary artery disease; OR
    - Peripheral arterial disease; OR
    - Patient has undergone a coronary or other arterial revascularization procedure (e.g., coronary artery bypass graft surgery, percutaneous coronary intervention, angioplasty, coronary stent procedures) in the past; AND
- Lodoco is being added onto a background regimen of other atherosclerotic disease medications according to the prescriber. Examples of medications recommended for patients with atherosclerotic disease include aspirin, antiplatelet agents, anticoagulants, lipid-lowering agents, beta blockers, angiotensin converting enzyme inhibitors, and/or angiotensin receptor blockers; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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- Patient does not have severe hepatic impairment according to the prescriber; AND
- Patient has a creatinine clearance of ≥50 mL/min; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient does not have pre-existing blood dyscrasias (e.g., myelosuppression, leukopenia, granulocytopenia, thrombocytopenia, pancytopenia, or aplastic anemia); AND
- Lodoco will not be used in combination with strong CYP3A4 inhibitors or P-glycoprotein inhibitors (e.g., atazanavir, clarithromycin, itraconazole, ketoconazole, nefazodone, ritonavir).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Lodoco (colchicine) in patients not on a background regimen of other atherosclerotic disease medications or who have a creatinine clearance less than 50 mL/min to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Lodoco (colchicine) when the patient selection criteria are not met (except those noted above as **not medically necessary****) to be **investigational.***

Background/Overview

Lodoco contains a new strength of colchicine, 0.5 mg, and is indicated to reduce the risk of myocardial infarction, stroke, coronary revascularization, and cardiovascular (CV) death in adults with established atherosclerotic disease or with multiple risk factors for CV disease. Although the mechanism of action of Lodoco for preventing CV events is not completely known, it is believed to have anti-inflammatory properties. Other colchicine formulations are available at the 0.6 mg strength (Colcrys®, Mitigare®, generic)‡ that are indicated for the prevention and treatment of gout, as well as for the treatment of familial Mediterranean fever. For these indications, higher daily doses are generally recommended. The recommended dose of Lodoco for CV risk reduction is 0.5 mg once

daily. Colchicine is associated with gastrointestinal adverse events (e.g., diarrhea, vomiting), as well as myalgia. Patients with severe renal and/or hepatic impairment should not use Lodoco. Additionally, drug-drug interactions should be considered as Lodoco is contraindicated in combination with strong cytochrome P450 (CYP) 3A4 inhibitors or P-glycoprotein (Pgp) inhibitors.

Cardiovascular disease (CVD) is an umbrella term for conditions of the heart or blood vessels. The most common CVD is coronary artery disease (narrow or blocked coronary arteries caused by plaques), which can lead to chest pain, heart attacks, or stroke. This is also known as atherosclerotic CVD (ASCVD). ASCVD is the leading cause of morbidity and mortality in the United States, affecting more than 26 million Americans. Risk factors for certain types of CVD include smoking, high blood pressure, high cholesterol or dyslipidemia, diabetes, and overweight or obesity. Inflammatory markers, such as C-reactive protein (CRP) have also been associated with increased cardiovascular events.

Prevention of CVD in individuals at very high risk (primary prevention) and prevention of CV events in those patients with established disease (secondary prevention) includes lifestyle modifications in addition to guideline-directed medical therapies. The guideline-directed medical therapies include aspirin, antiplatelet agents, anticoagulants, lipid-lowering agents, beta blockers, angiotensin converting enzyme inhibitors, and/or angiotensin receptor blockers. The 2023 guidelines for the management of patients with chronic coronary disease from the American Heart Association and the American College of Cardiology state that the addition of colchicine for secondary prevention in patients with chronic coronary disease may be considered to reduce recurrent ASCVD events.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Lodoco was approved in June 2023 to reduce the risk of myocardial infarction, stroke, coronary revascularization, and cardiovascular death in adult patients with established atherosclerotic disease or with multiple risk factors for cardiovascular disease.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical

practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The evidence for the efficacy of colchicine in patients with cardiovascular events is derived from the published LoDoCo2 trial along with other supportive studies.

The LoDoCo2 trial was an investigator-initiated, randomized, placebo controlled, double-blind, event-driven trial conducted to assess the efficacy of colchicine 0.5 mg once daily orally in patients with stable coronary artery disease. The study included 5522 patients, in which 2762 were assigned to the colchicine group and 2760 to placebo. Patients were treated for chronic coronary disease, with 99.7% taking an antiplatelet agent or an anticoagulant, 96.6% a lipid-lowering agent, 62.1% a beta-blocker, and 71.7% an inhibitor of the renin-angiotensin system. Included patients were between 35-85 years of age, had proven coronary artery disease, were clinically stable for at least 6 months, and did not have comorbidities that would preclude to follow up or a contraindication to colchicine use. The primary endpoint of the trial was a composite endpoint of cardiovascular death, spontaneous myocardial infarction, ischemic stroke, or ischemia-driven coronary revascularization. It was found that 0.5 mg of colchicine once daily resulted in a 31% lower relative risk of the primary composite endpoint events compared to placebo (HR, 0.69; 95% CI 0.57 to 0.83; $p<0.001$) and the number needed to treat was 36.

References

1. Lodoco [package insert]. Agepha Pharma USA, LLC. Parsippany, NJ. Updated August 2023.
2. Lodoco Drug Evaluation. Express Scripts. Updated August 2023.
3. Lodoco New Drug Review. IPD Analytics. Updated July 2023.

Policy History

Original Effective Date: 01/08/2024
Current Effective Date: 01/08/2024
12/07/2023 Medical Policy Committee review
12/13/2023 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 12/2024

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.