colchicine (Lodoco®)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO286

Description

Colchicine (Lodoco) is an orally administered alkaloid. The mechanism of action of colchicine (Lodoco) in prevention of major cardiovascular events is not well understood at this time.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
colchicine (Lodoco)	Cardiovascular risk reduction in patients with established atherosclerotic cardiovascular disease (ASCVD) or with multiple risk factors for cardiovascular disease	0.5mg tablet	30 tablets/30 days

Initial Evaluation

I. **Colchicine (Lodoco)** may be considered medically necessary when the following criteria are met:
   A. Member is 35 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a provider specializing in heart disease (i.e., cardiology, lipidology); **AND**
   C. A diagnosis of **established Atherosclerotic Cardiovascular Disease (ASCVD)** when the following are met:
      1. Diagnosis is confirmed by one of the following:
         i. Primary prevention failure (e.g., member has had a stroke, myocardial infarction, percutaneous coronary intervention [PCI], etc.); **OR**
         ii. Evidence of clinical atherosclerotic disease on invasive or non-invasive testing (e.g., coronary angiography, CT angiography, etc.); **AND**
      2. Blood pressure is controlled and stable on current antihypertensive therapy; **AND**
      3. Provider attestation that member does not have any of the following comorbidities:
         i. Renal failure (i.e., CrCl <15 mL/min)
         ii. Severe liver impairment
         iii. Pre-existing blood dyscrasias
         iv. Concurrent use of strong CYP3A4 or P-gp inhibitors; **AND**

4. Member will continue background therapy with maximally tolerated statin (e.g., atorvastatin, rosuvastatin, simvastatin, etc.); **OR**
    i. If statin intolerant, member will continue background therapy with maximally tolerated non-statin lipid-lowering agents (e.g., ezetimibe, Repatha, Praluent, fenofibric acid, etc.) unless contraindicated or not tolerated; **AND**
5. Treatment with colchicine 0.6mg (Colcrys) has been ineffective, contraindicated, or not tolerated

II. Colchicine (Lodoco) is considered not medically necessary when criteria above are not met and/or when used for:
    A. Gout
    B. Familial Mediterranean fever

III. Colchicine (Lodoco) is considered investigational when used for all other conditions, including but not limited to:
    A. Actinic Keratosis
    B. Amyloidosis
    C. Behcet's syndrome
    D. Pericarditis, acute or recurrent
    E. Post-pericardiotomy syndrome

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has not experienced a major cardiovascular event (e.g., stroke, myocardial infarction); **OR**
    - If member has experienced a major cardiovascular event, the provider attests continuation of therapy is medically necessary AND clinical rationale of medical necessity has been provided and reviewed by a Moda Health clinician; **AND**
IV. Member will continue background therapy with maximally tolerated statin (e.g., atorvastatin, rosuvastatin, simvastatin, etc.); **OR**

- If statin intolerant, member will continue background therapy with maximally tolerated non-statin lipid-lowering agents (e.g., ezetimibe, Repatha, Praluent, fenofibric acid, etc.) unless contraindicated or not tolerated; **AND**

V. Treatment with colchicine 0.6mg (Colcrys) has been ineffective, contraindicated, or not tolerated

Supporting Evidence

I. Colchicine (Lodoco) 0.5mg tablets was evaluated in one pivotal phase 3, randomized, double-blind, placebo-controlled trial (LoDoCo2) to evaluate the safety and efficacy in patients with chronic coronary artery disease in 5,522 adult patients aged 35 to 82 years old. The primary composite endpoint of time to first cardiovascular (CV) death, spontaneous (non-procedural) myocardial infarction (MI), ischemic stroke, or ischemia-driven coronary revascularization was statistically significant compared to placebo, with an incidence rate per 100 person-years of 2.5 and 3.6 events, respectively [(hazard ratio, 0.69; 95% confidence interval [CI], 0.57 to 0.83; P<0.001)]. The key secondary endpoint of composite of CV death, spontaneous MI, or ischemic stroke was also met, with incidence rates of 1.5 and 2.1 events per 100 person-years in the colchicine and placebo groups, respectively [hazard ratio, 0.72; 95% CI, 0.57 to 0.92; P = 0.007)].

II. The most commonly adverse event reported during the LoDoCo2 clinical trial was myalgia, which occurred in 21.2% of colchicine (Lodoco) treated patients and 18.5% of patients in the placebo group. Colchicine (Lodoco) also carries labeled contraindications for use in patients with renal failure (e.g., CrCl <15 mL/min), severe hepatic impairment, and pre-existing blood dyscrasias due to higher risk of toxicity in this population.

III. Insight from cardiology specialists indicate that diagnosis of clinical ASCVD in the absence of a cardiovascular event can be achieved by angiography, ischemia on stress test, or stenosis of 50% or more using other imaging techniques. The inclusion trial for the LoDoCo2 clinical trial also included patients who had proven coronary disease by a Coronary Artery Calcium score ≥400; Although coronary calcium scores are not typically used as a diagnostic tool for ASCVD, this could be accepted as a verification of ASCVD based on the population colchicine (Lodoco) was studied in.

IV. Emerging data has shown that inflammation, in addition to hyperlipidemia, contributes to the risk of future atherothrombotic events. A collaborative analysis of three randomized trials observed that inflammation of high-sensitivity C-reactive protein (CRP) was a stronger predictor for risk of future CV events and death than cholesterol assessed by low-density lipoprotein cholesterol (LDL-C). The 2021 ESC guidelines for secondary prevention of CV events indicates that colchicine is an appropriate therapy to consider in patients with established ASCVD (secondary prevention) who remain at very high risk of future CV events, particularly if other risk factors are insufficiently controlled or if recurrent CV events occur under optimal therapy (i.e., controlled blood pressure, controlled hyperlipidemia, etc.). Guidelines indicate that statins

continue to provide the strongest level LDLC reduction and protection against CV events; however, in those who do not tolerate statin therapy, use of other anti-hyperlipidemic therapy is appropriate to reduce LDL.

V. Although colchicine 0.6mg tablet has not specifically been studied in the setting of CV prevention, this is likely due to the lack of availability of this formulation in the geography of the clinical trial (i.e., Europe). There is no anticipated clinically meaningful difference in the effect of colchicine 0.5mg (Lodoco) compared to 0.6mg; therefore, the off-label use of colchicine 0.6mg tablets is required as cost-effective step therapy.

Investigational or Not Medically Necessary Uses

I. Colchicine (Lodoco) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Gout
      i. Colchicine 0.6mg (Colcrys) is currently FDA-approved for the treatment of gout. Although there is no anticipated clinically meaningful difference in the effect of colchicine 0.5mg (Lodoco) compared to 0.6mg, therapies are only considered medically necessary when prescription drug or prescription drug dose recommended for this condition is cost-effective compared to alternative interventions, including no intervention. Since colchicine 0.6mg tablets are considered a cost-effective therapy, use of colchicine 0.5mg (Lodoco) is considered not medically necessary for this indication.
   B. Familial Mediterranean fever
      i. Colchicine 0.6mg (Colcrys) is currently FDA-approved for the treatment of familial mediterranean fever. Although there is no anticipated clinically meaningful difference in the effect of colchicine 0.5mg (Lodoco) compared to 0.6mg, therapies are only considered medically necessary when prescription drug or prescription drug dose recommended for this condition is cost-effective compared to alternative interventions, including no intervention. Since colchicine 0.6mg tablets are considered a cost-effective therapy, use of colchicine 0.5mg (Lodoco) is considered not medically necessary for this indication.
   C. Actinic Keratosis
   D. Amyloidosis
   E. Behcet's syndrome
   F. Pericarditis, acute or recurrent
   G. Post-pericardiotomy syndrome

Appendix

I. Table 1: Examples of CYP3A4 and P-gp inhibitors

Strong CYP3A4 inhibitors	Atazanavir
	Clarithromycin
	Darunavir/ritonavir
	Indinavir
	Itraconazole
	Ketoconazole
	Lopinavir/ritonavir
	Nefazodone
	Nelfinavir
	Ritonavir
	Saquinavir
	Telithromycin
	Tipranavir/ritonavir
Moderate CYP3A4 inhibitors	Amprenavir
	Aprepitant
	Diltiazem
	Erythromycin
	Fluconazole
	Fosamprenavir (prodrug of amprenavir)
	Verapamil
P-gp inhibitors	Cyclosporine
	Ranolazine

References

1. LODOCO. Package inset. Agepha Pharma USA, LLC; June 2023.
2. Nidorf SM, Fiolet ATL, Mosterd A, et al. Colchicine in Patients with Chronic Coronary Disease. N Engl J Med. 2020;383(19):1838-1847. doi:10.1056/NEJMoa2021372
3. Ridker PM, Bhatt DL, Pradhan AD, et al. Inflammation and cholesterol as predictors of cardiovascular events among patients receiving statin therapy: a collaborative analysis of three randomized trials. *Lancet* 2023; 401: 1293-301.
4. IPD Analytics. RX Insights: Cardiovascular – Lodoco for Cardiovascular Risk Reduction. Published July 2023.
5. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. European Heart Journal (2021); 42, 3227-3337.
6. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease. *Circulation*. 2019; 140: e596-e646.

Related Policies

Policy Name	Disease state
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitor Policy	Atherosclerotic cardiovascular disease (ASCVD)
Bempedoic acid, bempedoic acid/ezetimibe (Nexletol™, Nexlizet™)	As an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with established atherosclerotic cardiovascular disease who require additional lowering of LDL-C

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	09/2023