Clinical Policy: Colchicine (Colcrys)
Reference Number: CP.PPA.11
Effective Date: 05/11
Last Review Date: 05/176
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Colchicine (Colcrys®) is an alkaloid.

FDA approved indication
Colcrys is indicated:
- For the prophylaxis and treatment of gout flares in adults
- For the treatment of ffamilial Mediterranean fever in adults and children 4 years or older

Limitation of use: Colcrys is not an analgesic medication and should not be used to treat pain from other causes.

Policy/Criteria
Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Colcrys is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Familial Mediterranean Fever (FMF) (must meet all)**:**
1. Diagnosis of fFamilial Mediterranean fFever (FMF);
2. ~~Age ≥ 4 years;~~
3.2. ~~Request~~Dose does not exceed 2.4 mg per ~~/~~day (4 tablets per day).

Approval duration: 12 months

B. Gout – Treatment of Acute Attack (must meet all)**:**
1. Diagnosis of acute gout attack;
2. Age ≥ 16 years;
3. Failure of a ~~full dose~~ nonsteroidal anti-inflammatory drug (NSAID) (e.g., naproxen, indomethacin, sulindac) within the last 30 days unless m~~M~~ember has one of the following contraindications ~~to NSAID use~~:
   a. Heart failure or uncontrolled hypertension;
   b. Current use of ~~-~~an anticoagulant (aspirin, warfarin, low molecular weight heparin, direct thrombin inhibitors, factor Xa inhibitors, and clopidogrel);
   c. Active duodenal or gastric ulcer (not gastroesophageal reflux disease [GERD]);
   d. Current use of~~-~~ corticosteroid;
   e. Chronic kidney disease with ~~creatinine clearance (~~CrCl~~)~~ ~~of less than~~<~~ 60 mL/min per 1.73 m^2;

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4. ~~Request~~ Dose does not exceed 1.8 mg for the initial dose (3 tablets) followed by 1.2 mg per ~~/~~day (2 tablets per day) thereafter.

Approval duration: 2 weeks (no more than 30 tablets)

C. Gout – Anti-Inflammatory Prophylaxis ~~with Hyperuricemia/Chronic Use~~ (must meet all)**:**

~~1. Age ≥ 16 years;~~
~~2. Member meets at least one of the following conditions:~~
~~3.~~1. Diagnosis of gout with clinical evidence of disease activity indicated by at least one of the following~~and failure of adherent use of allopurinol at maximum tolerated doses for ≥ 3 consecutive months within the last 6 months, unless contraindicated.~~:~~
   a. 1 or more tophi detected on physical examination;
   b. Recent acute gout attacks;
   c. Chronic gouty arthritis; ~~Diagnosis of gout with contraindication to allopurinol, and failure of ≥ 3 consecutive months of therapy with of colchicine/probenecid at maximum tolerated doses in the last 6 months, unless contraindicated;~~
   ~~a.~~
   ~~b. Diagnosis of hyperuricemia and will be initiating/ has recently initiated therapy with a urate-lowering medication, within a 6 month period;~~
   ~~c.~~d. Current (within ~~prior~~ the last 30 days) serum urate ≥ 6.~~5~~0 mg/dL;
2. Age ≥ 16 years;
3. Member is currently taking or will be initiating a urate-lowering therapy (e.g., allopurinol, probenecid) within the next 6 months, unless contraindicated;
~~Failure or clinically significant adverse effect to an NSAID, unless~~
4. ~~Request~~Dose does not exceed 1.2 mg per~~/~~ day (2 tablets per day).

Approval duration: 6 months

D. Pericarditis (off-label) (must meet all)**:**

1. Diagnosis of pericarditis classified as one of the following (a or b):
   a. Acute (new onset);
   b. Recurrent (recurring after a symptom-free interval of at least 4 weeks);
2. Prescribed by or in consultation with a cardiologist;
3. Colchicine will be used concurrently with an NSAID;
4. Dose does not exceed 1.2 mg per day (2 tablets per day).

Approval duration: 3 months for acute pericarditis; 6 months for recurrent pericarditis

~~D.~~E. Other diagnoses/indications

1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. ~~All Indications~~FMF (must meet all)**:**

~~1. Member is currently receiving colchicine for chronic treatment of gout (not for hyperuricemia/acute gout flare) or FMF via centene benefit;~~

~~1. If colchicine will be used for gout prophylaxis or acute gout attack, member must meet initial approval criteria for these indications;~~
1. ~~Request does not exceed 2.4mg/day for FMF and 1.2mg/day for gout.~~Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy (e.g., reduction/normalization of C-reactive protein (CRP) or serum amyloid A (SAA) levels; reduction of flare frequency, symptom severity, or duration);
~~2.~~3. If request is for a dose increase, new dose does not exceed 2.4 mg per day (4 tablets per day).

Approval duration: 12 months

B. Gout – Treatment of Acute Attack (must meet all)**:**
1. Member meets all initial approval criteria.

Approval duration: 2 weeks (no more than 30 tablets)

C. Gout – Anti-Inflammatory Prophylaxis (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is currently taking a urate-lowering therapy (e.g., allopurinol, probenecid) at up to maximally indicated doses, unless contraindicated;
3. Documentation of positive response to therapy;
4. If request is for a dose increase, new dose does not exceed 1.2 mg per day (2 tablets per day).

Approval duration: 6 ~~12~~ months

D. Pericarditis (off-label) (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. Pericarditis has recurred after a symptom-free interval of at least 4 weeks since the last request for colchicine;
4. Colchicine will be used concurrently with an NSAID;
5. If request is for a dose increase, new dose does not exceed 1.2 mg per day (2 tablets per day).

Approval duration: 6 months

~~B.~~**E. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 12~~12~~ months or duration of request (~~,~~whichever is less)

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CrCl: creatinine clearance
FDA: Food and Drug Administration
FMF: familial Mediterranean fever
GERD: gastroesophageal reflux disease
NSAID: nonsteroidal anti-inflammatory drug

Appendix B: Inadequate Response to Acute Gout Treatment
Per the American College of Rheumatology 2012 guidelines for the management of gout, an inadequate response to therapy is defined as < 20% improvement in pain score within 24 hours or < 50% improvement in pain score at ≥ 50%.

~~V.~~ V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
FMF	*4-6 years*: 0.3 mg to 1.8 mg daily *6-12 years*: 0.9 mg to 1.8 mg daily ≥ *12 years*: 1.2 mg to 2.4 mg daily	2.4 mg/day
Prophylaxis of gout flares	0.6 mg once or twice daily	1.2 mg/day
Treatment of gout flares	1.2 mg at first sign of flare, followed by 0.6 mg one hour later	1.8 mg/treatment
Pericarditis (off-label)	*< 70 kg*: 0.5 mg daily* *≥ 70 kg*: 0.5 mg twice daily*	1 mg/day*

** This is the recommended dosing per the European Society of Cardiology guidelines. Note that the 0.5 mg dosage form is not available in the US.*

VI. Product Availability

Tablet: 0.6 mg

VII. Workflow Document

CP.PPA.11
Colchicine (Colcrys)

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VIII. References

1. ~~Colchicine Monograph. Clinical Pharmacology. Accessed May 2016. http://www.clinicalpharmacology-ip.com~~ Colcrys Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; December 2015. Available at: www.colcrys.com. Accessed January 12, 2017.
2. Khanna D, Fitzgerald JD, Khanna PJ, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systemic nonpharmacologic and pharmacologic approaches to hyperuricemia. Arthritis Care & Research. 2012; 64(10): 1431-1446.
2. ~~Becker MK. Treatment of acute gout. Schumacher RH (Ed), UpToDate. Accessed May 2016.~~
3. ~~Becker MK. Prevention of recurrent gout. Schumacher RH (Ed), UpToDate. Accessed May 2016.~~
3. Khanna D, Khanna PJ, Fitzgerald JD, et al. ~~American College of Rheumatology.~~ 2012 American College of Rheumatology g~~G~~uidelines for m~~M~~anagement of ~~G~~gout. Part 2: ~~T~~therapy and ~~A~~antiinflammatory p~~P~~rophylaxis of a~~A~~cute g~~G~~outy a~~A~~rthritis. Arthritis Care & Research. 2012; 64(10): 1447-1461~~Available at: http://www.rheumatology.org/Portals/0/Files/Gout_Part_2_ACR-12.pdf. Accessed May 2016~~.
4. Ozen S, Demirkaya E, Erer B, et al. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis. 2016; 75(4): 644-651.
5. Lilly LS. Clinician update: treatment of acute and recurrent idiopathic pericarditis. Circulation. 2013; 127: 1723-1726.
6. Adler Y, Charron P, Imazio M, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases: the Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2015; 36(42): 2921-2964.
~~4.~~7. Bach DS. Latest in cardiology: 2015 ESC guidelines for pericardial disease. American College of Cardiology. Published October 30, 2015. Available at: http://www.acc.org/latest-in-cardiology/ten-points-to-remember/2015/10/30/12/01/2015-esc-guidelines-for-the-diagnosis-and-management-of-pericardial-diseases. Accessed February 6, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added the following section in the Criteria for Approval: "Information needed for approval: A. Baseline Serum Urate Levels B. Recent Serum Urate Levels C. History of acute gouty flares Added warnings on drug interactions with CYP3A4 inhibitors to the Special Instructions.	05/12	05/12
Special instruction: Added "hepatic disease; renal impairment/disease contraindications" and "Dosage adjustments are needed in patients with normal renal and hepatic function taking interacting medications"	05/13	05/13

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Criteria for approval: Added "Concomitant use upon initiation of allopurinol therapy" for gout prophylaxis and noted "3 months with initiation of allopurinol therapy" in the initial approval. Criteria for approval: Added "Baseline CBC and Alkaline phosphatase" to information needed for approval because colchicine has been associated with decreased blood count and hepatic enzyme elevation. Added: "severe adverse reaction and contraindication" to the definition of trial and failure. Note: Added "and adolescents" Description: Rewording and added that "Colchicine is not effective for other types of pain. It is not an analgesic and does not affect uric acid clearance." Updated references		
Updated references	05/15	05/15
Converted to new template Modified criteria specify required time frame for allopurinol use to be considered a failure; Modified criteria to require use of colchicine/probenecid in patients who cannot use allopurinol, added a specified time frame for use to be considered a failure Added criteria for treatment of acute gout attack with quantity limit	08/15	08/15
Modify the criteria for chronic use of gout to allow for gout prophylaxis in members with hyperuricemia , initiating therapy with a urate lowering medication and changed approval duration to 6 months; Specified the maximum allowable dose for FMF and gout; Modify renewal criteria to identify the diagnoses for which continued treatment may be approved. References updated	05/16	05/16

~~Clinical changes made to criteria~~
- Treatment of gout: added option for failure of NSAID (per ACR guidelines: those with inadequate response to initial therapy should be switched to alternate monotherapy)
- Prophylaxis of gout:
  - Removed diagnosis of hyperuricemia as colchicine is indicated for gout and does not alter urate levels
  - Added requirement for evidence of active gout and modified serum urate level from 6.5 mg/dL to 6 mg/dL per ACR guideline minimum target
	03~~1~~/17	05/17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
- Removed requirement for trial/failure of urate lowering therapies (per ACR guidelines: colchicine is 1st line for anti-inflammatory prophylaxis and should be used with or just prior to initiating ULT) - Continuation: added requirement for use of ULT; modified approval duration to 6 months Pericarditis: developed criteria set for this off-label indication (per ESC guidelines, which were supported by ACC, and per AHA clinician update: colchicine is a 1st line agent that can be added to conventional NSAID therapy to improve response to therapy, increase remission, and reduce recurrence) *Note: the maximum dose enforced in this criteria reflects the available 0.6 mg dosage form and allows up to 2 tablets per day* - ~~Non-clinical changes made to criteria~~ - Converted to new template - Removed age restriction for FMF per updated template; age restriction is maintained for gout indications per package insert and per age edits currently in place - Added quantity limit for gout treatment (max 30 tablets) - Continuation: separated into individual criteria sets; added requirement for documentation of positive response for FMF and anti-inflammatory prophylaxis of gout - Updated references		

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the

administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.