Clinical Policy: Febuxostat (Uloric)

Reference Number: CP.PMN.57
Effective Date: 08.01.13
Last Review Date: 02.22
Line of Business: HIM, Medicaid

Revision Log

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

Description

Febuxostat (Uloric®) is a xanthine oxidase inhibitor.

FDA Approved Indication(s)

Uloric is indicated for the chronic management of hyperuricemia in patients with gout who have an inadequate response to a maximally titrated dose of allopurinol, who are intolerant to allopurinol, or for whom treatment with allopurinol is not advisable.

Limitation(s) of use: Uloric is not recommended for the treatment of asymptomatic hyperuricemia.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

I. Initial Approval Criteria

A. Hyperuricemia (must meet all)**:**

1. Diagnosis of hyperuricemia associated with gout;
2. Current (within the last 30 days) serum urate ≥ 6 mg/dL;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. Failure of combination urate-lowering therapy (allopurinol and probenecid **OR** allopurinol and probenecid/colchicine) at up to maximally tolerated doses;
   b. Member has intolerance or contraindication to combination urate-lowering therapy, and failure of allopurinol or probenecid, at up to maximally tolerated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
5. Uloric is not prescribed concurrently with azathioprine or mercaptopurine;
6. Dose does not exceed 80 mg (1 tablet) per day.

Approval duration:
HIM – 12 months
Medicaid – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Hyperuricemia (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters:
   a. Reduced frequency of gout attacks;
   b. Serum urate level < 6 mg/dL;
3. If request is for a dose increase, new dose does not exceed 80 mg (1 tablet) per day.

Approval duration:
HIM – 12 months
Medicaid – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy;
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
allopurinol (Zyloprim®)	100 mg PO QD; may be increased by 100 mg every 2 to 4 weeks until serum	800 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	urate concentration is ≤ 6 mg/dL or until maximum of 800 mg/day is reached	
probenecid	250 mg PO BID for the first week, then 500 mg PO BID	2 g/day
colchicine (Colcrys®, Mitigare®)	0.5 mg to 1 mg/day PO QD or BID	1.8 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): patients being treated with azathioprine or mercaptopurine
- Boxed warning(s): none reported

Appendix D: General Information

- In November 2017, the FDA MedWatch issued an alert to the public regarding the preliminary results from a safety clinical trial that showed an increased risk of heart-related death with febuxostat compared to allopurinol. The febuxostat drug labels already carried a Warning and Precaution about cardiovascular events because the clinical trials conducted before approval showed a higher rate of heart-related problems in patients treated with febuxostat compared to allopurinol. These problems included heart attacks, strokes, and heart-related deaths. As a result, the FDA required an additional safety clinical trial after the drug was approved and on the market to better understand these differences, and that trial result continued to show increased heart-related death with febuxostat.
- Per ACR, the minimum threshold for all patients on urate-lowering therapy is < 6.8 mg/dL. For patients with non-palpable, non-tophaceous disease in long-term clinical remission (for several years) and whose serum urate level is < 6.8 mg/dL, there is not a need for drug therapy to be up titrated for the sole purpose of reaching a goal of serum urate < 6 mg/dL. However, for all other patients with gout and recent symptoms of gout or tophi, the recommended target goal is a serum urate level < 6 mg/dL.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hyperuricemia in patients with gout	40 mg or 80 mg PO QD	80 mg/day

VI. Product Availability

Tablets: 40 mg, 80 mg

VII. References

1. Uloric Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc; February 2019. Available at: www.uloric.com. Accessed November 20, 2021.
2. Khanna D, Fitzgerald JD, Khanna PJ, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. Arthritis Care Res 2012; 64(10): 1431-1446.

3. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care & Research. June 2020; 0 (0): 1-17.
4. Richette P, Doherty M, Pascual E, et al. 2016 Updated EULAR evidence-based recommendations for the treatment of gout. Ann Rhem Dis 2016; 0:1–14. doi:10.1136/annrheumdis-2016-209707.
5. Qaseem A, Harris RP, Forciea MA, et al. Management of acute and recurrent gout: A clinical practice guideline from the American College of Physicians. Ann Intern Med. 2017; 166(1): 58-68.
6. Fitzgerald JD, Mikuls TR, Neogi T, et al. Development of the American College of Rheumatology electronic clinical quality measures for gout. Arthritis Care & Research. 2018;70(5):659-671. doi: 10.1002/acr.23500.
7. Fitzgerald JD, Terkeltaub R, Khanna D, Khanna P. July 2018 author statement explaining different serum urate targets in 2012 ACR gout guideline and 2018 ACR electronic clinical quality measures for gout. American College of Rheumatology. Available at: https://www.rheumatology.org/Portals/0/Files/ACR-Gout-Guideline-Author-Statement.pdf.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: policies combined for HIM and Medicaid; added age limit following the safety guidance endorsed by Medical Affairs; added drug interactions with azathioprine and mercaptopurine following the safety guidance; References reviewed and updated.	11.20.17	02.18
Medicaid: changed approval duration to length of benefit	03.04.18	05.18
1Q 2019 annual review: removed requirement for trial within the last 6 months; modified max dose requirement to max dose tolerated; no significant changes from previously approved corporate policy; references reviewed and updated.	10.30.18	02.19
No significant changes: added updated FDA indication: Uloric is indicated for use after inadequate response, intolerance, or unable to take allopurinol; references reviewed and updated.	03.08.19	
No significant changes: clarified combination urate-lowering therapy requirement to require monotherapy if member is unable to use combination regimen.	05.02.19	
1Q 2020 annual review: no significant changes; updated verbiage for tiered redirection; references reviewed and updated.	10.28.19	02.20
1Q 2021 annual review: no significant changes; added examples of positive response included in Appendix D to section II; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.16.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated	11.20.21	02.22

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.

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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.