Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Prior Authorization Criteria Update: Gout

Date of Review: February 2020

Purpose of the Update:
In 2017, a safety study showed an increased risk of heart-related death in patients randomized to febuxostat compared to allopurinol.[1] In 2018 results from the Cardiovascular Safety of Febuxostat and Allopurinol in Patients with Gout and Cardiovascular Morbidities (CARES) trial were made available and were analyzed by the Food and Drug Administration (FDA). Labeling was changed in 2019 with the addition of a boxed warning to febuxostat prescribing information which identified an increase in risk of heart-related deaths and death from all-causes with febuxostat use.[2]

The CARES trial was a multicenter, double-blind, noninferiority trial in patients (n=6190) with gout and cardiovascular (CV) disease.[3] There were 15 heart-related deaths per 1000 patients treated with febuxostat compared to 11 deaths per 1000 patients treated with allopurinol over one year.[3] All-cause death was 26 per 1000 patients treated with febuxostat compared to 22 per 1000 patients treated with allopurinol for one year. The primary composite endpoint (CV death, nonfatal myocardial infarction, nonfatal stroke, or unstable angina with urgent revascularization) was similar between febuxostat and allopurinol, 10.8% versus 10.4%.[3] Subgroup analysis demonstrated no clear evidence of patients that may benefit or be at increased risk of harm from febuxostat therapy. It is recommended that febuxostat should be reserved for those who failed or cannot take allopurinol.

Boxed warning: Cardiovascular death
- Gout patients with established cardiovascular (CV) disease treated with febuxostat had a higher rate of CV death compared to those treated with allopurinol in a CV outcomes study.[4]
- Consider the risks and benefits of febuxostat when deciding to prescribe or continue patients on therapy. Febuxostat should only be used in patients 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.[4]

Utilization: In quarter 3 of 2019, there were 2 claims for febuxostat. Allopurinol and cholchicine/probenecid are the preferred treatments for the class.

Recommendation:
1. After review, the committee voted to reject the addition of new febuxostat prior authorization (PA) criteria to confirm that the patient has been accessed for CV risk and that the benefits outweigh the risks.

References:

1. Food and Drug Administration. FDA to evaluate increased risk of heart-related death and death from all causes with the gout medicine febuxostat (Uloric). 15 November 2017. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-evaluate-increased-risk-heart-related-death-and-death-all-causes. Accessed 8 November 2019.
2. Food and Drug Administration. FDA adds boxed warning for increased risk of death with gout medicine Uloric (febuxostat). 21 February 2019. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-adds-boxed-warning-increased-risk-death-gout-medicine-uloric-febuxostat. Accessed 8 November 2019.
3. White W, Saag K, Becker M, et al. Cardiovascular safety of febuxostat or allopurinol in patients with gout. NEJM 2018;378:1200-10.
4. Uloric (febuxostat) [product information]. Deerfield, IL: Takeda Pharmaceuticals America, Inc., February 2019.

Appendix 1. Proposed Prior Authorization Criteria

Agents for Gout

Goal(s):

- To provide evidenced-based step-therapy for the treatment of acute gout flares, prophylaxis of gout and chronic gout.

Length of Authorization:

- Up to 12 months

Requires PA:

- Non-preferred drugs

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Will the provider switch to a preferred product? Note: Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics Committee. Preferred products are available without a PA	**Yes:** Inform prescriber of covered alternatives in the class	**No:** Go to #3
3. Is the request for colchicine?	**Yes:** Go to #4	**No:** Go to #5
4. Has the patient tried and failed NSAID therapy or have contraindications to NSAIDs or is a candidate for combination therapy (i.e., multiple joint involvement and severe pain)?	**Yes:** Approve for 12 months	**No:** Pass to RPh. Deny; recommend trial of NSAID
5. Is the request for febuxostat?	**Yes:** Go to #6	**No:** Go to #
6. Has the patient tried and failed allopurinol or has contraindications to allopurinol?	**Yes:** Approve for 12 months	**NO:** Pass to RPh. Deny; recommend trial of allopurinol
7. Is the request for lesinurad?	**Yes:** Go to #	**No:** Pass to RPh. Deny; Medical appropriateness
8. Is the patient concomitantly taking a xanthine oxidase inhibitor (e.g., allopurinol, febuxostat)?	**Yes:** Go to #	**No:** Pass to RPh. Deny; medical appropriateness
9. Is the estimated CrCl < 45 mL/min?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Approve for 12 months at a maximum daily dose of 200 mg

Appendix 2: Search Strategy

1. FDA boxed warnings from 1/01/2015 – 11/14/2019
2. FDA drug safety communications 1/01/2015 – 11/14/2019