MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY:	Gout	**P&T DATE:**	5/24/2022
THERAPEUTIC CLASS:	Rheumatologic Disorders	**REVIEW HISTORY:** (MONTH/YEAR)	2/21, 2/20, 2/19, 2/18, 2/17, 11/15, 5/11, 5/09
LOB AFFECTED:	MCL		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

Effective 1/1/2022, the Pharmacy Benefit is regulated by Medi-Cal Rx. Please visit https://medi-calrx.dhcs.ca.gov/home/ for portal access, formulary details, pharmacy network information, and updates to the pharmacy benefit.

OVERVIEW

Gout is a disorder derived from an excess amount of uric acid in the body that typically presents as acute episodic arthritis but can manifest as chronic arthritis as well. Although there is advanced understanding of how to treat gout, there are still significant shortfalls in gout management due to shortfalls in patient education and adherence. The American College of Rheumatology has developed recommendations for the overall management and treatment of not only active gout flares, but also for prophylaxis of gouty attacks. This review will examine the management guidelines of gout, the currently available agents for gout management, and their coverage criteria (please note information regarding anti-inflammatory agents can be found in the non-opioid pain management policy).

Table 1: Available Agents for the Management of Gout *(Current as of 3/2022)*

Class	Drug	CPT Code	Available Strengths	Pharmacy Benefit	Medical Benefit
Anti-Gout Agent	Colchicine (Colcrys)	--	*Tablet:* 0.6mg	Yes	No
NSAIDS	Celecoxib (Celebrex)	--	*Capsule:* 50mg, 100mg, 200mg, 400mg	Yes	No
	Indomethacin (Indocin)	--	*Capsule IR:* 25mg, 50mg	Yes	No
		--	*Capsule ER:* 75mg		
		--	*Suppository:* 50mg		
		--	*Suspension:* 25mg/5mL		
	Sulindac (Clinoril)	--	*Tablet:* 150mg, 200mg	Yes	No
	Naproxen (Naprosyn)	--	*Tablet IR:* 250mg, 375mg, 500mg, 550mg	Yes	No
		--	*Tablet DR:* 500mg		
		--	*Suspension:* 125mg/5mL		
Oral Corticosteroids*	Dexamethasone (DexPak)	--	*Tablet:* 0.5mg, 0.75mg, 1mg, 1.5mg, 2mg, 4mg, 6mg	Yes	No
			Solution: 0.5mg/5mL		
	Prednisone (Deltasone)	--	*Tablet:* 1mg, 2.5mg, 5mg, 10mg, 20mg, 50mg	Yes	No
			Solution: 5mg/5mL		
	Prednisolone (Millipred)	--	*Tablet*: 5mg	Yes	No
			Solution/Syrup: 5mg/5mL, 15mg/5mL		
	Methylprednisolone (Medrol)	--	*Tablet:* 2mg, 4mg, 8mg, 16mg, 32mg	Yes	No
Uricosuric Agent	Probenecid	--	*Tablet:* 500mg	Yes	No
Uric Acid Transporter 1 Inhibitor	Lesinurad (Zurampic)	--	Tablets: 200mg	Discontinued	No

Xanthine Oxidase Inhibitors	Allopurinol (Zyloprim)	--	100mg, 300mg	Yes	No
	Febuxostat (Uloric)	--	40mg, 80 mg	Yes	No
Urate-Oxidase (Recombinant) Enzyme	Pegloticase (Krystexxa)	J2507 INJECTION, PEGLOTICASE, 1 MG	8mg/mL	Yes	Yes
Combinations	Colchicine/Probenecid	--	0.5mg/500mg	Yes	No
UA Transporter inhibitor/XOI	Lesinurad/Allopurinol (Duzallo)	--	200mg/300mg, 200mg/200mg	Discontinued	No

Clinical Justification:

Urate lowering therapy (ULT) is a primary focus in the management of gout. Although both Allopurinol and Febuxostat are recommended as first line pharmacologic ULT, Febuxostat has not been shown to be more cost effective than Allopurinol. However, due to the possibility of a severe allergic reaction to Allopurinol in certain subsets of patients, Febuxostat is available for patients with positive HLA-B*5801 alleles. In cases where monotherapy with a xanthine oxidase inhibitor is insufficient to reaching the serum urate target, the addition of a uricosuric agent is appropriate. During initiation of prophylaxis with ULT, colchicine may be used at 0.6mg twice daily dosing for up to 6 months while agents such as allopurinol are titrated to optimal doses.

In regard to treating or preventing acute gouty arthritis attacks, recommended first line agents include colchicine, NSAIDS, or glucocorticoids. The dosing of colchicine during an acute gouty attack is a maximum of 1.8 mg over 1 hour, followed by 0.6 mg QD to BID until the attack has resolved.

Regarding other ULT agents, Zurampic (Lesinurad) and Duzallo (Lesinurad/Allopurinol) have been discontinued in the U.S. while Krystexxa (Pegloticase) is indicated for use in patient's refractory to conventional therapy such as xanthine oxidase inhibitors and uricosurics. The benefits of using Kystexxa only outweigh the safety risks and cost in patients with severe disease (patients who have frequent gout flares or nonresolving subcutaneous tophi).

Triage:

- ***Appropriate diagnosis***
- ***Anti-gout/uricosuric/xanthine oxidase inhibitor medications tried***
- ***Clinical documentation/labs presenting gout history/significant allergic reactions***

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Urate-Oxidase (Recombinant) Enzyme

Pegloticase (Krystexxa)

- ❒ **Coverage Criteria:** Krystexxa (pegloticase) is reserved for patients with all of the following:
  - Patient has one of the following:
    i. At least 2 gout flares per year that were inadequately controlled by colchicine, NSAIDs, or corticosteroids; OR
    ii. At least 1 non-resolving gout tophus.
  - Documented contraindication, intolerance, or treatment failure (inability to reduce serum uric acid to < 6 mg/dL, frequent gout flares, or nonresolving tophi) to three months of either of the following:
    i. Allopurinol at 800mg/day. If unable to tolerate allopurinol at maximum dosing, febuxostat at 80mg/day is required; OR
    ii. Maximum medically appropriate xanthine oxidase inhibitor AND uricosuric agent.
  - Must be prescribed by rheumatology, nephrology, or podiatry.
- ❒ **Limits:** N/A
- ❒ **Required Information for Approval:** Prescription history or medical authorization history showing at least 1) a three-month trial of allopurinol 800mg/day or febuxostat 80mg/day or 2) a three-month trial of maximum medically-appropriate xanthine oxidase inhibitor and uricosuric agent except if intolerable or contraindicated.
- ❒ **Notes:** Providers should not use concurrent oral antihyperuricemic agents. Patients at increased risk for G6PD deficiency (eg, African, Mediterranean [including Southern European and Middle Eastern], and Southern Asian ancestry) should be screened prior to initiation of therapy.

REFERENCES

1. Khanna D, FitzGeral JD, Khanna PP, 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 (Hoboken). 2012 Oct; 64(10): 1447-1461.
2. Khanna D, Khanna PP, FitzGeral JD, et al. 2012 American College of Rheumatology Guidelines for Management of Gout. Part 2: Therapy and Antiinflammatory Prophylaxis of Acute Gouty Arthritis. Arthritis Care Res (Hoboken). 2012 Oct; 64(10): 1447-1461.
3. Duzallo [package insert]. Ironwood Pharmaceuticals Inc, Cambridge, MA; September 2017. http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125293s089lbl.pdf. Accessed February 12, 2017.
4. Zurampic [package insert]. Astra Zeneca Pharmaceuticals LP, Wilmington, DE; December 2015. http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207988lbl.pdf. Accessed February 13,2017.
5. Shekelle PG, Newberry SJ, FitzGerald JD, Motala A, O'Hanlon CE, Tariq A, et al. Management of Gout: A Systematic Review in Support of an American College of Physicians Clinical Practice Guideline. Ann Intern Med. 2017;166:37-51.
6. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Annals of the Rheumatic Diseases 2017;76:29-42.
7. Sundy JS, Becker MA, Baraf HS, Barkhuizen A, Moreland LW, Huang W, Waltrip RW 2nd, Maroli AN, Horowitz Z; Pegloticase Phase 2 Study Investigators Reduction of plasma urate levels following treatment with multiple doses of pegloticase (polyethylene glycol-conjugated uricase) in patients with treatment-failure gout: results of a phase II randomized study. *Arthritis and Rheumatism* 2008 Sep;58(9):2882-91.
8. Sundy JS, Baraf HSB, Yood RA, Edwards NL, Gutierrez-Urena SR, Treadwell EL, Vázquez-Mellado J, White WB, Lipsky PE, Horowitz Z, Huang W, Maroli AN, Waltrip RW, Hamburger SA, Becker MA. Efficacy and Tolerability of Pegloticase for the Treatment of Chronic Gout in Patients Refractory to Conventional Treatment Two Randomized Controlled Trials. *JAMA.* 2011;306(7):711-720.
9. Saag, K. G., Fitz-Patrick, D., Kopicko, J., Fung, M., Bhakta, N., Adler, S., Storgard, C., Baumgartner, S. and Becker, M. A. (2017), Lesinurad Combined With Allopurinol: A Randomized, Double-Blind, Placebo-Controlled Study in Gout

Patients With an Inadequate Response to Standard-of-Care Allopurinol (a US-Based Study). Arthritis & Rheumatology, 69: 203–212.
10. Bardin T, Keenan RT, Khanna PP, *et al.* Lesinurad in combination with allopurinol: a randomised, double-blind, placebo-controlled study in patients with gout with inadequate response to standard of care (the multinational CLEAR 2 study). *Annals of the Rheumatic Diseases* Published Online First: 07 November 2016. doi: 10.1136/annrheumdis-2016-209213.
11. Dalbeth N, Jones G, Terkeltaub R, *et al.* SAT0329 Lesinurad, A Novel Selective Uric Acid Reabsorption Inhibitor, in Combination with Febuxostat, in Patients with Tophaceous Gout: the Crystal Phase III Clinical Trial. *Annals of the Rheumatic Diseases* 2015;**74:**778.
12. Federal Drug Administration. Uloric (febuxostat): Drug Safety Communication-FDA to Evaluate Increased Risk of Heart-related Death. 11/15/2017
13. Colcrys [package insert]. Takeda Pharmaceuticals America, Inc., Deerfield, IL; December 2015.
14. FitzGerald, JD, et al. 2020 American College of Rheumatology Guidelines for Management of Gout. Arthritis Care Res (Hoboken). 2020 June; 72(6): 744-760.
15. Krystexxa (pegloticase) [package insert]. Lake Forect, IL: Horizon Pharma USA, Inc.; 2016.

REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Uloric – Febuxostat v3 5-13-09.docx	5/2009	Allen Shek PharmD BCPS
Update to Policy	Formulary Realignment 5-11.xlsx	5/2011	Allen Shek PharmD BCPS
Update to Policy	HPSJ Coverage Policy – Rheumatologic Disorders – Gout 2015-11.docx	11/2015	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Rheumatologic Disorders – Gout 2017-02.docx	2/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Rheumatologic Disorders – Gout 2018-02.docx	2/2018	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Rheumatologic Disorders – Gout 2019-02.docx	2/2019	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Rheumatologic Disorders – Gout 2020-02.docx	2/2020	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Rheumatologic Disorders – Gout 2021-02.docx	2/2021	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Rheumatologic Disorders – Gout 2022-05.docx	5/2022	Matthew Garrett, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy