MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY:	Gout	**P&T DATE:**	2/12/2019
THERAPEUTIC CLASS:	Rheumatologic Disorders	**REVIEW HISTORY:** (MONTH/YEAR)	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.

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 2/2019)*

Class	Drug	Available Strengths	Restrictions	Cost/RX	Notes
Anti-Gout Agent	Colchicine (Colcrys)	*Tablet:* 0.6mg	ST, QL, FL	$75.16	Step therapy to allopurinol filled within the last 30 days. Limited to 61 tablets per 30 days, 6 fills per 365 days.
NSAIDS*	Celecoxib (Celebrex)	*Capsule:* 50mg, 100mg, 200mg, 400mg	ST, AL	$31.87	Step therapy to failure of 3 different NSAIDs (including meloxicam or etodolac) unless over 65 or at high risk for GI events.
	Indomethacin (Indocin)	*Capsule IR:* 25mg, 50mg		$9.07	Indomethacin Suspension is non-formulary.
		Capsule ER: 75mg		$43.43	
		Suppository: 50mg		--	
		Suspension: 25mg/5mL	NF	--	
	Sulindac (Clinoril)	*Tablet:* 150mg, 200mg		$8.12	
	Naproxen (Naprosyn)	*Tablet IR:* 250mg, 375mg, 500mg, 550mg		$7.88	Naproxen Suspension is non-formulary.
		Tablet DR: 500mg		$23.83	
		Suspension: 125mg/5mL	NF	$147.99	
Oral Corticosteroids*	Dexamethasone (DexPak)	*Tablet:* 0.5mg, 0.75mg, 1mg, 1.5mg, 2mg, 4mg, 6mg		$5.21	
		Solution: 0.5mg/5mL		$16.44	
	Prednisone (Deltasone)	*Tablet:* 1mg, 2.5mg, 5mg, 10mg, 20mg, 50mg		$2.40	
		Solution: 5mg/5mL		$16.19	
	Prednisolone (Millipred)	*Tablet*: 5mg		--	
		Solution/Syrup: 5mg/5mL, 15mg/5mL		$3.21	

	Methylprednisolone (Medrol)	*Tablet:* 2mg, 4mg, 8mg, 16mg, 32mg		$8.02	
Uricosuric Agent	Probenecid	*Tablet:* 500mg		$32.42	
Uric Acid Transporter 1 Inhibitor	Lesinurad (Zurampic)	200mg	NF	$378.42	Non-formulary.
Xanthine Oxidase Inhibitors	Allopurinol (Zyloprim)	100mg, 300mg		$4.01	
	Febuxostat (Uloric)	40mg, 80 mg	PA	$347.54	Reserved for patients allergic to allopurinol.
Urate-Oxidase (Recombinant) Enzyme	Pegloticase (Krystexxa)	8mg/mL	NF	--	Non-formulary.
Combinations	Colchicine/Probenecid	0.5mg/500mg		$79.68	
UA Transporter inhibitor/XOI	Lesinurad/Allopurinol (Duzallo)	200mg/300mg, 200mg/200mg	NF	--	Non-formulary

NF = Non-Formulary, QL = Quantity Limit, PA = Prior Authorization required, ST = Step Therapy, FL = Fill Limit

*Over-estimated as some of these agents are also used for the treatment of pain, asthma/COPD exacerbations, and other anti-inflammatory disease states

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 regards to treating or preventing acute gouty arthritis attacks, the recommended first line agent is colchicine, followed by NSAIDS or oral corticosteroids (monotherapy or as combination therapy). 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 newer agents approved for use in gout. As Zurampic (Lesinurad) must be administered with a first line xanthine oxidase inhibitor, overall is similar in mechanism to a uricosuric agent like probenecid, and has additional risks of acute renal failure, Zurampic will remain as non-formulary. Regarding Krystexxa (Pegloticase), as there are safety concerns for methemeglobinemia, risk of cardiovascular related death, and is indicated for use in patient's refractory to conventional therapy, Krystexxa will remain as non-formulary. Duzallo was approved by the FDA using the same clinical trials for Zurampic. As such, Duzallo will remain as non-formulary.

⌗ 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).

Anti-Gout Agents

Colchicine (Colcrys)

- ❒ **Coverage Criteria:** Step therapy to allopurinol filled within the last 30 days.
- ❒ **Limits:**
  - Quantity limit: 61 tablets per 30 days
  - Fill limit: 6 per 365 days

- ❒ **Required Information for Approval:** N/A
- ❒ **Notes:** To encourage chronic gout prevention, ensure that use of urate lowering therapy agents such as allopurinol are on board at optimal doses of up to 800mg per day. Alternatives: Allopurinol for prevention, Naproxen for inflammation, colchicine for gout flares.

Uricosuric Agent

Probenecid, Probenecid with Colchicine

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** N/A
- ❒ **Non-Formulary: Lesinurad (Zurampic), Lesinurad/Allopurinol (Duzallo)**

Xanthine Oxidase Inhibitor

Allopurinol (Zyloprim), Febuxostat (Uloric)

- ❒ **Coverage Criteria:**
  - Febuxostat: Reserved for patients who are allergic to allopurinol.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:**
  - Febuxostat: Clinical documentation/labs supporting allergy to allopurinol.

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.

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

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