Clinical Policy Title:	pegloticase
Policy Number:	RxA.182
Drug(s) Applied:	Krystexxa®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Pegloticase (Krystexxa®) is a PEGylated uric acid specific enzyme.

Krystexxa® is indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pegloticase (Krystexxa®)	Chronic gout	8 mg intravenously every 2 weeks	8 mg/2 weeks

Dosage Forms

- Vial: 8 mg of uricase protein/1 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Chronic Gout (must meet all)**:**

1. Diagnosis of chronic gout;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Positive for symptomatic gout with one or more of the following:
   a. At least 2 gout flares in the previous 12 months;
   b. At least 1 gout tophus;
   c. Chronic gouty arthritis;

5. Failure to normalize uric acid to < 6 mg/dL with at least 3 months each of allopurinol and Uloric®, at maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of one uricosuric agent (e.g., probenecid or Zurampic®), at maximally indicated doses, in combination with allopurinol or Uloric® unless contraindicated or clinically significant adverse effects are experienced;
7. Has tested negative for glucose-6-phosphate dehydrogenase (G6PD) deficiency;
8. Dose does not exceed 8 mg (uricase protein) every two weeks.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Chronic Gout (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by a decrease in plasma uric acid levels;
3. Member is not concurrently taking any oral urate-lowering agents (e.g., allopurinol, Uloric®, probenecid);
4. If request is for a dose increase, new dose does not exceed 8 mg (uricase protein) every two weeks.

Approval Duration
Commercial: 6 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
G6PD: glucose-6-phosphate dehydrogenase
PEGylated: Poly Ethylene glycated

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
allopurinol (Zyloprim®)	400-600 mg orally once daily	800 mg/day
febuxostat (Uloric®*)	40 mg orally once daily	120 mg/day
probenecid	500 mg orally twice daily	2 gm/day

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - G6PD deficiency

- Boxed Warning(s):
  - Anaphylaxis and infusion reactions;
  - Should pre-medicate with antihistamines and corticosteroids;
  - G6PD deficiency-associated hemolysis and methemoglobinemia.

APPENDIX D: General Information

- Anaphylaxis: Anaphylaxis may occur with any Krystexxa® infusion. Pre-medicate and monitor patients.
- Infusion Reactions: Infusion reactions occurred in patients treated with Krystexxa®. Pre-medicate and monitor patients.
- G6PD Deficiency Associated Hemolysis and Methemoglobinemia: Screen patients at risk for G6PD deficiency. Do not administer Krystexxa® to patients with G6PD deficiency.
- Gout Flares: Gout flare prophylaxis is recommended for at least the first 6 months of Krystexxa® therapy.
- Congestive Heart Failure: Congestive heart failure exacerbation may occur. Monitor patients closely following infusion.
- Discontinue oral urate-lowering agents before starting Krystexxa.

References

1. Krystexxa® Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; March 2021. Available at: https://www.hzndocs.com/KRYSTEXXA-Prescribing-Information.pdf. Accessed July 12, 2021.
2. Khanna D, Fitzgerald, 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 gout. Arthritis Care Res. October 2012; 64(10): 1431-1446. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3683400/. Accessed July 12, 2021.
3. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed June 19, 2020.
4. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care Res (Hoboken). June 2020;72(6):744-760. doi:10.1002/acr.24180. Available at: https://onlinelibrary.wiley.com/doi/full/10.1002/acr.24180. Accessed July 12, 2021.
5. Krystexxa®. Lexi-Drugs. Hudson, OH: Lexicomp, 2021. http://online.lexi.com/. Updated June 21, 2021. Accessed July 12, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Background was updated to include limitations of use. 3. Initial Approval Criteria I.A.2 was added to specify prescriber type. 4. Initial Approval Criteria I.A.4a was updated to 2 flares within 12 months. 5. Initial Approval criteria I.A.6 updated to	07/09/2020	09/14/2020

remove losartan and add Zurampic® as uricosuric agent. 6. Initial Approval criteria I.A.8 was added to include negative G6PD deficiency result due to contraindication. 7. Initial and Continued Therapy approval durations updated to exactly 6 months. 8. Continued Therapy Criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 9. Appendix B updated to remove losartan and add Zurampic® as therapeutic alternative. 10. Appendix C updated to add requirement of pre-medication with antihistamines and corticosteroids. 11. References were updated.		
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Continued Therapy Criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…”. 3. Appendix A was updated to include abbreviation “PEGylated”. 4. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance…". 5. Appendix B: Therapeutic Alternatives maximum dose for allopurinol (Zyloprim®) was updated from "600 mg/day" to "800 mg/day”. 6. Appendix B: Therapeutic Alternatives maximum dose for febuxostat (Uloric®*) was updated from “80 mg/day” to “120 mg/day”. 7. Appendix B was updated to remove generic drug name "lesinurad" as it is currently unavailable.. 8. Appendix B was updated to remove discontinued brand-name drug Zurampic.	07/12/2021	09/14/2021

9. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 10. Appendix D was updated to include several warnings and precautions: “Anaphylaxis…”, “Infusion Reactions…”, “G6PD Deficiency Associated Hemolysis and Methemoglobinemia…”, “Gout Flares…”, “Congestive Heart Failure…”, and “Discontinue oral urate-lowering agents…”. 11. References were reviewed and updated. 12.		