Clinical Policy: Pegloticase (Krystexxa)
Reference Number: CP.PHAR.115
Effective Date: 06.01.13
Last Review Date: 02.21
Line of Business: Commercial, HIM, Medicaid

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

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

FDA Approved Indication(s)
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.

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 Krystexxa is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Chronic Gout (must meet all):
      1. Diagnosis of chronic gout;
      2. Age ≥ 18 years;
      3. Positive for symptomatic gout with one or more of the following:
         a. At least 3 gout flares in the previous 18 months;
         b. At least 1 gout tophus;
         c. Chronic gouty arthritis;
      4. Failure to normalize uric acid to < 6 mg/dL with allopurinol and Uloric® at maximally indicated doses, each used for at least 3 months unless clinically significant adverse effects are experienced or both are contraindicated;
      5. Failure of one uricosuric agent (e.g., probenecid or losartan), at maximally indicated doses, in combination with allopurinol or Uloric unless clinically significant adverse effects are experienced or all are contraindicated;
      6. Krystexxa is not prescribed concurrently with oral urate-lowering agents (e.g., allopurinol, Uloric, probenecid);
      7. Dose does not exceed 8 mg (uricase protein) every two weeks.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member’s renewal date, whichever is longer
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): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Chronic Gout (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 a decrease in plasma uric acid levels;
      3. Krystexxa is not prescribed concurrently with 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:
   Medicaid/HIM – 12 months
   Commercial – 6 months or to the member’s renewal date, whichever is longer

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
      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): CP.CPA.09 for commercial, 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 – CP.CPA.09 for commercial, 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
   G6PD: glucose-6-phosphate dehydrogenase

   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.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>allopurinol (Zyloprim®)</td>
<td>400-600 mg PO QD</td>
<td>600 mg/day</td>
</tr>
<tr>
<td>Uloric (febuxostat)</td>
<td>40 mg PO QD</td>
<td>80 mg/day</td>
</tr>
<tr>
<td>probenecid</td>
<td>500 mg PO BID</td>
<td>2 gm/day</td>
</tr>
<tr>
<td>losartan (Cozaar®)*</td>
<td>50 mg PO QD</td>
<td>50 mg/day</td>
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</tbody>
</table>

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.

*Off-label

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): G6PD deficiency
- Boxed warning(s): anaphylaxis and infusion reactions; G6PD deficiency-associated hemolysis and methemoglobinemia

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic gout</td>
<td>8 mg IV every 2 weeks</td>
<td>8 mg/2 weeks</td>
</tr>
</tbody>
</table>

VI. Product Availability

Vial: 8 mg of uricase protein/1 mL

VII. References

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>J2507</td>
<td>Injection, pegloticase, 1 mg</td>
</tr>
</tbody>
</table>
## Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under renewal criteria, added “baseline” to “decrease in plasma uric acid levels”</td>
<td>04.17</td>
<td>05.17</td>
</tr>
<tr>
<td>- Converted to new template.</td>
<td>09.22.17</td>
<td>11.17</td>
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<tr>
<td>- Added requirement to fail one uricosuric agent in combination with a xanthine oxidase inhibitor, after failure of xanthine oxidase inhibitors alone, per treatment guidelines.</td>
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<td>- Added age limit per package labeling.</td>
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<td>- Removed requirement for concomitant gout flare prophylactic therapy.</td>
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<tr>
<td>- For continued approval, added the requirement to confirm the absence of concurrent oral urate-lowering agents.</td>
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<tr>
<td>- Changed approval durations from 3 and 6 months to 6 and 12 months for initial and continued approvals, respectively.</td>
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<tr>
<td>1Q18 annual review: No significant changes. Policies combined for Medicaid and Commercial lines of business. References reviewed and updated.</td>
<td>11.22.17</td>
<td>02.18</td>
</tr>
<tr>
<td>1Q 2019 annual review: removed the requirement for G6PD deficiency testing to align with the previously approved Corporate approach for G6PD deficiency testing; references reviewed and updated.</td>
<td>11.06.18</td>
<td>02.19</td>
</tr>
<tr>
<td>1Q 2020 annual review: no significant changes; added HIM line of business; references reviewed and updated.</td>
<td>10.28.19</td>
<td>02.20</td>
</tr>
<tr>
<td>1Q 2021 annual review: no significant changes; added requirement in continued therapy that member is not concurrently taking other oral urate-lowering therapy to Section I for initial approval; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.</td>
<td>11.16.20</td>
<td>02.21</td>
</tr>
</tbody>
</table>

### 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...
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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.

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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.

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