Clinical Policy: Mercaptopurine (Purixan)
Reference Number: CP.CPA.110
Effective Date: 11.16.16
Last Review Date: 05.19
Line of Business: Commercial

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

Description
Mercaptopurine (Purixan®) is a nucleoside metabolic inhibitor that is an analogue of the purine bases adenine and hypoxanthine.

FDA Approved Indication(s)
Purixan is indicated for the treatment of patients with acute lymphoblastic leukemia (ALL) as part of a combination maintenance therapy regimen.

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 Purixan is medically necessary when the following criteria are met:

I. Initial Approval Criteria
A. Acute Lymphoblastic Leukemia or Acute Myeloid Leukemia (must meet all):
   1. Diagnosis of ALL or acute promyelocytic leukemia;
   2. Prescribed by or in consultation with an oncologist or hematologist;
   3. One of the following (a or b):
      a. Medical justification supports inability to use mercaptopurine tablets (e.g., contraindications to excipients in mercaptopurine tablets);
      b. Member has a documented swallowing disorder or an inability to swallow tablets or capsules;
   4. Request meets one of the following (a or b):
      a. Dose does not exceed 5 mg/kg or 75 mg/m² per day;
      b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: Length of Benefit

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.
II. Continued Therapy

A. Acute Lymphoblastic Leukemia or Acute Myeloid Leukemia (must meet all):
   1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Purixan for a covered indication and has received this medication for at least 30 days;
   2. Member is responding positively to therapy;
   3. If request is for a dose increase, request meets one of the following (a or b):
      a. New dose does not exceed 5 mg/kg or 75 mg/m² per day;
      b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

   Approval duration: Duration of request or 12 months (whichever is less); or
   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.

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 policy – CP.CPA.09 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ALL: acute lymphoblastic leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

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</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>mercaptopurine</td>
<td>1.5 to 2.5 mg/kg (50 to 75 mg/m²) PO QD</td>
<td>Dose should be adjusted to maintain an absolute neutrophil count (ANC) at a desirable level</td>
</tr>
</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.

Appendix C: Contraindications/Boxed Warnings
None reported
Appendix D: General Information

- Typical maintenance therapy regimen consists of daily 6-mercaptopurine, weekly methotrexate, and monthly vincristine/prednisone pulses for 2-3 years.
- Oral mercaptopurine can have highly variable drug and metabolite concentrations as many factors (e.g. thiopurine S-methyl transferase (TPMT) polymorphisms and drug-drug-interactions with other chemotherapeutic agents) can affect bioavailability and impact the ability of maintenance regimens to prevent disease relapse.
- Mercaptopurine dose adjustments may be needed to manage clinically significant adverse effects (e.g. myelosuppression including anemia, neutropenia, lymphopenia and thrombocytopenia). Mercaptopurine oral suspension may be more amendable to dose adjustments in patients who continue to have poor clinical response despite dose adjustments with the tablet form.
- Micromedex lists mercaptopurine as a Class IIb recommendation for both Crohn’s disease and ulcerative colitis.
- NCCN treatment guidelines for ALL state that lymphoblastic lymphoma is indistinguishable from ALL based on morphologic, genetic, and immunophenotypic features. Patients with lymphoblastic lymphoma generally benefit from treatment with ALL-like regimens.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>1.5 to 2.5 mg/kg (50 to 75 mg/m²) PO QD</td>
<td>2.5 mg/kg/day or 75 mg/m²/day</td>
</tr>
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VI. Product Availability

Oral suspension: 2000 mg/100 mL (20 mg/mL)

VII. References


Reviews, Revisions, and Approvals

<table>
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<th>Date</th>
<th>P&amp;T Approval Date</th>
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<td>01.12.17</td>
<td>11.17</td>
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<td>08.02.18</td>
<td>11.18</td>
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</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 benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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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