Clinical Policy: Mercaptopurine (Purixan)

Reference Number: CP.PHAR.447
Effective Date: 03.01.20
Last Review Date: 05.23
Line of Business: Commercial, HIM, Medicaid Revision Log

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 chemotherapy maintenance 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 (off-label);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member must use mercaptopurine tablets, unless one of the following (a, b, or c):
   a. Mercaptopurine tablets are contraindicated or clinically significant adverse effects are experienced;
   b. Member has a documented swallowing disorder or an inability to swallow tablets or capsules;
   c. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 2.5 mg/kg or 75 mg/m^2 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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/m^2 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:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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.

Drug	Dosing Regimen	Dose Limit/Maximum Dose
mercaptopurine (Purinethol®)	1.5 to 2.5 mg/kg (50 to 75 mg/m^2) PO QD	Dose should be adjusted to maintain an absolute neutrophil count (ANC) at a desirable level

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 for Crohn's disease as a Class I recommendation for adults and Class Ia for pediatrics. Ulcerative colitis has a Class IIb recommendation for both adult and pediatrics.

- 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.

Appendix E: States with Regulations against Redirections in Certain Oncology Settings

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to HIM requests only** For stage 4 metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ALL	1.5 to 2.5 mg/kg (50 to 75 mg/m^2) PO QD	2.5 mg/kg/day or 75 mg/m^2/day

VI. Product Availability

Oral suspension: 2,000 mg/100 mL (20 mg/mL)

VII. References

1. Purixan Prescribing Information. Leicester, UK: Nova Laboratories Ltd; April 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9fd27952-7787-47d9-b6cf-7af2dc38217b . Accessed January 4, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 19, 2023.
3. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 19, 2023.
4. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed January 19, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved policy CP.CPA.110; retire CP.CPA.110l added Medicaid LOB; no significant changes from previously approved corporate policy; references reviewed and updated.	10.30.19	02.20
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.11.20	05.20
2Q 2021 annual review: no significant changes; added HIM line of business; references reviewed and updated.	02.12.21	05.21
2Q 2022 annual review: modified commercial approval duration from length of benefit to "12 months or duration of request, whichever is less"; modified redirection language from "medical justification" to "member must use"; references reviewed and updated.	02.02.22	05.22
Template changes applied to other diagnoses/indications.	09.27.22	
2Q 2023 annual review: added by-passing of redirection if state regulations do not allow step therapy in certain oncology settings; clarified HIM approval durations align with Medicaid; references reviewed and updated.	01.04.23	05.23

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.