Clinical Policy: Thioguanine (Tabloid)

Reference Number: CP.PHAR.437
Effective Date: 09.04.18
Last Review Date: 11.22
Line of Business: HIM, Medicaid

Revision Log

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

Description

Thioguanine (Tabloid®) is an antimetabolite.

FDA Approved Indication(s)

Tabloid is indicated for remission induction and remission consolidation treatment of acute nonlymphocytic leukemias *[also known as acute myeloid leukemia; AML per the National Cancer Institute's Dictionary of Cancer Terms]*. However, it is not recommended for use during maintenance therapy or similar long-term continuous treatments due to the high risk of liver toxicity.

Tabloid is not effective in chronic lymphocytic leukemia, Hodgkin's lymphoma, multiple myeloma, or solid tumor.

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 Tabloid is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Myeloid Leukemia (must meet all)**:**

1. Diagnosis of AML:
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Prescribed for induction or consolidation therapy;
4. Request meets one of the following (a or b):*
   a. Dose does not exceed 3 mg/kg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant labeled or off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 3 months

B. Acute Lymphoblastic Leukemia (off-label) (must meet all)**:**

1. Diagnosis of relapsed/refractory acute lymphoblastic leukemia (ALL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age < 18 years;

4. Disease is one of the following (a or b):
   a. Philadelphia chromosome-negative;
   b. Philadelphia chromosome-positive, and prescribed in combination with Sprycel® or imatinib;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 3 months

C. Glioma (off-label) (must meet all)**:**
1. Diagnosis of recurrent or progressive pilocytic astrocytoma (PA);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Prescribed in combination with PCV (procarbazine, lomustine, and vincristine; carmustine may be used in place of lomustine);
5. Member has had prior fractionated external beam radiation therapy;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 3 months

D. 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: 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: 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: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acute Myeloid Leukemia (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Tabloid 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 3 mg/kg per day;

b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant labeled or off-label use (*prescriber must submit supporting evidence*).

Approval duration: 3 months

B. Acute Lymphoblastic Leukemia and Glioma (off-label) (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Tabloid 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, new dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 3 months

C. 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: 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: 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: 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 – 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

AML: acute myeloid leukemia
ALL: acute lymphoblastic leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
PA: pilocytic astrocytoma

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): thioguanine should be not used in patients whose disease has demonstrated prior resistance to this drug
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

AML	Induction and consolidation therapy:
	• Combination therapy:
	  ○ Because the usual therapies for adult and pediatric acute nonlymphocytic leukemias involve the use of thioguanine with other agents in combination, physicians responsible for administering these therapies should be experienced in the use of cancer chemotherapy and in the chosen protocol.
	• Single agent therapy:
	  ○ On those occasions when single-agent chemotherapy with thioguanine may be appropriate, the usual initial dosage for pediatric patients and adults is approximately 2 mg/kg of body weight per day. If, after 4 weeks on this dosage, there is no clinical improvement and no leukocyte or platelet depression, the dosage may be cautiously increased to 3 mg/kg/day. The total daily dose may be given at one time.
	Maintenance therapy:
	• Thioguanine is not recommended for use during maintenance therapy or similar long-term continuous treatments due to the high risk of liver toxicity.
		Varies

VI. Product Availability

Tablet: 40 mg

VII. References

1. Tabloid Prescribing Information. Mason,OH: Prasco Laboratories; May 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/012429s028lbl.pdf. Accessed August 1, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 1, 2022.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 1, 2022.
4. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed August 1, 2022.

5. National Comprehensive Cancer Network. Central Nervous System Cancers Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed August 2, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adopted from HIM.PA.13 (to be retired); Medicaid line of business added; AML relabeled as "myeloid" and ALL age limited to pediatrics per NCCN guidelines; mercaptopurine trial removed from AML given the drug's lack of FDA label and from ALL given the new pediatric age restriction; dosing restated in criteria and Section V, with guidance from Clinical Pharmacology, Micromedex and NCCN; durations extended to 3 months; references reviewed and updated.	08.20.19	11.19
4Q 2020 annual review: AML dosing information limited to package insert information or directive for providers to forward protocol dosing information (there is no NCCN guidance here); the off-label ALL criteria is presented separately with standard off-label dosing language; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: moved requirement for use as remission induction/consolidation from ALL to AML per FDA label and NCCN; for ALL, specified that disease should be relapsed/refractory and added requirement for use in combination with imatinib or Sprycel if Ph+ per NCCN; added 12 month approval durations for Legacy WellCare – off-label dosing for ALL not retained per rationale above (WCG.CP.PHAR.437 retired); references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	06.28.21	11.21
4Q 2022 annual review: added off-label indication Glioma (pilocytic astrocytoma) per NCCN; approval durations for Legacy Wellcare consolidated to 3 months; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.01.22	11.22

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.