Clinical Policy: Thioguanine (Tabloid)

Reference Number: ERX.SPA.353
Effective Date: 12.01.19
Last Review Date: 11.21
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Acute Myeloid Leukemia (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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*).

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

Approval duration: 3 months

B. Acute Lymphoblastic Leukemia (off-label) (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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

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://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4490128b-e73f-4849-9d6e-e8591639d771. Accessed July 15, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 28, 2021.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed July 15, 2021.
4. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed July 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.03.19	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; references reviewed and updated.	06.28.21	11.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.