Clinical Policy: Thioguanine (Tabloid)
Reference Number: CP.PHAR.437
Effective Date: 09.04.18
Last Review Date: 11.20
Line of Business: HIM, Medicaid

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].

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. Request meets one of the following (a, b, or c):
         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).
   Approval duration: 3 months

   B. Acute Lymphoblastic Leukemia (off-label) (must meet all):
      1. Acute lymphoblastic leukemia (ALL);
      2. Prescribed by or in consultation with an oncologist or hematologist;
      3. Age < 18 years;
      4. Thioguanine is prescribed for remission induction/consolidation;
      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 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): HIM.PHAR.21 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 (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).*
   Approval duration: 3 months

   C. 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 6 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): HIM.PHAR.21 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.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   *Prescribed regimen must be FDA-approved or recommended by NCCN
   Appendix A: Abbreviation/Acronym Key
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

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<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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| AML        | Induction and consolidation therapy:  
- Combination therapy:  
o 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:  
o 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

Reviews, Revisions, and Approvals

<table>
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<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>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.</td>
<td>08.20.19 11.19</td>
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<td>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.</td>
<td>08.11.20 11.20</td>
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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.

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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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