BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

SYNRIBO® (omacetaxine mepesuccinate) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Synribo (omacetaxine mepesuccinate) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Chronic or accelerated phase chronic myeloid leukemia (CML) with resistance and/or intolerance to two or more tyrosine kinase inhibitors (TKI)

b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. Individual has completed **ALL** the following **baseline tests** before initiation of treatment and will have continued monitoring as clinically appropriate:
   a. Negative pregnancy test in a woman of childbearing potential
   b. Eastern Cooperative Oncology Group (ECOG) performance status 0-2

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual does not have **ANY** of the following:
   a. New York Heart Association (NYHA) class III or IV heart disease
   b. Active ischemia
   c. Other uncontrolled cardiac condition

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Synribo (omacetaxine mepesuccinate) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual has documentation of positive clinical response to therapy defined as **ALL** of the following:
   a. No evidence of disease progression
   b. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
   a. Myelosuppression such as severe thrombocytopenia, neutropenia, and anemia
   b. Hemorrhage
   c. Hyperosmolar non-ketotic hyperglycemia

Renewal duration: 12 months

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- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

Synribo (omacetaxine mepesuccinate) injection is indicated for the treatment of adult patients with chronic or accelerated phase chronic myeloid leukemia (CML) with resistance and/or intolerance to two or more tyrosine kinase inhibitors (TKI). Omacetaxine mepesuccinate is a cephalotaxine ester. It is a protein synthesis inhibitor. Omacetaxine mepesuccinate is an extract from the leaves of *Cephalotaxus sp.*

CML is a form of cancer that causes abnormal/immature white blood cells (WBCs) to increase. Many patients with CML develop a genetic translocation that results in a "Philadelphia Chromosome (BCR-ABL gene)," which results in the production of tyrosine kinase, an enzyme that is involved in the excess production of WBCs. This enzyme can be targeted by drugs known as tyrosine kinase inhibitors (TKIs).

CML is divided into 3 general phases based on the percentage of immature (or blast cells), in the bone marrow – chronic stable (<10%), accelerated (10-19%), and blast crisis (≥20%). The chronic stable phase (a relatively indolent phase) is controlled with oral agents while the more aggressive accelerated phase is more difficult to control. The disease culminates with the blast crisis (acute leukemia), generally refractory to treatment. Blast crisis can occur de novo or develop slowly or rapidly during TKI therapy of the chronic phase. Treatment of blast crisis depends upon the lineage of the blasts (i.e., myeloid versus lymphoid).

The mechanism of action of omacetaxine mepesuccinate has not been fully clarified but includes inhibition of protein synthesis and is independent of direct BCR-ABL binding. Omacetaxine mepesuccinate binds to the A-site cleft in the peptidyl-transferase center of the large ribosomal subunit from a strain of archaeabacteria. *In vitro*, omacetaxine mepesuccinate reduced protein levels of the BCR-ABL oncoprotein and Mcl-1, an antiapoptotic Bcl-2 family member.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Chronic myeloid leukemia (CML): An indolent (slow growing) cancer in which too many myeloblasts are found in the blood and bone marrow. Myeloblasts are a type of immature blood cell that makes white blood cells called myeloid cells. Chronic myeloid leukemia may get worse over time as the number of myeloblasts increases in the blood and bone marrow. This may cause fever, fatigue, easy bleeding, anemia, infection, a swollen spleen, bone pain, or other signs and symptoms. Chronic myeloid leukemia is usually marked by a chromosome change called the Philadelphia chromosome, in which a piece of chromosome 9 and a piece of chromosome 22 break off and trade places with each other. It usually occurs in older adults and rarely occurs in children. Also called chronic granulocytic leukemia, chronic myelogenous leukemia, and CML.

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Tyrosine kinase inhibitors (TKIs) with FDA indication treatment of chronic or accelerated phase CML:

- Bosutinib (Bosulif®)
- Dasatinib (Sprycel®)
- Imatinib (Gleevec®)
- Nilotinib (Tasigna®)
- Ponatinib (Iclusiq®)

Accelerated Phase of CML:

- 10-19% blasts in the peripheral blood or bone marrow
- Peripheral blood basophils ≥ 20%
- Platelets < 100,000/microL, unrelated to therapy
- Platelets > 1,000,000/microL, unresponsive to therapy
- Progressive splenomegaly and increasing white cell count, unresponsive to therapy
- Cytogenetic evolution (defined as the development of chromosomal abnormalities in addition to the Philadelphia chromosome)

Blast Phase of CML:

- ≥ 2% peripheral blood or bone marrow blasts
- Large foci or clusters of blasts on the bone marrow biopsy
- Presence of extramedullary blastic infiltrates (e.g., myeloid sarcoma, also known as granulocytic sarcoma or chloroma)

Resources:

Synribo (omacetaxine mepesuccinate) SQ injection product information, revised by Cephalon, Inc. 09-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 07,2024. **Discontinued 12-27-2023.**

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Myeloid Leukemia Version 3.2025. Updated November 27, 2024. Available at https://www.nccn.org. Accessed May 10, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

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