BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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SYNRIBO® (omacetaxine mepesuccinate)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Synribo (omacetaxine mepesuccinate) is considered ***medically necessary*** and will be approved when **ALL** of 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. 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. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Negative pregnancy test in a woman of child bearing potential
     b. Eastern Cooperative Oncology Group (ECOG) performance status 0-2

  5. 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) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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

  2. Individual's condition has responded while on therapy
     a. Response is defined as:
        i. No evidence of disease progression
        ii. 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. Individual has not developed any significant adverse drug effects that may exclude continued use
     a. Significant adverse effect such as:

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i. Myelosuppression such as severe thrombocytopenia, neutropenia, and anemia
ii. Hemorrhage
iii. Hyperosmolar non-ketotic hyperglycemia

5. There are no significant interacting drugs

Renewal duration: 12 months

- 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 a Non-Cancer Medications**

2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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.

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Definitions:

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.

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) product information, revised by Cephalon, Inc. 11-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on June 09, 2021.

Schiffer CA, Atallah E. Overview of the treatment of chronic myeloid leukemia. In: UpToDate, Larsen RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 14, 2021.

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Schiffer CA, Atallah E. Initial treatment of chronic myeloid leukemia in chronic phase. In: UpToDate, Larsen RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 14, 2021.

Negrin RS, Schiffer CA. Treatment of chronic myeloid leukemia in chronic phase after failure of initial therapy. In: UpToDate, Larsen RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 14, 2021.

Negrin RS, Schiffer CA. Treatment of chronic myeloid leukemia in accelerated phase. In: UpToDate, Larsen RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 14, 2021.

Negrin RS, Schiffer CA. Treatment of chronic myeloid leukemia in blast phase. In: UpToDate, Larsen RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 14, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Myeloid Leukemia Version 3.2021 – Updated January 13, 2021. Available at https://www.nccn.org. Accessed on June 14, 2021.

National Comprehensive Cancer Network (NCCN) Compendium: Synribo (omacetaxine mepesuccinate). National Comprehensive Cancer Network (NCCN). NCCN Drugs & Biologics Compendium. Available at: http://www.nccn.org. Accessed on June 14, 2021.

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.