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Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	January 1, 2013
Subject:	Synribo	**Page:**	1 of 4

Last Review Date: September 6, 2024

Synribo

Description

Synribo (omacetaxine mepesuccinate)

Background
Synribo is a protein synthesis inhibitor used in the treatment of adults with chronic or accelerated chronic myelogenous leukemia. Chronic myelogenous leukemia (CML) is a myeloproliferative disorder that accounts for 15 - 20% of leukemias in adults. Synribo is a semi-synthetic formulation of the cytotoxic plant alkaloid homoharringtonine, isolated from the evergreen tree *Cephalotaxus harringtonia* (1-2).

Regulatory Status
FDA-approved indication: Synribo for 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) (2).

Synribo contains warnings for several serious adverse effects including: (2)

- Myelosuppression: severe and fatal thrombocytopenia, neutropenia and anemia.
- Bleeding: severe thrombocytopenia and increased risk of hemorrhage. Fatal cerebral hemorrhage and severe, non-fatal gastrointestinal hemorrhage.
- Hyperglycemia: glucose intolerance and hyperglycemia including hyperosmolar non-ketotic hyperglycemia.
- Embryo-fetal toxicity: Can cause fetal harm. Advise females of reproductive potential to avoid pregnancy while being treated with Synribo.
- IV administration may be associated with acute cardiac toxicity. Synribo is FDA approved for subcutaneous administration.

The safety and efficacy of Synribo in pediatric patients have not been established (2).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Synribo may be considered **medically necessary** if the conditions indicated below are met.

Synribo may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Chronic phase myeloid leukemia (CML) that is resistant and/or intolerant to two or more tyrosine kinase inhibitors (TKI)
2. Accelerated phase chronic myeloid leukemia (CML) that is resistant and/or intolerant to two or more tyrosine kinase inhibitors (TKI)

AND the following:

a. Subcutaneous administration

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Chronic phase myeloid leukemia (CML) that is resistant and/or intolerant to two

or more tyrosine kinase inhibitors (TKI)
2. Accelerated phase chronic myeloid leukemia (CML) that is resistant and/or intolerant to two or more tyrosine kinase inhibitors (TKI)

AND ALL of the following:
a. Show clinical benefit from therapy
b. Subcutaneous administration

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval *Renewal* Limits
Same as above

Rationale

Summary
Synribo is medically necessary 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). This indication is based upon response rate. There are no trials verifying an improvement in disease-related symptoms or increased survival with Synribo. Synribo warnings include myelosuppression, bleeding, hyperglycemia, and for female patients, the potential to cause fetal toxicity. Synribo may be associated with acute cardiac toxicity when administered intravenously. Synribo is FDA-approved for subcutaneous administration (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Synribo (omacetaxine mepesuccinate) while maintaining optimal therapeutic outcomes.

References
1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012; 62:10.
2. Synribo [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc; May 2021.

3. NCCN Drugs & Biologics Compendium® Omacetaxine 2024. National Comprehensive Cancer Network, Inc. Accessed on July 18, 2024.

Policy History

Date	Action
November 2012	New addition to PA
March 2013	Addition of the subcutaneous administration due to acute cardiac toxicity with IV administration
March 2014	Annual review
March 2015	Annual review and reference update
December 2015	Annual editorial review
June 2016	Annual editorial review and reference update Policy code changed from 5.04.31 to 5.21.31
June 2017	Annual editorial review and reference update
June 2018	Annual editorial review and reference update
June 2019	Annual review and reference update
June 2020	Annual review and reference update
September 2021	Annual review and reference update
September 2022	Annual review and reference update
September 2023	Annual review and reference update
September 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.