

POLICY: Oncology – Synribo® (omacetaxine mepesuccinate injection for subcutaneous use – Teva)

APPROVAL DATE: 09/04/2019

OVERVIEW

Synribo 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.¹ Synribo can be administered by someone other than a healthcare professional (e.g., patient or a caregiver), if appropriate. The mechanism of action of Synribo has not been fully determined but involves inhibition of protein synthesis. The safety and efficacy of Synribo in pediatric patients have not been established.

Disease Overview

CML is a myeloproliferative neoplasm that comprises 15% of newly-diagnosed adult leukemias with an incidence of 1 to 2 cases per 100,000 adults.^{2,3} In 2019, it was estimated that 8,990 patients would be diagnosed in the US, and 1,140 patients would die from the disease.² The median age at onset is 67 years; however, CML occurs in all age groups. CML is diagnosed by persistent unexplained leukocytosis with the presence of the Philadelphia chromosome abnormality characterized by a reciprocal translocation between chromosomes 9 and 22 that gives rise to the breakpoint cluster region (*BCR*) Abelson murine leukemia (*ABL*) 1 fusion gene which is believed to play a central role in the initial development of CML. Approximately 50% of patients with CML that are diagnosed in the US are asymptomatic.³ Diagnosis often occurs following a routine physical examination or blood test.^{2,3} CML occurs in three different phases (chronic phase [CP], accelerated phase [AP], or blast phase [BP]) and is usually diagnosed in CP. Common signs and symptoms of CP CML are related to anemia and splenomegaly. These include fatigue, weight loss, malaise, and left upper quadrant pain or fullness. Untreated CP CML will eventually progress to advanced disease in 3 to 5 years. Certain mutations are associated with high rates of disease progression and relapse. The T315I mutation is a commonly noted example, which occurs in about 5% to 15% of cases.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for CML (version 1.2020 – August 26, 2019) recommends Synribo as a treatment option for patients who have experienced disease progression to accelerated phase CML on TKI therapy.² It is not an option among patients who present with accelerated phase CML. Synribo is also a treatment option for patients with the T315I mutation. Synribo is stated as an option for patients with disease that is resistant and/or intolerant to two other TKIs.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Synribo. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Synribo as well as the monitoring required for adverse events and long-term efficacy, approval requires Synribo to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Synribo is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Chronic Myeloid Leukemia (CML).** Approve for 6 months if the patient meets the following criteria (A, B, and C):
 - A) Synribo is prescribed by or in consultation with an oncologist; AND
 - B) The patient is ≥ 18 years of age; AND
 - C) The patient meets one of the following criteria (i or ii):
 - i. The patient is T315I-positive, OR
 - ii. The patient has tried at least two tyrosine kinase inhibitors indicated for use in CML (e.g., Gleevec[®] [imatinib tablets], Sprycel[®] [dasatinib tablets], Tasigna[®] [nilotinib capsules], Bosulif[®] [bosutinib tablets], Iclusig[®] [ponatinib tablets]).

Dosing. Approve up to 1.25 mg/m² given by subcutaneous injection twice daily for up to 14 days once every 28 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Synribo has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Synribo[®] injection for subcutaneous use [prescribing information]. North Wales, PS: Teva Pharmaceuticals; June 2017.
2. The NCCN Chronic Myeloid Leukemia Clinical Practice Guidelines in Oncology (Version 1.2020 – August 26, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 30, 2019.
3. Jabbour E, Kantarjian H. Chronic myeloid leukemia: 2018 update on diagnosis, therapy and monitoring. *Am J Hematol.* 2018;93:442-459.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New policy	Not applicable.	07/25/2018
Annual revision	The Dosing section were revised to provide for the maximum range of dosing (see Policy). Additionally, the following sections were removed: initial/extended approval, duration of therapy, and labs/diagnostics. The waste management section was also deleted. Additional changes per the specific indications were as follows: <ol style="list-style-type: none">1. Chronic Myeloid Leukemia: The wording of the criteria requiring the patient to be an adult ≥ 18 years of age was changed to just state "≥ 18 years of age". Also, the modifier "at least" was added to the criteria that requires that the patient try two tyrosine kinase inhibitors indicated for use in chronic myeloid leukemia.	09/04/2019