Synribo® (omacetaxine mepesuccinate)
(Subcutaneous)

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Document Number: IC-0488

Last Review Date: 02/01/2024
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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

Synribo 3.5 mg for injection single-dose vial:
- Induction**:** 28 vials every 28 days (*until hematologic response is achieved, then begin maintenance*)
- Maintenance**:** 14 vials every 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 9,800 billable units every 28 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Patient's disease is confirmed by either a Philadelphia chromosome-positive (Ph+) or *BCR::ABL1* positive laboratory test result; **AND**

Chronic Myeloid Leukemia (CML) † Φ [1-3]

- Used as single agent therapy; **AND**
- Patients is resistant, intolerant, or had an inadequate response after at least 3 months of therapy with at least TWO tyrosine kinase inhibitor (TKI) therapies (e.g., asciminib, bosutinib, imatinib, dasatinib, ponatinib, or nilotinib); **AND**
  - Patient has chronic phase disease; **OR**
  - Patient has advanced phase disease that has progressed to accelerated phase

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-3]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: myelosuppression (e.g., severe neutropenia, thrombocytopenia, or anemia), hemorrhage (including cerebral and gastrointestinal), uncontrolled hyperglycemia, etc.; **AND**
- Treatment response as indicated by one of the following BCR::ABL1 (IS) transcript levels:
  - ≤ 10% at 3 months; **OR**
  - ≤ 10% at 6 months; **OR**
  - ≤ 0.1% or a ≥ 3-log reduction in *BCR-ABL1* transcripts from the standardized baseline, if qPCR (IS) is not available; **OR**
  - ≤0.01% MR4.0 or ≤0.0032% MR4.5

  Note: cytogenetic assessment of response may be used if quantitative reverse transcriptase polymerase chain reaction RT-PCR (qPCR) using International Scale (IS) for *BCR::ABL1* is not available

V. Dosage/Administration [1]

Indication	Dose
Chronic Myeloid Leukemia	Induction Dose: 1.25 mg/m^2 administered by subcutaneous injection twice daily for 14 consecutive days of a 28-day cycle. Repeat until a hematologic response is achieved, then begin maintenance. Maintenance Dose: 1.25 mg/m^2 administered by subcutaneous injection twice daily for 7 consecutive days of a 28-day cycle. Treatment should continue as long as patients are clinically benefiting from therapy.
– Synribo should be prepared/reconstituted in a healthcare facility by a healthcare professional. – Synribo may be administered by the patient or caregiver with appropriate training on proper handling, storage conditions, administration, disposal, and clean-up of accidental spillage of the product.	

VI. Billing Code/Availability Information

HCPCS Code:

- J9262 – Injection, omacetaxine mepesuccinate, 0.01 mg; 1 billing unit = 0.01 mg

NDC:

- Synribo 3.5 mg single-dose vial for injection: 63459-0177-xx

VII. References (STANDARD)

1. Synribo [package insert]. Parsippany, NJ; Teva Pharmaceuticals USA, Inc.; September 2022. Accessed December 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for omacetaxine. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed December 2023.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Chronic Myeloid Leukemia 2.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed December 2023.
4. Cortes J, Digumarti R, Parikh M, et al. Phase 2 study of subcutaneous omacetaxine mepesuccinate for chronic-phase chronic myeloid leukemia patients resistant to or intolerant of tyrosine kinase inhibitors. Am J Hematol. 2013 May;88(5):350-4. doi: 10.1002/ajh.23408. Epub 2013 Mar 7.
5. Cortes J, Lipton J, Rea D, et al. Phase 2 study of subcutaneous omacetaxine mepesuccinate after TKI failure in patients with chronic-phase CML with T315I mutation. Blood. 2012 Sep 27;120(13):2573-80.doi: 10.1182/blood-2012-03-415307. Epub 2012 Aug 15.

VIII. References (ENHANCED)

1e. Khoury HJ, Cortes J, Baccarani M, et al. Omacetaxine mepesuccinate in patients with advanced chronic myeloid leukemia with resistance or intolerance to tyrosine kinase inhibitors. Leuk Lymphoma. 2015 Jan;56(1):120-7.

2e. Cortes JE, Kantarjian HM, Rea D, et al. Final analysis of the efficacy and safety of omacetaxine mepesuccinate in patients with chronic- or accelerated-phase chronic myeloid leukemia: Results with 24 months of follow-up. Cancer. 2015;121(10):1637–1644.

3e. Talpaz M, Silver RT, Druker BJ, et al. Imatinib induces durable hematologic and cytogenetic responses in patients with accelerated phase chronic myeloid leukemia: results of a phase 2 study. Blood. 2002 Mar 15;99(6):1928-37.

4e. Palandri F, Castagnetti F, Alimena G, et al. The long-term durability of cytogenetic responses in patients with accelerated phase chronic myeloid leukemia treated with imatinib 600 mg: the GIMEMA CML Working Party experience after a 7-year follow-up. Haematologica. 2009;94(2):205–212.

5e. Kantarjian H, Cortes J, Kim DW, et al. Phase 3 study of dasatinib 140 mg once daily versus 70 mg twice daily in patients with chronic myeloid leukemia in accelerated phase resistant or intolerant to imatinib: 15-month median follow-up. Blood. 2009;113(25):6322–6329.

6e. le Coutre PD, Giles FJ, Hochhaus A, et al. Nilotinib in patients with Ph+ chronic myeloid leukemia in accelerated phase following imatinib resistance or intolerance: 24-month follow-up results. Leukemia. 2012 Jun;26(6):1189-94.

7e. Gambacorti-Passerini C, Kantarjian HM, Kim DW, et al. Long-term efficacy and safety of bosutinib in patients with advanced leukemia following resistance/intolerance to imatinib and other tyrosine kinase inhibitors. Am J Hematol. 2015;90(9):755–768.

8e. Cortes J, Lipton JH, Rea D, et al. Phase 2 study of subcutaneous omacetaxine mepesuccinate after TKI failure in patients with chronic-phase CML with T315I mutation. Blood. 2012;120(13):2573–2580.

9e. Cortes J, Digumarti R, Parikh PM, et al. Phase 2 study of subcutaneous omacetaxine mepesuccinate for chronic-phase chronic myeloid leukemia patients resistant to or intolerant of tyrosine kinase inhibitors. Am J Hematol. 2013;88(5):350–354.

10e. Cortes JE, Kim DW, Pinilla-Ibarz J, et al. Ponatinib efficacy and safety in Philadelphia chromosome-positive leukemia: final 5-year results of the phase 2 PACE trial. Blood. 2018;132(4):393–404.

11e. Kantarjian HM, O'Brien S, Cortes JE, et al. Imatinib mesylate therapy for relapse after allogeneic stem cell transplantation for chronic myelogenous leukemia. Blood. 2002 Sep 1;100(5):1590-5.

12e. Prime Therapeutics Management. Synribo Clinical Literature Review Analysis. Last updated December 2023. Accessed December 2023.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdictio	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC