Synribo® (omacetaxine mepesuccinate)
(Subcutaneous)

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I. Length of Authorization

Coverage will be provided for six 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]:

Induction:
- 9,800 billable units every 28 days until hematologic response is achieved, then begin maintenance

Maintenance:
- 4,900 billable units every 28 days

III. Initial Approval Criteria [1,2,3]

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

- Used as single agent therapy; **AND**
- Patient 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., bosutinib, imatinib, dasatinib, ponatinib or nilotinib); **AND**

- Patient has chronic phase disease; **OR**
- Patient has advanced disease that has progressed to accelerated phase; **OR**
- Used for post-allogeneic hematopoietic stem cell transplant (HSCT) follow-up therapy in patients with molecular relapse (*BCR-ABL1* transcript positive) following complete cytogenetic response (CCyR); **OR**
- Used for post-allogeneic HSCT follow-up therapy in patients with relapse or those who are not in CCyR; **OR**
- Patient has T315I mutation positive disease

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

IV. Renewal Criteria [1-5]

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**
- Patient has been adherent to therapy; **AND**
- Treatment response as indicated by one of the following:
  - Patient has *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* mRNA from the standardized baseline, if qPCR (IS) is not available

    Note: cytogenetic assessment of response may be used if quantitative RT-PCR (QPCR) using International Scale (IS) for *BCR-ABL1* is not available

V. Dosage/Administration

Indication	Dose
Chronic Myeloid Leukemia	Induction Dose: 1.25 mg/m² 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/m² 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 and storage of the reconstituted product

VI. Billing Code/Availability Information

HCPCS:

- 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

1. Synribo [package insert]. North Wales, PA; Teva Pharmaceuticals USA, Inc.; May 2021. Accessed November 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for omacetaxine. National Comprehensive Cancer Network, 2021. 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 November 2021.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Chronic Myeloid Leukemia 2.2022. National Comprehensive Cancer Network, 2021. 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 November 2021.
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.

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)

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**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