Clinical Policy: Omacetaxine (Synribo)

Reference Number: PA.CP.PHAR.108
Effective Date: 01/2018
Last Review Date: 04/2024

Description
Omacetaxine (Synribo®) is cephalotaxine ester that inhibits protein synthesis by binding to the A-site in the peptidyl-transferase center of the large ribosomal subunit.

FDA Approved Indication(s)
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 (TKIs).

Policy/Criteria
It is the policy of PA Health & Wellness that Synribo is **medically necessary** when one of the following criteria are met:

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia (must meet all):

1. Diagnosis of chronic myeloid leukemia (CML);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, Bosulif®, Sprycel®, Tasigna®, Iclusig®);
   b. Member has T315I mutation and has received prior treatment with Iclusig and Scemblix®;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 2.5 mg/m^2 per day for 14 consecutive days for induction and 7 consecutive days for maintenance of each 28-day cycle.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Chronic Myeloid Leukemia (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policye (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 2.5 mg/m^2 per day for 14 consecutive days for induction and 7 consecutive days for maintenance of each 28-day cycle;

b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policye (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CML: chronic myelogenous leukemia
FDA: Food and Drug Administration
TKI: tyrosine kinase inhibitors

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
imatinib (Gleevec®)	Adult: • 400-600 mg/day PO for chronic phase • 600-800 mg/day PO for accelerated phase or blast crisis (800 mg given as 400 BID)	Adult: 800 mg/day
Bosulif® (bosutinib)	400 mg PO QD	600 mg/day
Sprycel® (dasatinib)	Adults: • Chronic phase: 100-140 mg/day PO • Accelerated, myeloid phase, or lymphoid blast phase: 140-180 mg/day PO	Adults: 180 mg/day
Tasigna® (nilotinib)	Adults: 300 mg PO BID	Adults: 600 mg/day
Iclusig® (ponatinib)	Starting dose 45 mg PO QD	45 mg/day
Scemblix® (asciminib)	200 mg PO BID	200 mg/day

Appendix C: Contraindications/Boxed Warnings
None reported

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CML	Induction dose: 1.25 mg/m^2 subcutaneous twice daily for 14 consecutive days of a 28-day cycle Maintenance dose: 1.25 mg/m^2 subcutaneous twice daily for 7 consecutive days of a 28-day cycle	2.5 mg/m^2 per day

V. Product Availability

Single-use vial: 3.5 mg of omacetaxine mepesuccinate as a lyophilized powder

VI. References

1. Synribo Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; May 2021. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/203585Orig1s008lbl.pdf. Accessed January 8, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at http://www.nccn.org/professionals/drug_compendium. Accessed January 11, 2024.
3. National Comprehensive Cancer Network Guidelines. Chronic Myeloid Leukemia Version 2.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf.. Accessed January 11, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9262	Injection, omacetaxine mepesuccinate, 0.01 mg

Reviews, Revisions, and Approvals	Date
Q 2018 annual review: summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; references reviewed and updated.	02/2018
2Q 2019 annual review: hematologist added to CML/ALL criteria; added requirement for failure of 2 or more tyrosine kinase inhibitors prior to approval for CML; references reviewed and updated.	04/2019
2Q 2020 annual review: black box warnings removed; references reviewed and updated.	04/2020
2Q 2021 annual review: added, Member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, bosutinib, dasatinib, nilotinib, ponatinib); references reviewed and updated.	04/2021
2Q 2022 annual review: added additional prior therapy option requirement for T315I mutation that member has received prior treatment with Iclusig and	04/2022

Reviews, Revisions, and Approvals	Date
Scemblix as other TKIs are contraindicated in this specific mutation; references reviewed and updated.	
2Q 2023 annual review: clarified dosing to include allowance for dosing 14 consecutive days for induction and 7 consecutive days for maintenance of each 28-day cycle; references reviewed and updated.	04/2023
2Q 2024 annual review: no significant changes; references reviewed and updated.	04/2024