Clinical Policy: Omacetaxine (Synribo)

Reference Number: CP.PHAR.108
Effective Date: 04.01.13
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Synribo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia (must meet all)**:**

1. Diagnosis of Ph+ (BCR-ABL1-positive) CML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member has experienced resistance, toxicity, or intolerance to prior therapy with two or more TKIs (e.g., imatinib, Bosulif®, Sprycel®, Tasigna®, Iclusig®);
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).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM - 6 months
Commercial - 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Chronic Myeloid Leukemia (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Synribo for CML and has received this medication for at least 30 days;
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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM - 12 months
Commercial - 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

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

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

V. 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

VI. Product Availability

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

VII. 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 16, 2025.
2. National Comprehensive Cancer Network Guidelines. Chronic Myeloid Leukemia Version 3.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed February 11, 2025.

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	P&T Approval Date
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); updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.12.21	05.21
2Q 2022 annual review: added additional prior therapy option requirement for T315I mutation that member has received prior treatment with Iclusig and Scemblix as other TKIs are contraindicated in this specific mutation; 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.	02.02.22	05.22
Template changes applied to other diagnoses/indications.	09.30.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.06.23	05.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2024 annual review: no significant changes; references reviewed and updated.	01.08.24	05.24
2Q 2025 annual review: removed off-label use in T315I mutation as this is no longer supported by NCCN Compendium; references reviewed and updated.	01.16.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.