RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	omacetaxine
Policy Number:	RxA.615
Drug(s) Applied:	Synribo®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

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.
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 (TKI).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
omacetaxine (Synribo®)	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

Dosage Forms

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

Clinical Policy

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

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia (must meet all):

1. Request is for one of the following (a or b):
   a. Both i and ii;
      i. Diagnoses of either one of the following (1 or 2);
         1. Chronic phase CML;
         2. Accelerated phase CML;

ii. Resistance or intolerance to prior therapy with two or more TKI.

b. Member is receiving follow-up therapy after hematopoietic stem cell transplantation for either of the following:
   i. Molecular relapse (BCR-ABL1 transcript positive) following a previous complete cytogenetic response;
   ii. Cytogenetic relapse or not in complete cytogenetic response;

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. Dose does not exceed 2.5 mg/m^2 per day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Chronic Myeloid Leukemia (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indication 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;
   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
Commercial: 6 months
Medicaid: 12 months

III. Appendices

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

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None.

- Boxed Warning(s):
  - None.

APPENDIX D: General Information

- Synribo® acts independently of direct BCR-ABL1 binding. The mechanism of action has not been fully

elucidated. It reduces protein levels of both BCR-ABL1 and Mcl-1, an inhibitor of apoptosis, as demonstrated in vitro.

- Warnings and Precautions:
  - Myelosuppression: Severe and fatal thrombocytopenia, neutropenia and anemia. Monitor hematologic parameters frequently.
  - Bleeding: Severe thrombocytopenia and increased risk of hemorrhage. Fatal cerebral hemorrhage and severe, non-fatal gastrointestinal hemorrhage.
  - Hyperglycemia: Glucose intolerance and hyperglycemia including hyperosmolar non-ketotic hyperglycemia.
  - Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use an effective method of contraception.

References

1. Synribo Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; November 2019. Available at https://www.synribohcp.com/wp-content/uploads/synribo_pi.pdf . Accessed November 06, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 06, 2020.
3. National Comprehensive Cancer Network Guidelines. Chronic Myeloid Leukemia Version 2.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf . Accessed November 06, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy clinical title was updated as “omacetaxine”. 2. Lines of business policy applies to all lines of business. 3. Initial approval criteria I.A.1 was updated to add new request. 4. Continued therapy criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…”. 5. Commercial approval duration for initial and continued approval criteria was updated to 6 months respectively. 6. Appendix C was updated: Removed boxed warnings. 7. Appendix D was updated. 8. References were reviewed and updated.	11/06/2020	12/07/2020