Medical Policy:

Synribo (omacetaxine)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.168	January 2, 2024	July 15, 2019

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Synribo (omacetaxine): is a cephalotaxine ester derived from the evergreen tree, Cephalotaxus harringtonia. Omacetaxine inhibits protein synthesis by binding to the A-site in the peptidyl-transferase center of the large ribosomal subunit. It reduces protein levels of Bcr-Abl and Mcl-1 independent of direct Bcr-Abl binding. Omacetaxine may induce apoptosis through mitochondrial disruption and cytochrome c release leading to caspase-9 and caspase-3 activation in certain myeloid leukemia cell lines (i.e., HL60, HL60/MRP). Apoptosis may also be facilitated by a down-regulation of Mcl-1 and activation of PARP and caspase-8. The Bcr-Abl kinase is essential for the initiation, maintenance, and progression of chronic myelogenous leukemia (CML). A Bcr-Abl mutation that exchanges the amino acids threonine and isoleucine at position 315 (T315I mutation) represents a mechanism of resistance for the tyrosine kinase inhibitors (TKI). Omacetaxine has demonstrated activity in wild- type and T315I mutated Bcr-Abl in mice models and efficacy in CML patients with the T315I mutation who had failed previous TKI therapy.

Length of Authorization

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

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

- Induction:
  - 9,800 billable units every 28 days until hematologic response is achieved, then begin maintenance
- Maintenance:
  - 4,900 billable units every 28 days

Guideline

I. **Initial Approval Criteria**

Synribo *may be considered medically necessary when any of the following selection criteria is met:*

1. **Chronic Myelogenous Leukemia**
   A. The member has chronic phase **OR** accelerated phase CML **OR** is post-transplant; **AND**
   B. The member is Philadelphia chromosome (Ph+) or BCR-ABL positive; **AND**
   C. Has disease progression due to resistance and/or intolerance to **TWO** or more tyrosine kinase inhibitors: Such as Gleevec (imatinib), Tasigna (nilotinib), Sprycel (dasatinib), Iclusig (ponatinib) or Bosulif (bosutinib) **OR**
   D. The member has a T315I mutation.

Limitations/Exclusions

Synribo is not considered medically necessary for when any of the following selection criteria is met:

1. Disease progression while taking Synribo (omacetaxine).
2. Concurrent use with Gleevec (imatinib), Sprycel (dasatinib), Tasigna (nilotinib), Sprycel (dasatinib), Iclusig (ponatinib) or Bosulif (bosutinib).
3. Dosing exceeds single dose limit of Synribo (omacetaxine) 1.25 mg/m^2.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

II. **Renewal Criteria**

Patient continues to meet criteria in INITIAL APPROVAL CRITERIA.

Dosage/Administration

Indication	Dose
Chronic myelogenous leukemia	Induction dose: 1.25mg/m^2 subcutaneously twice daily for 14 days repeated every 28 days until a hematologic response is achieved. Maintenance dose: 1.25 mg/m^2 subcutaneously twice daily for 7 days repeated every 28 days for as long as a clinical benefit is observed.

Applicable Procedure Codes

Code	Description
J9262	Injection, omacetaxine mepesuccinate, 0.01 mg, 1 billable unit = 0.01 mg

Applicable NDCs

Code	Description
63459-0177-xx	Synribo 3.5 mg single-use vial for injection

ICD-10 Diagnoses

Code	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

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/2/2024	Annual Review: No Criteria changes
EmblemHealth & ConnectiCare	4/21/2023	Annual Review: added : Sprycel (dasatinib), Iclusig (ponatinib) to TKI
EmblemHealth & ConnectiCare	1/13/2023	Transfer to New Template
EmblemHealth & ConnectiCare	7/15/2019	New Policy

References

1. Synribo prescribing information. Teva Pharmaceuticals Inc. North Wales, PA. 2017.
2. Clinical Pharmacology Elsevier Gold Standard. 2018.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2018.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2018.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2018.