Synribo® (omacetaxine)

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Medical Guideline Disclaimer

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Definition

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 peptidyltransferase 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

Max Units (per dose and over time) [Medical Benefit]:

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

- Maintenance:
  - 4,900 billable units every 28 days
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 or BCR-ABL positive; **AND**
   c. Has disease progression due to resistance and/or intolerance to two or more of the following tyrosine kinase inhibitors: Gleevec (imatinib), Tasigna (nilotinib), 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), or Bosulif (bosutinib).
3. Dosing exceeds single dose limit of *Synribo* (omacetaxine) 1.25 mg/m².
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**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
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| Chronic myelogenous leukemia      | – Induction dose: 1.25mg subcutaneously twice daily for 14 days repeated every 28 days until a hematologic response is achieved.  
|                                   | – Maintenance dose: 1.25 mg/m² subcutaneously twice daily for 7 days repeated every 28 days for as long as a clinical benefit is observed.  |

**Applicable Procedure Codes**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>J9262</td>
<td>Injection, omacetaxine mepesuccinate, 0.01 mg, 1 billable unit = 0.01 mg</td>
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</table>

**Applicable NDCs**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>63459-0177-xx</td>
<td>Synribo 3.5 mg single-use vial for injection</td>
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Applicable Diagnosis Codes

<table>
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<tr>
<th>ICD-10</th>
<th>ICD-10 Description</th>
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<tbody>
<tr>
<td>C92.10</td>
<td>Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission</td>
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<tr>
<td>C92.11</td>
<td>Chronic myeloid leukemia, BCR/ABL-positive, in remission</td>
</tr>
<tr>
<td>C92.12</td>
<td>Chronic myeloid leukemia, BCR/ABL-positive, in relapse</td>
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References