Drug Therapy Guidelines

Afinitor® (everolimus)

<table>
<thead>
<tr>
<th>Medical Benefit</th>
<th>Applicable</th>
<th>Effective: 4/5/17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacy- Formulary 1</td>
<td>x</td>
<td>Next Review: 3/18</td>
</tr>
<tr>
<td>Pharmacy- Formulary 2</td>
<td>x</td>
<td>Date of Origin: 9/10</td>
</tr>
<tr>
<td>Pharmacy- Formulary 4/AON</td>
<td>x</td>
<td></td>
</tr>
</tbody>
</table>

I. Medication Description

Afinitor® (everolimus) blocks a special targeted protein known as the mammalian target of rapamycin or mTOR. Everolimus exerts its action by binding to intracellular proteins to form an inhibitory complex which leads to reduction of protein synthesis, inhibition of hypoxia-inducible factor (HIF-1) and reduced expression of vascular endothelial growth factor (VEGF). Blocking these pathways helps reduce the growth, division, and metabolism of cancer cells.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage is provided for the following:

- Hodgkin Lymphoma as a single agent for relapsed/refractory disease
- Renal Cell Carcinoma:
  - Subsequent therapy as a single agent or in combination with lenvatinib for relapsed or unresectable stage IV disease with predominant clear cell histology OR
  - Systemic therapy as a single agent or in combination with lenvatinib for relapsed or unresectable stage IV disease in patients with non-clear cell histology
- Soft Tissue Sarcoma: single agent therapy for PEComa and reoccurring angiomylipoma and lymphangioleiomyomatosis
- Waldenström's Macroglobulinemia/lymphoplasmacytic lymphoma: single agent salvage therapy for disease that does not respond to primary therapy or for progressive or relapsed disease
- Invasive Breast cancer:
  - For ER positive, HER2 negative recurrent or metastatic breast cancer as subsequent therapy in combination with exemestane in post-menopausal patients who progressed on or within 12 months of an aromatase inhibitor or were treated with tamoxifen at any time
- Thymomas and Thymic Carcinomas: second-line therapy as a single agent
- Neuroendocrine tumors
  - Lung: Stage IIIb-IV low or intermediate grade neuroendocrine carcinoma
  - Pancreas: single-agent for unresectable locoregional and/or distant metastatic disease in patients with symptoms, or clinically significant tumor burden or progression
- Osteosarcoma: Second-line therapy in combination with sorafenib
IV. **Quantity Limitations**

- Afinitor 2.5mg, 5mg, 7.5mg tablets: 30 tablets per 30 days
- Afinitor 10mg tablets: 60 tablets per 30 days
- Afinitor Disperz 2mg, 3mg: 28 tablets per 28 days
- Afinitor Disperz 5mg: 60 tablets per 30 days

V. **Coverage Duration**

Coverage is provided for 12 months and can be renewed.

VI. **Coverage Renewal Criteria**

Coverage can be renewed based upon the following criteria:

- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread **AND**
- Absence of unacceptable toxicity from the drug

VII. **Billing/Coding Information**

Available as Afinitor 2.5mg, 5mg, 7.5mg, and 10mg oral tablets as well as Afinitor Disperz 2mg, 3mg, and 5mg tablets for oral suspension.

VIII. **Summary of Policy Changes**

- 6/1/11: Addition of SEGA indication and dosing limitations
- 6/15/13: Use in RCC limited to after failure of treatment with any tyrosine kinase inhibitor (changed from only after Sutent or Nexavar)
- 6/15/14: clear and non-clear cell RCC, hodgkin lymphoma and soft tissue sarcoma added to policy; additional indication in ER-positive breast cancer added; Afinitor disperz tablets added to policy, SEGA removed from policy
- 6/15/15: thymomas and thymic carcinomas added to policy; use in clear cell RCC changed from first line to subsequent therapy after failure of treatment with a tyrosine kinase inhibitor
- 7/1/15: formulary distinctions made
- 6/15/16: Updated coverage to coincide with current NCCN treatment guidelines
- 4/5/17: policy updated to correspond with current NCCN treatment guidelines
IX. References


The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary agent will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.