1. **Background:**

Afinitor® (everolimus) is a kinase inhibitor indicated for the treatment of advanced renal cell carcinoma after treatment with Sutent® (sunitinib) or Nexavar® (sorafenib); for the treatment of subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) in those patients who require therapeutic intervention but are not a candidate for curative surgical resection; for the treatment of progressive neuroendocrine tumors of pancreatic origin (PNET) that are well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic; for treatment of renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery; and in postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ BC) in combination with Aromasin® (exemestane) after failure of treatment with Femara® (letrozole) or Arimidex® (anastrozole).\(^1\) The National Cancer Comprehensive Network (NCCN) also recommends use of Afinitor in Waldenström’s macroglobulinemia / lymphoplasmacytic lymphoma, lung neuroendocrine tumors with carcinoid histology, non-clear cell kidney cancer, soft tissue sarcomas, osteosarcomas, thymomas and thymic carcinomas, and Hodgkin lymphoma.\(^2\)

**Coverage Information:**

Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. **Coverage Criteria:**

   **A. Patients less than 19 years of age**

   1. **Afinitor** will be approved based on the following criterion:

      a. Patient is less than 19 years of age

      **Authorization will be issued for 12 months.**
B. Neuroendocrine Tumors

1. Initial Authorization

   a. Afinitor will be approved based on all of the following criteria:

      (1) Diagnosis of one of the following:
          (a) Neuroendocrine tumors of pancreatic origin
          (b) Neuroendocrine tumors of gastrointestinal origin
          (c) Neuroendocrine tumors of lung origin

      -AND-

      (2) Disease is progressive

      -AND-

      (3) One of the following:

          (a) Disease is unresectable
          (b) Disease is locally advanced
          (c) Disease is metastatic

   Authorization will be issued for 12 months.

2. Reauthorization

   a. Afinitor will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Afinitor therapy

   Authorization will be issued for 12 months.

C. Advanced Renal Cell Carcinoma

1. Initial Authorization

   a. Afinitor will be approved based on all of the following criteria:

      (1) Diagnosis of renal cell cancer

      \textbf{AND}

      (2) One of the following:
(a) Disease has relapsed

OR

(b) Both of the following:
   i. Medically or surgically unresectable tumor
   ii. Diagnosis of Stage IV disease

AND

(3) One of the following:

(a) Patient with non-clear cell histology

OR

(b) Both of the following:
   i. Patient with predominantly clear cell histology

AND

   ii. History of failure, contraindication, or intolerance to at least one prior tyrosine kinase inhibitor therapy [e.g., Nexavar (sorafenib), Sutent (sunitinib)]

Authorization will be issued for 12 months.

2. Reauthorization

   a. Afinitor will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Afinitor therapy

      Authorization will be issued for 12 months.

D. Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC)

1. Initial Authorization

   a. Afinitor will be approved based on the following criterion:

      (1) Diagnosis of renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery
Authorization will be issued for 12 months.

2. Reauthorization

a. Afinitor will be approved based on the following criterion:

   (1) Patient does not show evidence of progressive disease while on Afinitor therapy

   Authorization will be issued for 12 months.

E. Subependymal Giant Cell Astrocytoma

1. Initial Authorization

a. Afinitor will be approved based on both of the following criteria:

   (1) Diagnosis of subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS)

   -AND-

   (2) Patient is not a candidate for curative surgical resection

   Authorization will be issued for 12 months.

2. Reauthorization Criteria

a. Afinitor will be approved based on the following criterion:

   (1) Patient does not show evidence of progressive disease while on Afinitor therapy

   Authorization will be issued for 12 months.

F. Waldenström’s Macroglobulinemia or Lymphoplasmacytic Lymphoma (off-label)

1. Initial Authorization

a. Afinitor will be approved based on both the following criteria:

   (1) Diagnosis of one of the following:

   (a) Waldenström’s macroglobulinemia

   (b) Lymphoplasmacytic lymphoma
(2) **One** of the following:

(a) Disease is non-responsive to primary treatment  
(b) Disease is progressive  
(c) Disease has relapsed  

**Authorization will be issued for 12 months.**

2. **Reauthorization Criteria**

   a. **Afinitor** will be approved based on the following criterion:

   (1) Patient does not show evidence of progressive disease while on Afinitor therapy  

   **Authorization will be issued for 12 months.**

**G. Breast Cancer**

1. **Initial Authorization**

   a. **Afinitor** will be approved based on **all** of the following criteria:

   (1) Diagnosis of breast cancer  

   - **AND-**  

   (2) **One** of the following:

   (a) Disease is recurrent  
   (b) Disease is metastatic  

   - **AND-**  

   (3) Disease is hormone receptor positive (HR+) [i.e., estrogen-receptor-positive (ER+) or progesterone-receptor-positive (PR+)]  

   - **AND-**  

   (4) Disease is human epidermal growth factor receptor 2 (HER2)-negative...
(5) Patient is a postmenopausal woman

(6) **One** of the following:

(a) Disease progressed while on or within 12 months of non-steroidal aromatase inhibitor [e.g., Arimidex (anastrozole), Femara (letrozole)] therapy

(b) Patients was treated with tamoxifen at any time

(7) Used in combination with Aromasin (exemestane)

**Authorization will be issued for 12 months.**

2. **Reauthorization Criteria**

   a. **Afinitor** will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Afinitor therapy

      **Authorization will be issued for 12 months.**

H. **Hodgkin Lymphoma (off-label)**

1. **Initial Authorization**

   a. **Afinitor** will be approved based on both of the following criteria:

      (1) Diagnosis of classical Hodgkin lymphoma

      **AND**

      (2) **One** of the following:

      (a) Disease is refractory

      (b) Disease has relapsed

      **Authorization will be issued for 12 months.**

2. **Reauthorization Criteria**

   a. **Afinitor** will be approved based on the following criterion:
(1) Patient does not show evidence of progressive disease while on Afinitor therapy

Authorization will be issued for 12 months.

I. Soft Tissue Sarcoma (off-label)

1. Initial Authorization

   a. Afinitor will be approved based on one of the following criteria:

      (1) Diagnosis of PEComa (perivascular epithelioid cell tumor)
      (2) Diagnosis of recurrent angiomyolipoma
      (3) Diagnosis of lymphangioleiomyomatosis

      Authorization will be issued for 12 months.

2. Reauthorization Criteria

   a. Afinitor will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Afinitor therapy

      Authorization will be issued for 12 months.

J. Osteosarcoma (off-label)

1. Initial Authorization

   a. Afinitor will be approved based on all of the following criteria:

      (1) Diagnosis of osteosarcoma

      -AND-

      (2) History of failure, contraindication, or intolerance to at least one prior first-line chemotherapy regimen

      -AND-

      (3) Used in combination with Nexavar (sorafenib)

      Authorization will be issued for 12 months.
2. **Reauthorization Criteria**

   a. **Afinitor** will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Afinitor therapy

      **Authorization will be issued for 12 months.**

K. **Thymomas and Thymic Carcinomas (off-label)**

   1. **Initial Authorization**

      a. **Afinitor** will be approved based on **both** of the following criteria:

         (1) **One** of the following:
             (a) Diagnosis of thymic carcinoma
             (b) Diagnosis of thymoma

         **-AND-**

         (2) History of failure, contraindication, or intolerance to at least **one** prior first-line chemotherapy regimen.

         **Authorization will be issued for 12 months.**

   2. **Reauthorization Criteria**

      a. **Afinitor** will be approved based on the following criterion:

         (1) Patient does not show evidence of progressive disease while on Afinitor therapy

         **Authorization will be issued for 12 months.**

3. **Additional Clinical Rules:**

   - Supply limits may be in place.

4. **References:**


<table>
<thead>
<tr>
<th>Program</th>
<th>Prior Authorization/Notification - Afinitor (everolimus)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change Control</strong></td>
<td></td>
</tr>
<tr>
<td>8/2014</td>
<td>Annual review. Added coverage for soft tissue sarcomas, Hodgkin lymphoma, and non-clear cell kidney cancer. Updated breast cancer to include tamoxifen as part of trial/failure and ‘advanced’ to type of cancer. Updated formatting, Background and References.</td>
</tr>
<tr>
<td>8/2015</td>
<td>Annual review. Updated criteria for breast cancer, Hodgkin lymphoma, lung neuroendocrine tumors and Waldenström’s macroglobulinemia / lymphoplasmacytic lymphoma. Increased authorization and reauthorization from 5 months to 12 months for all indications. Updated background and references.</td>
</tr>
<tr>
<td>7/2016</td>
<td>Annual review. Consolidated neuroendocrine tumor criteria. Minor revision to Renal Cell Carcinoma. Added indications and criteria for Osteosarcoma and Thymoma/thymic carcinoma per NCCN guidelines. Updated background and references.</td>
</tr>
</tbody>
</table>