UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2018 P 1003-7
Program	Prior Authorization/Notification
Medication	Afinitor (everolimus)
P&T Approval Date	12/8/2009, 6/2010, 9/2010, 12/2010, 7/2011, 9/2011, 5/2012, 8/2012, 7/2013, 8/2014, 8/2015, 7/2016, 7/2017, 5/2018
Effective Date	8/1/2018; Oxford only: 8/1/2018

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; 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), and for the adjunctive treatment of TSC associated partial-onset seizures.[1] The National Cancer Comprehensive Network (NCCN) also recommends use of Afinitor in invasive breast cancer, Waldenström's macroglobulinemia / lymphoplasmacytic lymphoma, neuroendocrine tumors with carcinoid histology, non-clear cell kidney cancer, soft tissue sarcomas, osteosarcomas, dedifferentiated chondrosarcoma, high-grade undifferentiated pleomorphic sarcoma (UPS), thymomas and thymic carcinomas, Hodgkin lymphoma, follicular, Hürthle cell and papillary thyroid carcinomas, meningioma, and endometrial carcinoma.[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. <u>Patients less than 19 years of age</u>

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
(d) Neuroendocrine tumors of thymic 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

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. Waldenströms 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) Waldenströms macroglobulinemia
(b) Lymphoplasmacytic lymphoma

-AND-

(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) **One** of the following:

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

-OR-

(b) **Both** of the following:

i. Disease is hormone receptor negative (HR-)
ii. Disease has clinical characteristics that predict a HR+ tumor

-AND-

(4) Disease is human epidermal growth factor receptor 2 (HER2)-negative

-AND-

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

(a) Patient is a postmenopausal woman

-OR-

(b) **Both** of the following:

i. Patient is a premenopausal woman
ii. Patient is being treated with ovarian ablation/suppression

-OR-

(c) Patient is male

-AND-

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

(a) **Both** of the following:

i. Used in combination with Aromasin (exemestane)

-AND-

ii. **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

-OR-

b. Patient was treated with tamoxifen at any time

-OR-

(b) Used in combination with **one** of the following:

i. Fulvestrant
ii. Tamoxifen

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 epitheliod cell tumor)
(2) Diagnosis of recurrent angiomyolipoma
(3) Diagnosis of lymphangioleiomyomatosis
(4) **All** of the following:

(a) Diagnosis of Gastrointestinal Stromal Tumor (GIST)

-AND-

(b) Disease has progressed after single agent therapy

-AND-

(c) Used in combination with **one** of the following:

i. Gleevec (imatinib)
ii. Sutent (sunitinib)
iii. Stivarga (regorafenib)

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. Bone Cancer (off-label)

1. Initial Authorization

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

(1) One of the following:
(a) Diagnosis of osteosarcoma
(b) Diagnosis of dedifferentiated chondrosarcoma
(c) Diagnosis of high-grade undifferentiated pleomorphic sarcoma (UPS)

-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 carcinmoa
(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.

L. Thyroid Carcinoma (off-label)

1. **Initial Authorization**

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

      (1) Diagnosis of **one** of the following:

         (a) Follicular carcinoma
         (b) Hürthle cell carcinoma
         (c) Papillary carcinoma

      -AND-

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

         (a) Unresectable recurrent disease
         (b) Persistent locoregional disease
         (c) Metastatic disease

      -AND-

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

         (a) Patient has symptomatic disease
         (b) Patient has progressive disease

      -AND-

      (4) Disease is refractory to radioactive iodine treatment

   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.

M. Meningioma (off-label)

1. **Initial Authorization**

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

(1) Diagnosis of meningioma

-AND-

(2) Disease is recurrent or progressive

-AND-

(3) Surgery and/or radiation is not possible

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.

N. Endometrial Carcinoma (off label)

1. Initial Authorization

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

(1) Diagnosis of endometrial carcinoma

-AND-

(2) Used in combination with letrozole

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.

O. Tuberous Sclerosis Complex associated Partial-onset Seizures

1. **Initial Authorization**

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

      (1) Diagnosis of tuberous sclerosis complex associated partial-onset seizures

      -AND-

      (2) Used as adjunctive therapy

      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.

3. Additional Clinical Rules:

- Supply limits may be in place.

4. References:

1. Afinitor [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2018.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at http://www.nccn.org/professionals/drug_compendium/content/contents.asp. March 22, 2018.

Program	Prior Authorization/Notification - Afinitor (everolimus)
Change Control	
8/2014	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.
9/2014	Administrative change - Tried/Failed exemption for State of New

	Jersey removed.
8/2015	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.
7/2016	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.
7/2017	Annual review. Updated background and added criteria for thyroid carcinoma and the bone cancers, dedifferentiated chondrosarcoma, high-grade undifferentiated pleomorphic sarcoma (UPS) per NCCN guidelines. Updated references.
5/2018	Annual review. Updated background, added criteria for meningioma, gastrointenstinal stromal tumors, endometrial carcinoma, thymic neuroendocrine tumors, and updated breast cancer criteria per NCCN guidelines. Added criteria for new indication of tuberous sclerosis complex associated partial-onset seizures. Updated references.