UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2023 P 1003-12
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, 5/2019, 5/2020, 5/2021, 5/2022, 5/2023
Effective Date	8/1/2023; Oxford only: 8/1/2023

1. Background:

Afinitor® (everolimus) is a kinase inhibitor indicated for the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer in combination with Aromasin® (exemestane) after failure of treatment with Femara® (letrozole) or Arimidex® (anastrozole); in adults with progressive neuroendocrine tumors of pancreatic origin (PNET) and adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic; adults with advanced renal cell carcinoma (RCC) after failure of treatment with Sutent® (sunitinib) or Nexavar® (sorafenib); adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery; treatment of adult and pediatric patients aged 1 year and older with TSC who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected; and for the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.[1]

Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.

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, histiocytic neoplasms, 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.

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2. Coverage Criteria[a,b]:

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 **One** of the following criteria:

      (1) **All** of the following:

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

            (i) Neuroendocrine tumors of gastrointestinal origin
            (ii) Neuroendocrine tumors of lung origin
            (iii) Neuroendocrine tumors of thymic origin

            -AND-

         (b) Disease is progressive

            -AND-

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

            (i) Disease is unresectable
            (ii) Disease is locally advanced
            (iii) Disease is metastatic

      -OR-

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

         (a) Diagnosis of neuroendocrine tumors of pancreatic origin

            -AND-

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

            (i) Used for the management of recurrent, locoregional advanced disease and/or distant metastatic disease
            (ii) Used as preoperative therapy of locoregional insulinoma with or without diazoxide

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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/Kidney Cancer

1. **Initial Authorization**

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

(1) Diagnosis of advanced renal cell cancer/kidney cancer

-AND-

(2) Disease is **one** of the following:

(a) Relapsed
(b) Stage IV disease

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

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:

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(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 with Tuberous Sclerosis Complex

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

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.

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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 (HR)-positive [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-

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(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

1. **Initial Authorization**

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

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(1) Diagnosis of classic Hodgkin lymphoma

-AND-

(2) Disease is refractory to at least 3 prior lines of therapy

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

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 with **one** of the following:

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

-AND-

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

i. imatinib (Gleevec)
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:

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

Authorization will be issued for 12 months.

J. Thymomas and Thymic Carcinomas

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) **One** of the following:

(a) History of failure, contraindication, or intolerance to at least **one** prior first-line chemotherapy regimen
(b) Patient has extrathoracic metastatic disease

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. Thyroid Carcinoma

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:

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(a) Unresectable locoreginal recurrent disease
(b) Persistent 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.

L. Meningioma

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

-AND-

(4) Used in combination with bevacizumab (Avastin®, Mvasi™, etc.)

Authorization will be issued for 12 months.

2. **Reauthorization Criteria**

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

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

Authorization will be issued for 12 months.

M. Endometrial Carcinoma

1. **Initial Authorization**

   a. **Afinitor** will be approved based on **all** 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.

N. 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.

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O. Bone Cancer - Osteosarcoma

1. **Initial Authorization**

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

      (1) Diagnosis of osteosarcoma

      -AND-

      (2) Disease is **one** of the following:
      (a) Relapsed
      (b) Refractory
      (c) Metastatic

      -AND-

      (3) Used in combination with Nexavar (sorafenib)

      -AND-

      (4) **Not** used as first-line 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.

P. Histiocytic Neoplasms

1. **Initial Authorization**

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

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

      (a) Rosai-Dorfman Disease
      (b) Langerhans Cell Histiocytosis
      (c) Erdheim-Chester Disease

      Authorization will be issued for 12 months.

2. **Reauthorization**

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

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

Authorization will be issued for 12 months.

Q. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply

[b] Coverage of oncology medications may be approved based on state mandates.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Afinitor [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2022.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at https://www.nccn.org/professionals/drug_compendium/content/. March 16, 2023.

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.

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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.
5/2019	Annual review. Updated background. Removed criteria for bone cancer (no longer recommended per NCCN guidelines). Updated reference.
5/2020	Annual review. Updated background. Updated coverage criteria for soft tissue sarcoma, thymomas and thymic carcinomas, and meningiomas per NCCN guidelines. Updated references.
5/2021	Annual review. Addition of criteria for osteosarcoma and Histiocytic Neoplasms, and update to kidney cancer criteria according to NCCN guidelines. Updated references.
5/2022	Annual review. Updated background. Updated osteosarcoma criteria per NCCN guidelines. Updated references.
5/2023	Annual review. Updated background. Updated Neuroendocrine tumor and Hodgkin lymphoma criteria per NCCN guidelines. Added state mandate and oncology medications footnote. Updated references.

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