PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Everolimus Products Prior Authorization Policy
- Afinitor® (everolimus tablets – Novartis, generic)
- Afinitor Disperz® (everolimus tablets for oral suspension – Novartis)
- Torpenz™ (everolimus tablets – Upsher-Smith)

REVIEW DATE: 03/19/2025

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Afinitor, a kinase inhibitor, is indicated for the following uses:[1]

- **Breast cancer**, treatment of advanced hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative disease in combination with exemestane, after failure of treatment with letrozole or anastrozole in postmenopausal women.
- **Neuroendocrine tumors (NET)**, treatment of progressive disease of pancreatic origin and progressive, well-differentiated, non-functional NET of gastrointestinal or lung origin that are unresectable, locally advanced, or metastatic in adults. Limitation of Use: Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.
- **Renal cell carcinoma**, treatment of advanced disease after failure of treatment with sunitinib or sorafenib in adults.
- **Tuberous sclerosis complex (TSC)-associated renal angiomyolipoma,** treatment of adults not requiring immediate surgery.
- **TSC-associated subependymal giant cell astrocytoma (SEGA)**, treatment of patients ≥ 1 year of age who require therapeutic intervention but cannot be curatively resected.

Afinitor Disperz, a kinase inhibitor, is indicated for the following uses:[1]

- **TSC-associated SEGA**, treatment of patients ≥ 1 year of age who require therapeutic intervention but cannot be curatively resected.
- **TSC-associated partial-onset seizures**, adjunctive treatment of patients ≥ 2 years of age.

Torpenz, a kinase inhibitor, is indicated for the following uses:[2]

- **Breast cancer**, treatment of advanced HR+, HER2-negative disease in combination with exemestane, after failure of treatment with letrozole or anastrozole in postmenopausal women.
- **Renal angiomyolipoma and TSC,** treatment of adults not requiring immediate surgery.
- **TSC-associated SEGA**, treatment of patients ≥ 1 year of age who require therapeutic intervention but cannot be curatively resected.

Of note, Zortress® (everolimus tablets) is indicated in combination with other drugs for prophylaxis of organ rejection in adults undergoing kidney or liver transplant.[3] The tablet strengths and dosing are different for Zortress and Afinitor. Zortress is not targeted in this policy.

Guidelines

The National Comprehensive Cancer Network (NCCN) Compendium recommends use of everolimus for the indications listed in the FDA-Approved Indications and Other Uses with Supportive Evidence sections.[4]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of everolimus products. All approvals are provided for the duration noted below. In the clinical criteria, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: a woman is defined as an individual with the biological traits of a woman, regardless of the individual's gender identity or gender expression; men are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression.

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is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Breast Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, F, and G):
   A) Patient is ≥ 18 years of age; AND

B) Patient has recurrent or metastatic, hormone receptor positive (HR+) [i.e., estrogen receptor-positive {ER+} and/or progesterone receptor-positive {PR+}] disease; AND
C) Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
D) Patient has tried at least one prior endocrine therapy (e.g., anastrozole, letrozole, or tamoxifen); AND
E) Patient meets ONE of the following (i or ii):
  i. Patient is a postmenopausal woman* or a man*; OR
  ii. Patient is a pre/perimenopausal woman* and meets ONE of the following (a or b):
    a) Patient is receiving ovarian suppression/ablation with a gonadotropin-releasing hormone (GnRH) agonist; OR
    Note: Examples of a GnRH agonist include leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous implant).
    b) Patient has had surgical bilateral oophorectomy or ovarian irradiation; AND
F) Patient meets ONE of the following (i or ii):
  i. The medication will be used in combination with exemestane and the patient meets ONE of the following (a or b):
    a) Patient is a man* and the patient is receiving a gonadotropin-releasing hormone (GnRH) analog; OR
    Note: Examples of a GnRH analog include leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous implant), Firmagon (degarelix acetate subcutaneous injection), and Orgovyx (relugolix tablet).
    b) Patient is a woman*; OR
  ii. The medication will be used in combination with fulvestrant or tamoxifen; AND
G) Patient has not had disease progression while on everolimus.

*Refer to the Policy Statement.

2. Neuroendocrine Tumors of the Pancreas, Gastrointestinal Tract, Lung, and Thymus (Carcinoid Tumors). Approve for 1 year if the patient is ≥ 18 years of age.

3. Renal Cell Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient has relapsed or Stage IV disease; AND
C) Patient meets ONE of the following (i or ii):
  i. Patient has non-clear cell disease; OR
  ii. Patient meets BOTH of the following (a and b):
    a) Patient has clear cell disease; AND

b) Patient has tried at least one prior systemic therapy.
Note: Examples of prior systemic therapy include the following products: Inlyta (axitinib tablets), Lenvima (lenvatinib capsules), Cabometyx (cabozantinib tablets), Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), pazopanib, sunitinib.

4. **Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma.** Approve for 1 year.

5. **Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma (SEGA).** Approve for 1 year if therapeutic intervention is required but SEGA cannot be curatively resected.

6. **Tuberous Sclerosis Complex-Associated Partial Onset Seizures.** Approve for 1 year.

Other Uses with Supportive Evidence

7. **Endometrial Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) The medication will be used in combination with letrozole.

8. **Gastrointestinal Stromal Tumors.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried each of the following (i, ii, iii, and iv):
      i. One of imatinib or Ayvakit (avapritinib tablets); AND
      ii. One of sunitinib or Sprycel (dasatinib tablets); AND
      iii. Stivarga (regorafenib tablets); AND
      iv. Qinlock (ripretinib tablets); AND
   C) The medication will be used in combination with imatinib, sunitinib, or Stivarga (regorafenib tablets).

9. **Histiocytic Neoplasm.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i, ii, or iii):
      i. Patient has Langerhans cell histiocytosis; OR
      ii. Patient has Erdheim-Chester disease; OR
      iii. Patient has Rosai-Dorfman disease; AND
   C) Patient has a *PIK3CA* mutation.

10. **Classic Hodgkin Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B and C):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has relapsed or refractory disease; AND

C) Patient is not a candidate for high-dose therapy and autologous stem cell rescue.

11. **Meningioma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has recurrent or progressive disease; AND
    C) Patient meets BOTH of the following: (i and ii):
        i. Patient has surgically inaccessible disease; AND
        ii. Radiation therapy is not possible.
    D) Patient meets ONE of the following (i or ii):
        i. The medication will be used in combination with a somatostatin analogue; OR
        Note: Example of somatostatin analogue includes octreotide.
        ii. The medication will be used in combination with bevacizumab.

12. **Soft Tissue Sarcoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has ONE of the following (i or ii):
        i. Perivascular epithelioid cell tumor (PEComa); OR
        ii. Recurrent angiomyolipoma/lymphangioleiomyomatosis.

13. **Thymomas and Thymic Carcinomas.** Approve for 1 year if the patient meets BOTH of the following (A and B):
    A) Patient is ≥ 18 years of age; AND
    B) Patient meets ONE of the following (i or ii):
        i. Patient has tried at least one chemotherapy regimen; OR
        Note: Examples of a chemotherapy regimen include cisplatin, doxorubicin, and cyclophosphamide; cisplatin plus etoposide; carboplatin plus paclitaxel; carboplatin, paclitaxel, and Cyramza (ramucirumab intravenous infusion).
        ii. Patient cannot tolerate chemotherapy.

14. **Thyroid Carcinoma, Differentiated.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has differentiated thyroid carcinoma; AND
    Note: Examples of differentiated thyroid carcinoma include papillary, follicular, and oncocytic thyroid carcinoma.
    C) The disease is refractory to radioactive iodine therapy.

15. **Uterine Sarcoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C and D):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has advanced, recurrent, metastatic, or inoperable disease; AND
    C) Patient has a perivascular epithelioid cell tumor (PEComa); AND
    D) Patient has tried at least one systemic regimen.

Note: Examples of systemic regimen include doxorubicin, docetaxel, gemcitabine, ifosfamide, dacarbazine.

16. Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma. Approve for 1 year if the patient meets BOTH of the following (A and B):

A) Patient is ≥ 18 years of age; AND

B) Patient has tried at least one systemic regimen.

Note: Examples of a systemic regimen include one or more of the following agents: bortezomib, bendamustine, rituximab, cyclophosphamide, Imbruvica (ibrutinib capsules, tablets, and oral solution), Brukinsa (zanubrutinib capsules), Kyprolis (carfilzomib intravenous infusion), or Ninlaro (ixazomib capsules).

CONDITIONS NOT COVERED

- **Afinitor® (everolimus tablets (Novartis, generic)**
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is(are) considered experimental, investigational or unproven for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Afinitor® tablets, Afinitor Disperz® tablets for oral suspension [prescribing information]. East Hanover, NJ: Novartis; January 2025.
2. Torpenz™ tablets [prescribing information]. Maple Grove, MN: Upsher-Smith; March 2024.
3. Zortress® tablets [prescribing information]. East Hanover, NJ: Novartis; February 2024.
4. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 13, 2025. Search term: everolimus.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Meningioma**: Indication and criteria were removed from "Other uses with supportive evidence." **Uterine Sarcoma:** Condition of approval and criteria was added to "Other uses with supportive evidence."	03/08/2023
Selected Revision	**Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma:** The requirement that the patient is ≥ 18 years of age was removed.	03/29/2023
Annual Revision	**Classic Hodgkin Lymphoma:** Criterion which states that patient has tried at least three prior lines of therapy was added with a note with examples of therapy. **Histiocytic Neoplasm:** Criterion which states the patient has the following types of Langerhans cell histiocytosis: bone disease, central nervous system lesions, multisystem disease, and pulmonary disease was removed. **Meningioma**: Condition of approval and criteria were added.	03/06/2024
Selected Revision	Torpenz (everolimus tablets) was added to the policy with same criteria as the other everolimus products.	07/03/2024

HISTORY (CONTINUED)

Annual Revision	**Classic Hodgkin Lymphoma:** The qualifier that patient has tried at least three prior lines of chemotherapy and the Note with examples of chemotherapy were removed. The qualifier that patient is not a candidate for high-dose therapy and autologous stem cell rescue was added. **Meningioma:** The following option for approval was added, "the medication will be used in combination with bevacizumab." **Thymomas and Thymic Carcinomas:** The qualifier that the patient has tried "chemotherapy" was reworded to "at least one chemotherapy regimen." The Note was updated to include Carboplatin, paclitaxel, and Cyramza (ramucirumab intravenous infusion) as examples. **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma:** This condition of approval was previously worded as Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. The requirements that patient has not responded to primary therapy or patient has progressive or relapsed disease were removed. The requirement that the patient has tried at least one systemic regimen was added. The Note with examples of a systemic regimen was updated to,"Examples of a systemic regimen include one or more of the following agents: bortezomib, bendamustine, rituximab, cyclophosphamide, Imbruvica (ibrutinib capsules, tablets, and oral solution), Brukinsa (zanubrutinib capsules), Kyprolis (carfilzomib intravenous infusion), or Ninlaro (ixazomib capsules)." Previously the note stated, "Examples of primary therapy are bortezomib, dexamethasone, and rituximab; bendamustine and rituximab; cyclophosphamide, rituximab and dexamethasone; Imbruvica (ibrutinib capsules, tablets, and oral solution); and Brukinsa (zanubrutinib capsules)."	03/19/2025