PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 03/08/2023; selected revision 03/29/2023

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

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 subependymal giant cell astrocytoma (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.

Of note, Zortress® (everolimus tablets) is indicated in combination with other drugs for prophylaxis of organ rejection in adults undergoing kidney or liver transplant.[2] 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.[3]

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.

Afinitor® (everolimus tablets (Novartis, generic)
Afinitor Disperz® (everolimus tablets for oral suspension – Novartis)
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 the following criteria (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 conditions (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 conditions (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 the following criteria (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 criteria (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), Votrient (pazopanib tablets), 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 the following criteria (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 the following criteria (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 the following criteria (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 and one of the following (a, b, c, or d):
       - **a)** Bone disease; OR
       - **b)** Central nervous system lesions; OR
       - **c)** Multisystem disease; OR
       - **d)** Pulmonary disease; 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 the following criteria (A and B):
    - **A)** Patient is ≥ 18 years of age; AND
    - **B)** Patient has relapsed or refractory disease.

11. **Soft Tissue Sarcoma.** Approve for 1 year if the patient meets the following criteria (A and B):
    - **A)** Patient is ≥ 18 years of age; AND
    - **B)** Patient has one of the following conditions (i or ii):

i. Perivascular epithelioid cell tumor (PEComa); OR
ii. Recurrent angiomyolipoma/lymphangioleiomyomatosis.

12. Thymomas and Thymic Carcinomas. Approve for 1 year if the patient meets the following criteria (A and B):
A) Patient is ≥ 18 years of age; AND
B) Patient meets one of the following criteria (i or ii):
i. Patient has tried chemotherapy; OR
Note: Examples are cisplatin, doxorubicin, and cyclophosphamide; cisplatin plus etoposide; carboplatin plus paclitaxel.
ii. Patient cannot tolerate chemotherapy.

13. Thyroid Carcinoma, Differentiated. Approve for 1 year if the patient meets the following criteria (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 Hürthle cell thyroid carcinoma.
C) The disease is refractory to radioactive iodine therapy.

14. Uterine Sarcoma. Approve for 1 year if the patient meets the following criteria (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.

15. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Approve for 1 year if the patient meets the following criteria (A and B):
A) Patient is ≥ 18 years of age; AND
B) Patient meets one of the following (i or ii):
i. Patient has not responded to primary therapy; OR
Note: Examples of primary therapy are bortezomib, dexamethasone, and rituximab; bendamustine and rituximab; cyclophosphamide, rituximab, and dexamethasone; Imbruvica (ibrutinib capsules); and Brukinsa (zanubrutinib capsules).
ii. Patient has progressive or relapsed disease.

CONDITIONS NOT COVERED

Afinitor® (everolimus tablets (Novartis, generic)
Afinitor Disperz® (everolimus tablets for oral suspension – Novartis) is(are) considered experimental, investigational, or unproven for ANY other use(s).

REFERENCES

1. Afinitor® tablets, Afinitor Disperz® tablets for oral suspension [prescribing information]. East Hanover, NJ: Novartis; February 2022.
2. Zortress® tablets [prescribing information]. East Hanover, NJ: Novartis; January 2021.
3. The NCCN Drugs & Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 6, 2023. Search term: everolimus.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Breast Cancer:** Stage IV disease was reworded to metastatic disease. References to female or male were reworded to woman or man. Use of GnRH "agonist" was changed to GnRH "analog" for combination use with exemestane in a man. **Neuroendocrine Tumors of the Pancreas, Gastrointestinal Tract, Lung, and Thymus (Carcinoid Tumors**): Advanced, unresectable, or metastatic was removed from the condition of approval. **Renal Cell Carcinoma**: Clear cell or non-clear histology was removed from the condition of approval and moved into the criteria. **Endometrial Carcinoma:** The requirement that the patient has recurrent, metastatic, or high-risk disease was removed from the criteria. **Gastrointestinal Stromal Tumors.** An option of trial of Sprycel (dasatinib tablets) was added to trial of Sutent (sutinitib capsules). **Histiocytic Neoplasm:** Condition was added to Other Uses with Supportive Evidence section. **Soft Tissue Sarcoma**: Perivascular Epitheloid Cell Tumors, Recurrent Angiomyolipoma, Lymphangioleiomyomatosis was removed from the condition of approval and added to the criteria. **Thymomas and Thymic Carcinomas:** An option for patients who cannot tolerate chemotherapy was added. **Thyroid Carcinoma, Differentiated:** The requirement that patient has "differentiated" thyroid carcinoma was added to the criteria. A note was added with examples of differentiated thyroid carcinoma.	02/16/2022
Selected Revision	**For all indications:** The duration of approval was changed from 3 years to 1 year.	06/22/2022
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