

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: 02/16/2022

OVERVIEW

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

- **Breast cancer**, treatment of postmenopausal women with 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.
- **Neuroendocrine tumors (NET)**, treatment of adults with progressive disease of pancreatic origin and adults with progressive, well-differentiated, non-functional NET of gastrointestinal or lung origin that are unresectable, locally advanced, or metastatic. Limitation of Use: Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.
- **Renal cell carcinoma**, treatment of adults with advanced disease after failure of treatment with Sutent[®] (sunitinib capsules) or Nexavar[®] (sorafenib tablets).
- **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 is also FDA-approved for this indication.
- **TSC-associated partial-onset seizures**, adjunctive treatment of patients ≥ 2 years of age. Afinitor Disperz is FDA-approved for this indication.

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 is different for Zortress than with 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of everolimus products is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Breast Cancer.** Approve for 3 years 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 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 3 years if the patient is ≥ 18 years of age.
3. **Renal Cell Carcinoma.** Approve for 3 years 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 one of the following products: Inlyta (axitinib tablets), Lenvima (lenvatinib capsules), Cabometyx (cabozantinib tablets), Keytruda

(pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Votrient (pazopanib tablets), Sutent (sunitinib capsules).

4. **Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma.** Approve for 3 years if the patient is ≥ 18 years of age.
5. **Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma (SEGA).** Approve for 3 years if therapeutic intervention is required but SEGA cannot be curatively resected.
6. **Tuberous Sclerosis Complex-Associated Partial Onset Seizures.** Approve for 3 years.

Other Uses with Supportive Evidence

7. **Endometrial Carcinoma.** Approve for 3 years 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 3 years 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 following (i, ii, iii, and iv):
 - i. One of imatinib or Ayvakit (avapritinib tablets); AND
 - ii. One of Sutent (sunitinib capsules) 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, Sutent (sunitinib capsules), or Stivarga (regorafenib tablets).
 9. **Histiocytic Neoplasm.** Approve for 3 years if the patient meets 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 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 3 years 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. **Meningioma.** Approve for 3 years if the patient meets the following criteria (A and B):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient has recurrent or progressive disease.
 12. **Soft Tissue Sarcoma.** Approve for 3 years if the patient meets the following criteria (A and B):
 - A) Patient is ≥ 18 years of age; AND
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- B) Patient has one of the following conditions (i or ii):
 - i. Perivascular epitheloid cell tumor (PEComa); OR
 - ii. Recurrent angiomyolipoma/lymphangiomyomatosis.

13. Thymomas and Thymic Carcinomas. Approve for 3 years 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.

14. Thyroid Carcinoma, Differentiated. Approve for 3 years 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.

15. Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma. Approve for 3 years 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 RECOMMENDED FOR APPROVAL

Coverage of everolimus products is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. 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; December 2021.
2. Zortress® tablets [prescribing information]. East Hanover, NJ: Novartis; January 2021.
3. The NCCN Drugs & Biologics Compendium. © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on February 7, 2021. Search term: everolimus.

HISTORY

| Type of Revision | Summary of Changes | Review Date |
|-----------------------|--|-------------|
| Early Annual Revision | All throughout policy, where applicable, changed examples to list in Note. | 01/27/2021 |

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|-------------------|--|------------|
| | <p>Hodgkin Lymphoma Classical (nodular sclerosis, mixed cellularity, lymphocyte depleted, and lymphocyte-rich subtypes of Hodgkin lymphoma): Changed indication name to “Classic Hodgkin Lymphoma” and deleted the subtypes in parentheses to be in-line with other policies with this indication.</p> <p>Perivascular Epithelioid Cell Tumors (PEComa), Recurrent Angiomyolipoma, Lymphangioliomyomatosis. Added “Soft Tissue Sarcoma” to indication heading to group the subtypes listed under one disease state.</p> | |
| Selected Revision | <p>Breast Cancer: A requirement was added that the patient is ≥ 18 years of age.</p> <p>Neuroendocrine Tumors of the Pancreas, Gastrointestinal Tract, Lung and Thymus (Carcinoid Tumors) – Advanced, Unresectable, or Metastatic: A requirement was added that the patient is ≥ 18 years of age.</p> <p>Renal Cell Carcinoma (Clear Cell or Non-Clear Cell Histology): A requirement was added that the patient is ≥ 18 years of age.</p> <p>Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma: A requirement was added that the patient is ≥ 18 years of age.</p> <p>Differentiated (i.e., papillary, follicular, and Hürthle cell) Thyroid Carcinoma: A requirement was added that the patient is ≥ 18 years of age.</p> <p>Endometrial Carcinoma: A requirement was added that the patient is ≥ 18 years of age.</p> <p>Gastrointestinal Stromal Tumor: A requirement was added that the patient is ≥ 18 years of age. Ayvakit (avapritinib tablets) was added as an option to requirement, “Patient has tried imatinib.” Qinlock (ripretinib tablets) was added as a therapy patient has to try.</p> <p>Meningioma: A requirement was added that the patient is ≥ 18 years of age.</p> <p>Soft Tissue Sarcoma – Perivascular Epithelioid Cell Tumors, Recurrent Angiomyolipoma, Lymphangioliomyomatosis: A requirement was added that the patient is ≥ 18 years of age.</p> <p>Thymomas and Thymic Carcinomas: A requirement was added that the patient is ≥ 18 years of age.</p> <p>Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma: A requirement was added that the patient is ≥ 18 years of age.</p> | 06/23/2021 |
| Selected Revision | <p>Targeting was added for Afinitor and everolimus 10 mg tablet strength. As a result, the policy now targets all strengths of Afinitor and everolimus so reference to the various strengths of the drug were removed. The name of the policy was changed from “Oncology – Afinitor PA Policy” to “Oncology – Everolimus Products PA Policy.”</p> | 09/29/2021 |
| Annual Revision | <p>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.</p> <p>Neuroendocrine Tumors of the Pancreas, Gastrointestinal Tract, Lung, and Thymus (Carcinoid Tumors): Advanced, unresectable, or metastatic was removed from the condition of approval.</p> <p>Renal Cell Carcinoma: Clear cell or non-clear histology was removed from the condition of approval and moved into the criteria.</p> <p>Endometrial Carcinoma: The requirement that the patient has recurrent, metastatic, or high-risk disease was removed from the criteria.</p> <p>Gastrointestinal Stromal Tumors. An option of trial of Sprycel (dasatinib tablets) was added to trial of Sutent (sunitinib capsules).</p> <p>Histiocytic Neoplasm: Condition was added to Other Uses with Supportive Evidence section.</p> <p>Soft Tissue Sarcoma: Perivascular Epithelioid Cell Tumors, Recurrent Angiomyolipoma, Lymphangioliomyomatosis was removed from the condition of approval and added to the criteria.</p> <p>Thymomas and Thymic Carcinomas: An option for patients who cannot tolerate chemotherapy was added.</p> <p>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.</p> | 02/16/2022 |