Generic Name: Everolimus

Therapeutic Class or Brand Name: Afinitor®, Afinitor Disperz®

Applicable Drugs (if Therapeutic Class): N/A

Preferred: Everolimus tablets (generic) or everolimus tablets for oral suspension (generic)

Non-preferred: Afinitor Afinitor Disperz

Date of Origin: 2/1/2013

Date Last Reviewed / Revised: 11/19/2023

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through IV are met)

I. Documented diagnosis of one of the following conditions A through F AND must meet criteria listed under applicable diagnosis:

A. Breast cancer

1. Documentation of hormone receptor-positive, HER2-negative disease.
2. Documentation of recurrent, unresectable, or metastatic disease.
3. Documented treatment failure on at least one aromatase inhibitor (ie, anastrozole, letrozole) or tamoxifen.
4. Patient meets one of the following conditions i or ii:
    i. Patient is a postmenopausal woman
        1. Everolimus will be used in combination with endocrine therapy (ie, exemestane, fulvestrant, or tamoxifen).
    ii. Patient is a pre/perimenopausal woman or natal male
        1. Everolimus will be used in combination with both of the following:
            a. A gonadotropin-releasing hormone agonist (eg, leuprolide) OR there is documentation of surgical bilateral oophorectomy or ovarian irradiation for pre/perimenopausal women.
            b. Endocrine therapy (ie, exemestane, fulvestrant, or tamoxifen).
5. Patient has not had disease progression while taking an everolimus-containing regimen.
6. Minimum age requirement: 18 years old.

B. Neuroendocrine tumors

1. Documentation of progressive, well-differentiated, and non-functional disease.
2. Documentation of one of the following i or ii:
    i. Documentation that the tumor is of gastrointestinal, lung, or thymic origin.
        1. Documentation of unresectable, locally advanced, or metastatic disease.

ii. Documentation that the tumor is of pancreatic origin and meets criteria 1 or 2:

1. Documentation of unresectable, locally advanced, or metastatic disease.
2. Documentation of locoregional insulinoma and everolimus will be used as preoperative therapy with or without diazoxide.

3. Minimum age requirement: 18 years old.

C. Renal angiomyolipoma and tuberous sclerosis complex (TSC)

1. Patient does not require immediate surgery.
2. Minimum age requirement: 18 years old.

D. Renal cell carcinoma (RCC)

1. Documentation of relapsed or metastatic disease.
2. Patient meets one of the following i or ii:
   i. Patient has non-clear cell disease.
   ii. Patient has clear cell disease and has failed at least one prior systemic therapy (eg, axitinib, lenvatinib, cabozantinib, pembrolizumab, nivolumab, sunitinib, etc).
3. Minimum age requirement: 18 years old.

E. Subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC)

1. Therapeutic intervention is required (ie, the condition is associated with functional impairment such as seizures, motor abnormalities, pain, etc).
2. Patient is not a candidate for curative surgical resection.
3. Minimum age requirement: 1 year old.

F. Tuberous sclerosis complex (TSC) associated partial-onset seizures

1. Everolimus will be used as adjunctive treatment.
2. Minimum age requirement: 2 years old.

II. The medication is prescribed by an oncologist or hematologist.

III. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

IV. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have documented treatment failure or contraindication to the preferred product(s).

Exclusion Criteria

- The treatment of patients with functional carcinoid tumors.
- Use of Zortress (everolimus) for oncology diagnoses.
- Use of Afinitor Disperz for diagnoses other than TSC-associated SEGA or TSC-associated partial-onset seizures.

Other Criteria

- Use of Afinitor with strong CYP3A4 inhibitors or inducers should be avoided. Exceptions may be made for higher doses (up to 56 tablets per 28 days) when used concurrently with CYP3A4 inducers (medications that decrease Afinitor serum concentrations) cannot be avoided (see Appendix Table 1).
- Other uses with supportive evidence per National Comprehensive Cancer Network (NCCN) guidelines:
    - Endometrial carcinoma
    - Gastrointestinal stromal tumors
    - Histiocytic neoplasm
    - Classic Hodgkin lymphoma
    - Meningioma
    - Soft tissue sarcoma
    - Thymomas and thymic carcinomas
    - Thyroid carcinoma, differentiated
    - Waldenstrom's macroglobulinemia/lymphoblasmacytic lymphoma

Quantity / Days Supply Restrictions

- TSC-associated SEGA: Quantities to provide 4.5 mg/m^2 daily with trough concentrations of 5 to 15 ng/mL.
- TSC-associated partial-onset seizures: Quantities to provide 5 mg/m^2 daily with trough concentrations of 5 to 15 ng/mL.
- All other diagnoses: 30 tablets per 30 days.
- See under Other Criteria for possible exceptions for higher doses (up to 56 tablets per 28 days).

Approval Length

- **Authorization:** 1 year.

- **Re-Authorization:** Updated letter of medical necessity or progress notes showing current medical necessity criteria are met and that the medication is effective (ie, there is no evidence of progressive disease while on Afinitor therapy)

APPENDIX

- Table 1. Examples of Strong CYP3A4 Inducers (Reduce Afinitor Serum Concentrations)

Carbamazepine (Tegretol®, Epitol®)	Rifabutin (Mycobutin®)
Efavirenz (Sustiva®)	Rifapentine (Priftin®)
Nevirapine (Viramune®)	Rifampin (Rifadin®)
Phenobarbital	St. John's Wort*
Phenytoin (Dilantin®)	

*St. John's Wort may decrease Afinitor exposure unpredictably and should be avoided.

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology. Breast Cancer v.4.2023. Updated March 23, 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
2. NCCN Clinical Practice Guidelines in Oncology. Neuroendocrine and Adrenal Tumors v.1.2023. Updated August 2, 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf
3. NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer v.1.2024. Updated June 21, 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf
4. French JA, Lawson JA, Yapici Z, et al. Adjunctive everolimus therapy for treatment resistant focal-onset seizures associated with tuberous sclerosis (EXIST-3): a phase 3, randomised, double-blind, placebo-controlled study. *Lancet*. 2016;388(10056):2153-2163. doi: 10.1016/S0140-6736(16)31419-2.
5. Franz DN, Belousova E, Sparagana S, et al. Efficacy and safety of everolimus for subependymal giant cell astrocytomas associated with tuberous sclerosis complex (EXIST-1): a multicentre, randomised, placebo-controlled phase 3 trial. *Lancet*. 2013;381(9861):125-32. doi: 10.1016/S0140-6736(12)61134-9.
6. Afinitor/Afinitor Disperz. Prescribing information. Novartis; 2022. Accessed November 19, 2023. https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/afinitor.pdf