MEDICAL MUTUAL®

Drug Policy

Policy:	Afinitor, Afinitor Disperz (everolimus), everolimus	Annual Review Date: 01/19/2023 Last Revised Date: 01/19/2023

OVERVIEW

Afinitor, a kinase inhibitor, is FDA approved for: 1) treatment of postmenopausal women with advanced hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative breast cancer (advanced HR+ breast cancer) in combination with exemestane tablets, after failure of treatment with letrozole tablets ,or anastrozole tablets; 2) treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease. It is not indicated for the treatment of patients with functional carcinoid tumors; 3) treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with Sutent (sunitinib capsules) or Nexavar (sorafenib tablets); 4) treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC) not requiring immediate surgery; and 5) pediatric and adult patients with TSC for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected. Afinitor Disperz is indicated for the treatment of adult and pediatric patients aged ≥ 1 years with TSC who have SEGA that requires therapeutic intervention but cannot be curatively resected. Afinitor Disperz is also indicated for the adjunctive treatment of adult and pediatric patients aged ≥ 2 years with TSC-associated partial-onset seizures. Afinitor inhibits mammalian target of rapamycin (mTOR), a serine-threonine kinase. The mTOR pathway is dysregulated in several human cancers.

POLICY STATEMENT

This policy involves the use of Afinitor. Prior authorization is recommended for pharmacy benefit coverage of Afinitor. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Afinitor as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Afinitor be prescribed by or in consultation with a physician who specializes in the condition being treated. In order to be considered for coverage, Afinitor must be prescribed by or in consultation with a hematologist, oncologist, nephrologist, or urologist. All approvals for initial therapy are provided for the initial approval duration noted below

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Afinitor is recommended in those who meet the following criteria:

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For all indications:

Requested Product	Criteria
Afinitor (brand)	1. The patient must meet both of the following (A and B): **A)** Patient has tried generic everolimus tablets; AND **B)** Patient cannot continue to use generic everolimus tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**; OR **2.** If the patient has met the indication-specific clinical criteria listed below, but has not met the criterion 1 above: approve generic everolimus tablets.
Afinitor Disperz (brand)	**1.** The patient must meet both of the following (A and B): **A)** Patient has tried generic everolimus tablets for oral suspension; AND **B)** Patient cannot continue to use the generic everolimus tablets for oral suspension due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**; OR **2.** If the patient has met the indication-specific clinical criteria listed below, but has not met criterion 1 above: approve generic everolimus tablets for oral suspension.

1. Breast Cancer

Criteria. *Patient must meet the following criteria*

A. The patient meets the following set of criteria:
- **a.** The patient has advanced HR+ disease; AND
- **b.** The patient has HER2-negative breast cancer; AND
- **c.** Afinitor will be used in combination with exemestane, fulvestrant, or tamoxifen; AND
- **d.** The patient has tried letrozole, anastrazole, or tamoxifen; AND
- **e.** The patient meets one of the following:
  - **i.** The patient is a postmenopausal female; OR
  - **ii.** The patient is a male and will be on concomitant suppression of testicular steroidogenesis; OR
  - **iii.** The patient is a premenopausal female treated with ovarian ablation/suppression; OR

B. The patient meets the following set of criteria:
- **a.** Afinitor will be used in combination with fulvestrant or tamoxifen; AND
- **b.** The patient is a post-menopausal woman, man treated concomitantly to suppress testicular steroidogenesis, or pre-menopausal woman treated with ovarian ablation/suppression: AND
- **c.** The patient has recurrent or metastatic disease with symptomatic visceral disease

2. Advanced, Unresectable Neuroendocrine Tumors (i.e. lung, pancreas, thymus, gastrointestinal tract)

Criteria. *Approve.*

3. **Advanced Renal Cell Carcinoma (RCC)**
Criteria. *Approve if patient has failed treatment with sunitinib or sorafenib.*

4. **Tuberous Sclerosis Complex (TSC)-Associated Renal Cell Carcinoma (RCC)**
Criteria. *Approve if the requested product will be used as a single agent.*

5. **Patients with Tuberous Sclerosis Complex (TSC) for the Treatment of Subependymal Giant Cell Astrocytoma (SEGA) that Requires Therapeutic Intervention but Cannot be Curatively Resected.**
Criteria. *Approve.*

6. **Tuberous Sclerosis Complex (TSC) Associated Partial-Onset Seizures**
Criteria. *Approve in patients 2 years of age or older if being used for adjunctive treatment.*

7. **Perivascular Epitheloid Cell Tumors (PEComa), Recurrent Angiomyolipoma, Lymphangioleiomyomatosis**
Criteria. *Approve if Afinitor is requested as single-agent therapy.*

8. **Hodgkin's Lymphoma, Classical (nodular sclerosis, mixed cellularity, lymphocyte depleted, lymphocyte-rich subtypes)**
Criteria. *Approve in adult patients (18 years of age or older) with disease refractory to 3 prior lines of therapy AND the requested product will be used as a single agent.*

9. **Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL)**
Criteria. *Patient must meet the following criteria*
   - **A.** Afinitor will be used as single-agent therapy and the patient has not responded to primary therapy (e.g. Velcade with/without Rituxan, Velcade and dexamethasone with/without Rituxan, Kyprolis with Rituxan and dexamethasone, cyclophosphamide/ doxorubicin/vincristine/prednisone/Rituxan, Imbruvica, Rituxan, Rituxan with cyclophosphamide and dexamethasone, Thalomid with/without Rituxan); OR
   - **B.** The patient has progressive or relapsed disease.

10. **Osteosarcoma, Dedifferentiated Chondrosarcoma, and High-Grade Undifferentiated Pleomorphic Sarcoma (UPS)**
Criteria. *Approve if Afinitor is requested as second line treatment in combination with sorafenib.*

11. **Thymomas and Thymic Carcinomas**
Criteria. *Approve if the requested product will be used as a single agent.*

12. **Differentiated Thyroid Carcinoma (i.e. Papillary, Follicular, or Hürthle Cell), Iodine-Refractory**
Criteria. *Patient must meet the following criteria*

A. Other systemic therapies (including clinical trials) are not available or appropriate; AND
B. Disease is not amenable to radioactive iodine (RAI); AND
C. The patient meets one of the following:
  a. The patient has unresectable, recurrent, or persistent locoregional disease; OR
  b. The patient has distant metastatic disease.

13. Endometrial Carcinoma
Criteria. *Approve if used in combination with letrozole.*

14. Gastrointestinal Stromal Tumors (GIST)
Criteria. *Approve if used in combination with imatinib, sunitinib, or regorafenib for unresectable, recurrent/progressive or metastatic disease*.

15. Meningiomas
Criteria. *Approve if Afinitor will be used in combination with bevacizumab AND patient has surgically inaccessible, recurrent, or progressive disease AND radiation is not possible*.

16. Histiocytic Neoplasms (Langerhans Cell Histiocytosis [LCH], Erdheim-Chester Disease [ECD], Rosai-Dorfman Disease)
Criteria. *Approve if the requested agent will be used as a single agent and tumors are positive for PIK3CA mutation.*

17. Patients with another indication that is not listed but is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation
Criteria. *Prescriber will provide specific diagnosis for documentation.*

18. Patient has been started on Afinitor, Afinitor Disperz, or generic everolimus
Criteria. *Approve for an indication or condition addressed as an approval in this document.*

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Afinitor has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1) Afinitor®, Afinitor Disperz® [prescribing information]. East Hanover, NJ: Novartis; December 2021.
2) The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed 16 January 2023. Search term: Everolimus.
3) Everolimus. In: DRUGDEX [online database]. Truven Health Analytics. Greenwood Village, CO. Last updated 3 January 2023. Accessed on 17 January 2023.
4) Everolimus. In: Lexi-Drugs. Lexicomp. Wolters Kluwer Clinical Drug Information, Inc. Riverwoods, IL. Available at: http://www.online.lexi.com. Last updated 5 January 2023. Accessed on 17 January 2023.