Reference number
2021-A

SPECIALTY GUIDELINE MANAGEMENT

AFINITOR (everolimus)
AFINITOR DISPERZ (everolimus)
everolimus (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Hormone Receptor-Positive, HER2-Negative Breast Cancer
   Afinitor is indicated for the treatment of postmenopausal women with advanced hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer in combination with exemestane, after failure of treatment with letrozole or anastrozole.
2. Neuroendocrine Tumors (NET)
   a. Afinitor is indicated for the treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease.
   b. Afinitor is indicated for the treatment of adult patients with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin with unresectable, locally advanced or metastatic disease.
3. Renal Cell Carcinoma (RCC)
   Afinitor is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.
4. Tuberous Sclerosis Complex (TSC)-Associated Renal Angiomyolipoma
   Afinitor is indicated for the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.
5. Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA)
   Afinitor and Afinitor Disperz are indicated in adult and pediatric patients aged 1 year and older with tuberous sclerosis complex (TSC) for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.
6. Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures
   Afinitor Disperz is indicated for the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.

B. Compendial Uses
1. Relapsed or stage IV renal cell carcinoma
2. Soft tissue sarcoma subtypes:
   a. Perivascular epithelioid cell tumors (PEComa)
   b. Angiomyolipoma
   c. Lymphangioleiomyomatosis
3. Gastrointestinal stromal tumors (GIST)
4. Neuroendocrine tumors:
   a. Neuroendocrine tumors of the gastrointestinal tract, lung and thymus (carcinoid tumors)
   b. Neuroendocrine tumors of the pancreas
   c. Well differentiated Grade 3 neuroendocrine tumors

5. Thymomas and thymic carcinomas
6. Classic Hodgkin lymphoma
7. Central nervous system cancers:
   a. Meningiomas
   b. Glioma
   c. Subependymal giant cell astrocytoma (SEGA)
8. Thyroid carcinoma (papillary carcinoma, oncocytic/Hürthle cell carcinoma, and follicular carcinoma)
9. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
10. Uterine Neoplasms (uterine sarcoma, endometrial carcinoma)
11. HR+/HER2- breast cancer, recurrent unresectable or stage IV (M1)
12. Tuberous sclerosis complex
13. Histiocytic Neoplasms:
    a. Erdheim-Chester Disease (ECD)
    b. Langerhans Cell Histiocytosis (LCH)
    c. Rosai-Dorfman Disease

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

1. Documentation of the presence of phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) mutation (where applicable)
2. Hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status (where applicable)

III. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

Authorization of 12 months may be granted for subsequent treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative recurrent unresectable, advanced, or metastatic breast cancer when prescribed in combination with exemestane, fulvestrant, or tamoxifen.

B. Renal Cell Carcinoma

Authorization of 12 months may be granted for treatment of relapsed, advanced, or stage IV renal cell carcinoma when any of the following criteria are met:

1. The requested medication is given as a single agent or in combination with lenvatinib as subsequent therapy for clear cell histology; OR
2. The requested medication is given as single-agent or in combination with lenvatinib or bevacizumab for non-clear cell histology.

C. Neuroendocrine Tumors

Authorization of 12 months may be granted for the treatment of the following neuroendocrine tumors:

1. Neuroendocrine tumors of the gastrointestinal tract, lung, and thymus (carcinoid tumors)
2. Neuroendocrine tumors of the pancreas
3. Well differentiated Grade 3 neuroendocrine tumors

D. Tuberous Sclerosis Complex (TSC)

Authorization of 12 months may be granted for treatment of TSC.

E. Soft Tissue Sarcoma
Authorization of 12 months may be granted for treatment of any of the following subtypes of soft tissue sarcoma as single agent therapy: locally advanced unresectable or metastatic perivascular epithelioid cell tumor (PEComa), recurrent angiomyolipoma, or recurrent lymphangioleiomyomatosis.

F. Gastrointestinal Stromal Tumor (GIST)
Authorization of 12 months may be granted for treatment of residual, unresectable, recurrent, or metastatic/tumor rupture GIST in combination with either imatinib, sunitinib, or regorafenib for members who have failed at least four FDA-approved therapies (e.g., imatinib, sunitinib, regorafenib, ripretinib)

G. Thymoma and Thymic Carcinoma
Authorization of 12 months may be granted for treatment of thymoma or thymic carcinoma as a single agent.

H. Classic Hodgkin Lymphoma
Authorization of 12 months may be granted for treatment of relapsed or refractory classic Hodgkin lymphoma after at least three prior therapies, as a single agent.

I. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted for treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma as a single-agent therapy for previously treated disease.

J. Papillary, Oncocytic, or Follicular Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of progressive and/or symptomatic papillary, oncocytic/Hürthle cell, or follicular thyroid carcinoma not amenable to radioactive iodine (RAI) therapy.

K. Uterine Neoplasms
Authorization of 12 months may be granted for treatment of the following uterine neoplasms:
1. Endometrial carcinoma in combination with letrozole
2. Uterine sarcoma as a single agent for subsequent therapy

L. Central Nervous System Cancers
Authorization of 12 months may be granted for treatment of the following central nervous system cancers:
1. Glioma (including glioblastoma) or meningioma
2. Adjuvant treatment of subependymal giant cell astrocytoma (SEGA) as a single agent

M. Histiocytic Neoplasms
Authorization of 12 months may be granted for the treatment of any of the following histiocytic neoplasm subtypes as a single agent in members with a phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) mutation:
1. Symptomatic or relapsed/refractory Erdheim-Chester Disease (ECD)
2. Symptomatic or relapsed/refractory Rosai-Dorfman Disease
3. Langerhans Cell Histiocytosis (LCH)

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

V. REFERENCES

1. Afinitor and Afinitor Disperz [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2022.
2. Everolimus [package insert]. Chestnut Ridge, NY: Par Pharmaceutical; July 2021.
3. Everolimus tablet for suspension [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; March 2022.
4. The NCCN Drugs & Biologics Compendium 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed May 8, 2023.
5. Baselga J, Campone M, Piccart M, et al. Everolimus in postmenopausal hormone-receptor–positive advanced breast cancer. *N Engl J Med*. 2012;366(6):520-529.
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9. Darcy A. Krueger, Hope Northrup, et al. Tuberous Sclerosis Complex Surveillance and Management: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. *Pediatric Neurology*. 2013. 49: 255-265.
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12. Hainsworth, John D, et al. Phase II Study of concurrent radiation therapy, temozolomide, and bevacizumab followed by bevacizumab/everolimus as first-line treatment of patients with glioblastoma. *Clin adv Hematol*. Oncol. 2012. 10 (4): 240-6.