Clinical Policy: Everolimus (Afinitor, Afinitor Disperz)

Reference Number: PA.CP.PHAR.63
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for everolimus (Afinitor®, Afinitor Disperz®).

FDA Approved Indication(s)
Afinitor is indicated:

- For the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.
- For the treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) and adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic.
- For the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.
- For the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole (Femara) or anastrozole (Arimidex).

Afinitor and Afinitor Disperz are indicated:

- For the treatment of pediatric and adult patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness®that everolimus is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all):

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Disease is hormone-receptor positive and Human epidermal growth factor receptor 2 (HER2)-negative;
4. Disease is recurrent or metastatic;
5. Failure of a trial of a nonsteroidal aromatase inhibitor anastrozole (Arimidex®) or letrozole (Femara®) (at up to maximally indicated doses) unless contraindicated or clinically significant adverse effects are experienced;
6. Prescribed in combination with exemestane (Aromasin);
7. Dose does not exceed 10 mg/day.

Approval duration: 6 months

B. Neuroendocrine Tumor (must meet all):
1. Diagnosis of NET of one of the following origins:
   a. Pancreatic;
   b. GI tract;
   c. Lung;
   d. Thymus (off-label)
2. Prescribed by or in consultation with an oncologist;
3. Disease is unresectable, locally advanced or metastatic;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

C. Renal Cell Carcinoma (must meet all):
1. Diagnosis of advanced (relapsed or surgically unresectable stage IV disease) RCC;
2. Prescribed by or in consultation with an oncologist;
3. Meets a or b:
   a. For RCC with predominant clear cell histology both of the following (i and ii):
      i. Failure of a trial of one of the following, unless contraindicated or clinically significant adverse effects are experienced: Sutent, Votrient, Inlyta, Avastin in combination with Intron-A, Proleukin, Cabometyx, or Torisel;
      ii. Failure of a trial of Opdivo* or Cabometyx* (if not previously used as first-line therapy), unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization is required for Opdivo and Cabometyx*
   b. RCC with non-clear cell histology (off-label);
4. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Renal Angiomylipoma and Other PEComas (must meet all):
1. Diagnosis of renal angiomyolipoma and TSC, not requiring immediate surgery;
2. Prescribed by or in consultation with an oncologist;
3. Dose does not exceed 10 mg/day.

Approval duration: 6 months

E. Subependymal Giant Cell Astrocytoma Associated with Tuberous Sclerosis Complex (must meet all):

1. Diagnosis of subependymal giant cell astrocytoma (SEGA) associated with TSC;
2. Prescribed by or in consultation with an oncologist;
3. Member is not a candidate for curative surgical resection;

Approval duration: 6 months

F. NCCN Compendium Indications (off-label) (must meet all)**:**

1. Confirmed diagnosis of one of the following:
   a. Hodgkins Lymphoma;
   b. Soft Tissue Sarcoma:
      i. Gastrointestinal Stromal Tumors (GIST): Prescribed in combination with either imatinib, sunitinib, or regorafenib for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib
      ii. PEComa/Recurrent Angiomyolipoma/Lymphangioleiomyomatosis;
   c. Thymomas and Thymic Carcinomas (second line therapy as a single agent);
   d. Thyroid Carcinoma – follicular carcinoma, Hurthle cell carcinoma, papillary carcinoma;
   e. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic lymphoma (for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease);
   f. Endometrial carcinoma (in combination with letrozole);
2. Prescribed by or in consultation with an oncologist;
3. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

II. Continued Approval

A. All Indications Specifically Addressed in Section I (Initial Approval Criteria) (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (e.g., no disease progression or unacceptable toxicity);
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 10 mg/day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.PMN.53

Background
Description/Mechanism of Action:
Everolimus is an inhibitor of mammalian target of rapamycin (mTOR), a serine-threonine kinase, downstream of the PI3K/AKT pathway. The mTOR pathway is dysregulated in several human cancers. Inhibition of mTOR by everolimus has been shown to reduce cell proliferation, angiogenesis, and glucose uptake in *in vitro* or *in vivo* studies.

Formulations:
Afinitor - oral tablets
2.5, 5, 7.5 and 10 mg tablets
Afinitor Disperz - tablets for oral suspension
2, 3, 5 mg tablets

Appendices
Appendix A: Abbreviation Key
AML: angiomyolipoma
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
LAM: lymphangioleiomyomatosis
NET: neuroendocrine tumor
PEComa: perivascular epitheloid cell tumor
pNET: neuroendocrine tumor of the pancreas
RCC: renal cell carcinoma
SEGA: subependymal giant cell astrocytoma
TSC: tuberous sclerosis complex
UPS: undifferentiated pleomorphic sarcoma

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7527	Everolimus, oral, 0.25mg

Reviews, Revisions, and Approvals	Date	Approval Date
Removed dose form requirement by indication, no clinical difference expected (dosing is equivalent for SEGA indication). For RCC, included list of first line therapies per NCCN guidelines. For breast cancer, removed	02/18	

Reviews, Revisions, and Approvals	Date	Approval Date
compendium supported use after tamoxifen as this was removed from the 1.2017 NCCN guideline update. Added the following off-label NCCN compendium supported uses: GIST, lymphoplasmacytic lymphoma, osteosarcoma, endometrial carcinoma. References reviewed and updated.		

References

1. Afinitor Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2017. Available at: https://www.pharma.us.novartis.com/files/afinitor.pdf. Accessed November 9, 2017.
2. National Comprehensive Cancer Network. Kidney Cancer Version 1.2018. Available at: http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed November 9, 2017.
3. National Comprehensive Cancer Network. Neuroendocrine Tumors Version 3.2017. Available at: http://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed November 9, 2017.
4. National Comprehensive Cancer Network. Breast Cancer Version 2.2017. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November, 9, 2017.
5. Everolimus. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 9, 2017.
6. Yao, JC, Fazio N, Singh S, et al. Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study. Lancet. 2015 Dec 15. pii: S0140-6736(15)00817-X. doi: 10.1016/S0140-6736(15)00817-X. [Epub ahead of print].