Clinical Policy: Everolimus (Afinitor, Afinitor Disperz)

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

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®).

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. Disease is hormone-receptor positive and Human epidermal growth factor receptor 2 (HER2)-negative;
3. Disease is recurrent or metastatic;
4. Request is for Afinitor oral tablet in combination with exemestane;
5. Meets a or b:
   a. FDA approved use:
      i. Failure of or contraindication to letrozole or anastrozole;
   b. Off-label NCCN recommended use:
      i. Previous treatment with tamoxifen.

Approval duration: 6 months

B. Neuroendocrine Tumor (must meet all):
1. Meets a or b:
   a. FDA approved use (i. or ii.):
      i. Diagnosis of neuroendocrine tumor of pancreatic origin;
      ii. Diagnosis of neuroendocrine tumor of gastrointestinal or lung origin;
   b. Off-label NCCN recommended use:
      i. Diagnosis of neuroendocrine tumor of thymic origin:
2. Disease is recurrent, unresectable or metastatic;
3. Request is for Afinitor oral tablet.

Approval duration: 6 months

C. Renal Cell Carcinoma (must meet all):
1. Diagnosis of renal cell carcinoma;
2. Disease is recurrent, unresectable or metastatic;
3. Meets a or b:
   a. FDA approved use:
      i. As subsequent therapy after failed sunitinib or sorafenib treatment;
   b. Off-label NCCN recommended use:

i. As single agent or in combination with lenvatinib for one of the following (a or b):
   a) As subsequent therapy for predominant clear cell histology;
   b) As primary or subsequent therapy for non-clear cell histology;

4. Request is for Afinitor oral tablet.

Approval duration: 6 months

D. Renal Angiomylipoma and Other PEComas (must meet all):

1. Meets a or b:
   a. FDA approved use:
      i. Renal angiomyolipoma (AML) associated with tuberous sclerosis complex (TSC) and not requiring immediate surgery;
   b. Off-label NCCN recommended use:
      i. Perivascular epitheloid cell tumor (PEComa) (may include the following or other subtypes; subtypes may or may not be associated with TSC);
         a) AML (not limited to renal; must be recurrent);
         b) Lymphangioleiomyomatosis (LAM);
2. Request is for Afinitor oral tablet.

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. Member is not a candidate for curative surgical resection;
3. Request is for Afinitor oral tablet or Afinitor Disperz tablet for oral suspension.

Approval duration: 6 months

F. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

1. Oncology: The following NCCN recommended uses meeting NCCN categories 1, 2a or 2b are approved per the CP.PHAR.57 Global Biopharm Policy:
   a. Bone cancer: Osteosarcoma, dedifferentiated chondrosarcoma, or high-grade undifferentiated pleomorphic sarcoma (UPS);
   b. Classical Hodgkin lymphoma;
   c. Thymoma or thymic carcinoma;
   d. Thyroid carcinoma: Follicular, Hurthle cell or papillary subtypes;
   e. Waldenström's macroglobulinemia or lymphoplasmacytic lymphoma.

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. Documentation shows positive response to therapy (e.g., no disease progression or unacceptable toxicity).

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 CP.PHAR.57 - Global Biopharm Policy**.**

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

FDA Approved Indications:

Afinitor is an mTOR kinase inhibitor (available as oral tablet and tablet for oral suspension) indicated for the treatment of:

Afinitor (oral tablet):

- Advanced hormone receptor-positive, HER2-negative breast cancer
  - Postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole.
- Advanced neuroendrocine tumors (NET)*
  - Adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease.
  - Adult patients with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin with unresectable, locally advanced or metastatic disease
- Advanced renal cell carcinoma (RCC)

- Adult patients with advanced RCC after failure of treatment with sunitinib or sorafenib.
- Renal angiomyolipoma with tuberous sclerosis complex (TSC)
  - Adults with renal angiomyolipoma and TSC, not requiring immediate surgery.

Limitations of Use

- Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.

Afinitor (oral tablet) and Afinitor Disperz (tablet for oral suspension):

- Subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC)
  - Pediatric and adult patients with TSC for the treatment of SEGA that requires therapeutic intervention but cannot be curatively resected.

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

References

1. Afinitor prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2016. Available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/afinitor.pdf. Accessed March 30, 2017.
2. Everolimus. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed March 30, 2017.

3. Breast cancer (Version 1.2017) In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 30, 2017.
4. Kidney cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 30, 2017.
5. Neuroendocrine tumors (Version 2.2017), In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 31, 2017.
6. Soft tissue sarcoma (Version 2.2017), In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 31, 2017.
7. Central nervous system cancers (Version 1.2016), In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 31, 2017.
8. Owens J, Bodensteiner JB. Tuberocus sclerosis complex: Genetics, clinical features, and diagnosis. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at uptodate.com Accessed March 31, 2017.
9. Owens J, Bodensteiner JB. Tuberous sclerosis complex: Management. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at uptodate.com Accessed March 31, 2017.