Clinical Policy: Everolimus (Afinitor, Afinitor Disperz)

Reference Number: CP.PHAR.63
Effective Date: 06/11
Last Review Date: 05/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® 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 (a or b):
      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 Centene benefit or member has previously met all initial approval criteria;
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 Centene benefit and documentation supports positive response to therapy.
   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
Added efficacy data; corrected algorithm to match FDA indication for MBC, PNET, and SEGA. Removed Votrient from RCC failure question.	06/14	07/14
Edited FDA indications Edited algorithm to include both Afinitor and Afinitor Disperz, and the pediatric population for SEGA. Also changed initial approval periods from 6 months to 3 months for initial auths. Edited background & safety	05/15	05/15
Policy converted to new template; Added maximum dose and contraindications per PI; For breast cancer: added definition for advanced breast cancer; added that Afinitor may be used in after previous treatment with tamoxifen to comply with NCCN recommendation for use;	04/16	05/16

Reviews, Revisions, and Approvals	Date	Approval Date
For RCC, added definition for advanced RCC References updated		
NCCN and FDA uses separated in criteria sets; dosing removed if NCCN uses added. NET: "Non-functional" designation removed for NET of GI and lung origin; the term "locally advanced" is incorporated into recurrent, unresectable or metastatic. RCC: The term "advanced" RCC is restated as recurrent, unresectable or metastatic. The term "unless contraindicated" is removed from "failed sunitinib or sorafenib treatment." Safety information removed. Approval durations lengthened to 6 and 12 months.	04/17	05/17

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.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical

practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs,

and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.