Pharmacy Policy Bulletin: J-0127 Mechanistic Target of Rapamycin Kinase (mTOR) Inhibitors - Commercial and Healthcare Reform	
Number: J-0127	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0127-022	**Original Date:** 05/20/2009
Effective Date: 12/20/2024	**Review Date:** 12/04/2024

Drugs Product(s):	• Afinitor (everolimus) • Afinitor Disperz (everolimus tablets for oral suspension) • Torpenz (everolimus)

FDA-Approved Indication(s):	• Afinitor
	  ○ Treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole.
	  ○ Treatment of adults 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.
	  ○ Treatment of adults with advanced renal cell carcinoma after failure of treatment with sunitinib or sorafenib.
	  ○ Treatment of adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.
	  ○ Treatment of adult and pediatric patients aged 1 year and older with TSC who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.
	• Afinitor Disperz
	  ○ Treatment of adult and pediatric patients aged 1 year and older with TSC who have SEGA that requires therapeutic intervention but cannot be curatively resected.
	  ○ Adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.
	• Torpenz
	  ○ Treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole.
	  ○ Treatment of adults with renal angiomyolipoma and TSC, not requiring immediate surgery.

	○ Treatment of adult and pediatric patients aged 1 year and older with TSC who have SEGA that requires therapeutic intervention but cannot be curatively resected.

Background:	• Afinitor, Afinitor Disperz, and Torpenz (everolimus) require prior authorization to ensure use in the patient population approved by the Food and Drug Administration (FDA). • Afinitor, Afinitor Disperz, and Torpenz are inhibitors of mTOR, a serine-threonine kinase, downstream of the PI3K/AKT pathway. This pathway controls key cellular processes such as cell survival, growth, and proliferation, and is commonly dysregulated in several human cancers. • Everolimus binds to an intracellular protein, resulting in the formation of an inhibitory complex and inhibition of mTOR kinase activity. The inhibition of mTOR by everolimus has been shown to reduce cell proliferation, angiogenesis, and glucose uptake in both in vitro and in vivo studies. • ICD-10 Code Information: ○ ICD-10: Q85.1 “tuberous sclerosis” and ICD-10: D33.2 “benign neoplasm of brain, unspecified” may apply to Afinitor, Afinitor Disperz, and Torpenz in TSC with SEGA; however, the diagnosis must be specified. • Prescribing Considerations: ○ Everolimus should be prescribed under the supervision of a hematologist/oncologist. ○ Afinitor is not indicated for the treatment of patients with functional carcinoid tumors. ○ The most common toxicities associated with everolimus are stomatitis and pneumonitis. Other warnings and precautions include infections, angioedema, renal failure, risk of impaired wound healing, use in geriatric patients, metabolic disorders, myelosuppression, hypokalemia, and embryo-fetal toxicity.

Approval Criteria

I. Initial Authorization

A. Afinitor (everolimus)

1. Breast Cancer (ICD-10: C50)

When a benefit, coverage of Afinitor (everolimus) may be approved when all of the following criteria are met **(a. through f.)**:

a. The prescriber attests that the member is postmenopausal.
b. The member has a diagnosis of advanced breast cancer.
c. Disease is hormone receptor-positive, HER2-negative.
d. The member is using everolimus in combination with exemestane.
e. The member has experienced therapeutic failure to one (1) of the following **(i. or ii.)**:
  i. letrozole
  ii. anastrozole
f. If the request is for brand Afinitor, the member has experienced therapeutic failure or intolerance to generic everolimus tablets.

2. Neuroendocrine Tumors of Pancreatic Origin (ICD-10: C25.4)

When a benefit, coverage of Afinitor (everolimus) may be approved when all of the following criteria are met **(a. through d.)**:

a. The member is 18 years of age or older.

b. The member has a diagnosis of progressive neuroendocrine tumors of pancreatic origin (PNET).
c. Disease is unresectable, locally advanced or metastatic.
d. If the request is for brand Afinitor, the member has experienced therapeutic failure or intolerance to generic everolimus tablets.

3. Non-Functional Neuroendocrine Tumors (ICD-10: C7A.8)
When a benefit, coverage of Afinitor (everolimus) may be approved when all of the following criteria are met **(a. through f.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of non-functional neuroendocrine tumors (NET).
c. Disease is classified as progressive, well-differentiated, non-functional.
d. Disease is of gastrointestinal or lung origin.
e. Disease is unresectable, locally advanced or metastatic.
f. If the request is for brand Afinitor, the member has experienced therapeutic failure or intolerance to generic everolimus tablets.

4. Renal Cell Carcinoma (RCC) (ICD-10: C64)
When a benefit, coverage of Afinitor (everolimus) may be approved when all of the following criteria are met **(a. through d.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of advanced RCC.
c. The member has experienced therapeutic failure to one (1) of the following **(i. or ii.):**
i. sunitinib
ii. sorafenib
d. If the request is for brand Afinitor, the member has experienced therapeutic failure or intolerance to generic everolimus tablets.

5. Renal Angiomyolipoma and Tuberous Sclerosis Complex (TSC) (ICD-10: C64)
When a benefit, coverage of Afinitor (everolimus) may be approved when all of the following criteria are met **(a. through d.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of renal angiomyolipoma and TSC.
c. The prescriber attests that requirement for surgery is not immediate.
d. If the request is for brand Afinitor, the member has experienced therapeutic failure or intolerance to generic everolimus tablets.

6. TSC with Subependymal Giant Cell Astrocytoma (SEGA) (No ICD-10 Code)
When a benefit, coverage of Afinitor (everolimus) may be approved when all of the following criteria are met **(a. through d.)**:
a. The member is 1 year of age or older.
b. The member has a diagnosis of TSC with SEGA.
c. The member is not a candidate for curative surgical resection.
d. If the request is for brand Afinitor, the member has experienced therapeutic failure or intolerance to generic everolimus tablets.

B. Afinitor Disperz (everolimus tablets for oral suspension)

1. TSC with SEGA (No ICD-10 Code)
When a benefit, coverage of Afinitor Disperz (everolimus tablets for oral suspension) may be approved when all of the following criteria are met **(a. through e.)**:
a. The member is 1 year of age or older.
b. The member has a diagnosis of TSC with SEGA.
c. The member is not a candidate for curative surgical resection.
d. The member meets one (1) of the following criteria **(i. or ii.)**:

i. The member has experienced therapeutic failure or intolerance to plan-preferred, generic everolimus tablets.
ii. The member is unable to swallow generic everolimus tablets.

e. If the request is for brand Afinitor Disperz, the member has experienced therapeutic failure or intolerance to generic everolimus tablets for suspension.

2. TSC-associated Partial Onset Seizures (No ICD-10 Code)
When a benefit, coverage of Afinitor Disperz (everolimus tablets for oral suspension) may be approved when all of the following criteria are met **(a., b., and c.)**:

a. The member is 2 years of age and older.
b. The member is using Afinitor Disperz for the adjunctive treatment of TSC-associated partial-onset seizures.
c. If the request is for brand Afinitor Disperz, the member has experienced therapeutic failure or intolerance to generic everolimus tablets for suspension.

C. Torpenz

1. Breast Cancer (ICD-10: C50)
When a benefit, coverage of Torpenz may be approved when all of the following criteria are met **(a. through f.)**:

a. The prescriber attests that the member is postmenopausal.
b. The member has a diagnosis of advanced breast cancer.
c. Disease is hormone receptor-positive, HER2-negative.
d. The member is using Torpenz in combination with exemestane.
e. The member has experienced therapeutic failure to one (1) of the following **(i. or ii.)**:
i. letrozole
ii. anastrozole
f. The member has experienced therapeutic failure or intolerance to generic everolimus tablets.

2. Renal Angiomyolipoma and TSC (ICD-10: C64)
When a benefit, coverage of Torpenz may be approved when all of the following criteria are met **(a. through d.)**:

a. The member is 18 years of age or older.
b. The member has a diagnosis of renal angiomyolipoma and TSC.
c. The prescriber attests that the requirement for surgery is not immediate.
d. The member has experienced therapeutic failure or intolerance to generic everolimus tablets.

3. TSC with SEGA (No ICD-10 Code)
When a benefit, coverage of Torpenz may be approved when all of the following criteria are met **(a. through d.)**:

a. The member is 1 year of age or older.
b. The member has a diagnosis of TSC with SEGA.
c. The member is not a candidate for curative surgical resection.
d. The member has experienced therapeutic failure or intolerance to generic everolimus tablets.

II. Reauthorization
When a benefit, reauthorization of Afinitor, Afinitor Disperz, or Torpenz may be approved when all of the following criteria are met **(A. and B.)**:

A. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(1. or 2.)**:
1. Disease improvement
2. Delayed disease progression

B. If the request is for brand Afinitor or Afinitor Disperz, documentation that the AB-rated generic is ineffective or not tolerated.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.
II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
III. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR plans: If approved, up to a 24 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Afinitor [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2022.
2. Torpenz [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC.; June 2024.