Effective Date **10/1/2022**
Next Review Date… **10/1/2023**
Coverage Policy Number **IP0408**

Everolimus (Afinitor, Afinitor Disperz) for Non-Oncology Uses

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for everolimus (Afinitor, Afinitor Disperz) for non-oncology uses. The use of everolimus (Afinitor) for oncology indications is addressed in a separate coverage policy. Please refer to the related coverage policy link above (Oncology Medications).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Everolimus (Afinitor, Afinitor Disperz) is considered medically necessary when the following are met:

1. **Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma.** Individual meets **BOTH** of the following criteria:
    A. Individual is 18 years of age or older

B. Confirmation of angiomyolipoma greater than or equal to 3 cm diagnosed on radiographic imaging (for example, CT or MRI)

2. **Tuberous Sclerosis Complex-Associated Partial Onset Seizures.** Individual meets **ALL** of the following criteria (A, B, C, and D):
   A. Individual is 2 years of age or older
   B. Documentation of **ONE** of the following (i or ii):
      i. Individual has had an inadequate response to **TWO** antiepileptic drugs (for example, valproic acid, lamotrigine, topiramate, clonazepam, levetiracetam, zonisamide, Banzel, felbamate, clobazam, Fycompa, vigabatrin, epidiolex).
      ii. Individual has a contraindication per FDA label, significant intolerance, or is not a candidate* for **ALL** of the following (a, b, c, d, e, f, g, h, i, j, k, and l):±
         a. clobazam
         b. clonazepam
         c. epidiolex
         d. felbamate
         e. lamotrigine
         f. levetiracetam
         g. perampanel (Fycompa)
         h. rufinamide
         i. topiramate
         j. valproic acid
         k. vigabatrin
         l. zonisamide
   C. The drug will be used as adjunctive therapy (used in combination with other antiepileptic drugs)
   D. Prescribed by, or in consultation with, a pediatric neurologist or an adult neurologist with expertise in epilepsy

   **Note: Not a candidate due to being subject to a warning per the prescribing information (labeling), having a disease characteristic, individual clinical factor[s], or other attributes/conditions or is unable to administer and requires this dosage formulation*

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Coverage varies across plans and requires the use of preferred products. Refer to the customer's benefit plan document for coverage details.

Employer Group Non-Covered Products and the Preferred Covered Alternatives:

Non-Covered Product	Preferred Covered Alternatives Criteria
Afinitor tablets (everolimus)	**Effective 1/1/2023:** There is documentation of the following: A. The individual has tried **everolimus tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Afinitor Disperz (everolimus tablets for oral suspension)	**Effective 1/1/2023:** There is documentation of the following: B. The individual has tried **everolimus tablets for oral suspension** (the bioequivalent generic product) AND cannot take due to a formulation difference

Non-Covered Product	Preferred Covered Alternatives Criteria
	in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

Individual and Family Plan Non-Covered Products and Covered Alternative(s):

Non-Covered Product	Preferred Covered Alternatives Criteria
Afinitor tablets (everolimus)	There is documentation of the following: C. The individual has tried **everolimus tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Afinitor Disperz (everolimus tablets for oral suspension)	**Effective 1/1/2023:** There is documentation of the following: D. The individual has tried **everolimus tablets for oral suspension** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

Reauthorization Criteria

Everolimus (Afinitor, Afinitor Disperz) is considered medically necessary for continued use when ONE of the following is met:

1. **Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma.** Individual meets the following criteria:
   A. Initial criteria are met AND there is documentation of beneficial response (for example, stability or reduction in size of angiomyolipoma)
2. **Tuberous Sclerosis Complex-Associated Partial Onset Seizures.** Individual meets the following criteria:
   A. Initial criteria are met AND there is documentation of beneficial response (for example, reduced seizure severity, frequency, and/or duration)

Authorization Duration

Initial approval duration: up to 12 months.

Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Everolimus (Afinitor, Afinitor Disperz) for non-oncology uses is considered experimental, investigational or unproven for **ANY** other use.

Background

OVERVIEW

Afinitor, a kinase inhibitor, is indicated for the following uses:[1]

- **Breast cancer**, treatment of postmenopausal women with advanced hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative disease in combination with exemestane, after failure of treatment with letrozole or anastrozole.

- **Neuroendocrine tumors (NET)**, treatment of adults with progressive disease of pancreatic origin and adults with progressive, well-differentiated, non-functional NET of gastrointestinal or lung origin that are unresectable, locally advanced, or metastatic. Limitation of Use: Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.
- **Renal cell carcinoma**, treatment of adults with advanced disease after failure of treatment with Sutent® (sunitinib capsules) or Nexavar® (sorafenib tablets).
- **Tuberous sclerosis complex (TSC)-associated renal angiomyolipoma,** treatment of adults not requiring immediate surgery.
- **TSC-associated subependymal giant cell astrocytoma (SEGA)**, treatment of patients ≥ 1 year of age who require therapeutic intervention but cannot be curatively resected. Afinitor Disperz is also FDA-approved for this indication.
- **TSC-associated partial-onset seizures**, adjunctive treatment of patients ≥ 2 years of age. Afinitor Disperz is FDA-approved for this indication.

Of note, Zortress® (everolimus tablets) is indicated in combination with other drugs for prophylaxis of organ rejection in adults undergoing kidney or liver transplant.[2] The tablet strengths and dosing is different for Zortress than with Afinitor. Zortress is not targeted in this policy.

Guidelines
The National Comprehensive Cancer Network (NCCN) Compendium recommends use of everolimus for the indications listed in the FDA-Approved Indications.[3]

References

1. Afinitor® tablets, Afinitor Disperz® tablets for oral suspension [prescribing information]. East Hanover, NJ: Novartis; December 2021.
2. Zortress® tablets [prescribing information]. East Hanover, NJ: Novartis; January 2021.
3. The NCCN Drugs & Biologics Compendium. © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 7, 2021. Search term: everolimus.