

DRUG DETERMINATION POLICY

Title: DDP-14 Afinitor

Effective Date: 4/24/24



Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve Benefits. Coverage depends on the specific Benefit plan. Pharmacy Benefit Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Afinitor (everolimus) is a specialty drug indicated for a number of diagnoses and is associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

I. Neuroendocrine Tumors.

A. Diagnosis and severity:

1. Progressive, unresectable, locally advanced, or metastatic disease [must meet one listed below]:
 - a. Pancreatic neuroendocrine tumors.
 - b. Well-differentiated, nonfunctional Gastrointestinal or lung neuro-endocrine tumors.

B. Other therapies: contraindication, inadequate response, or significant adverse effects to National Comprehensive Cancer Network® (NCCN®) preferred therapies

C. Dosage regimen: Afinitor (everolimus): 10mg once daily.

D. Approval.

1. Initial: six months.

2. Re-approval: six months until disease progression or unacceptable toxicity.

II. Breast Cancer.

A. Diagnosis and severity [must meet all listed below]:

1. Postmenopausal.
2. Advanced hormone receptor-positive disease.
3. HER2-negative.

B. Other therapies: contraindication; inadequate response or significant adverse effects to NCCN preferred therapies.

C. Dosage regimen (everolimus).

1. 10mg once daily.
2. Combination with Aromasin (exemestane).

D. Approval.

1. Initial: six months.
2. Re-approval: six months until disease progression or unacceptable toxicity.

III. Renal Cell Carcinoma (RCC), Advanced.

A. Diagnosis and severity:

1. Advanced RCC with predominant clear cell histology.
2. Relapsed or medically unresectable RCC with non-clear cell histology.

B. Other therapies: contraindication; inadequate response, or significant adverse effects to NCCN preferred therapies

C. Dosage regimen Afinitor (everolimus): 10mg once daily.

D. Approval.

1. Initial: six months.
2. Re-approval: six months until disease progression or unacceptable toxicity.

IV. Tuberous Sclerosis Complex-Associated Partial Onset Seizures.

A. Age: at least two years

B. Diagnosis and severity: inadequate control of partial seizures (at least two seizures per week).

C. Other therapies: contraindication, inadequate response, or significant adverse effects to at least two preferred anti-epileptic drugs.

D. Dosage regimen (everolimus): 5mg per m² once daily.

E. Approval.

1. Initial: six months.

2. Re-approval: six months until disease progression or unacceptable toxicity.

V. Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma.

A. Diagnosis and severity [must meet both listed below]:

- a. Tuberous sclerosis complex
- b. Renal Angiomyolipoma.

B. Other therapies: contraindication, inadequate response, or significant adverse effects to NCCN kidney cancer preferred therapies.

C. Dosage regimen for Afinitor (everolimus): 10mg once daily.

D. Approval.

1. Initial: six months.

2. Re-approval: six months until disease progression or unacceptable toxicity.

VI. Tuberous Sclerosis Complex-Associated Sub-ependymal Giant Cell Astrocytoma.

A. Diagnosis and severity [must meet both diagnoses and severity listed below]:

1. Tuberous sclerosis complex.
2. Sub-ependymal Giant Cell Astrocytoma needs intervention and not curably resectable or symptomatic/growing after surgery.

B. Other therapies: contraindication; inadequate response, or significant adverse effects to NCCN Central Nervous System cancer preferred therapies.

C. Dosage regimen:

1. Initial: Afinitor (everolimus): 4.5mg per m² once daily.

2. Adjustment: Trough below 5mg/mL- increase 2 to 2.5mg per day; above 5mg/mL - decrease 2 to 2.5mg per day (at lowest dose give every other day).

D. Approval.

1. Initial: six months.

2. Re-approval: six months until disease progression or unacceptable toxicity.

VII. Appropriate medication use [must meet all listed below]:

A. Diagnosis: meets standard diagnostic criteria that designates signs, symptoms, and test results to support specific diagnosis.

B. The Food and Drug Administration (FDA) approval status [must meet one listed below]:

1. FDA approved: product, indication, and/or dosage regimen.

2. Non-FDA approved: compendium support (Lexicomp™) for use of a drug for a non-FDA approved indication or dosage regimen.

- C. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

4.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Afinitor, accessed February 2022.
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3. Available from: <http://www.uptodate.com/contents/metastatic-well-differentiated-pancreatic-neuroendocrine>.
4. Tuberous Sclerosis complex: Management. UpToDate [internet] Accessed April 2016. Available from: <http://www.uptodate.com/contents/tuberous-sclerosis-complex-management>.
5. Renal manifestations of tuberous sclerosis complex. UpToDate [internet] Accessed April 2016. Available from: <http://www.uptodate.com/contents/renal-manifestations-of-tuberous-sclerosis-complex>.
6. Long-term everolimus treatment in individuals with tuberous sclerosis complex: a review of current literature. 2015. *Pediatric Neurology*: 53;23-30.
7. Neuroendocrine and Adrenal Tumors. *NCCN Clinical Practice Guidelines in Oncology*. 2023; Version 1.2023. Accessed March 20, 2024. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf
8. Breast Cancer. *NCCN Clinical Practice Guidelines in Oncology*. 2024; Version 2.2024. Accessed March 20, 2024. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
9. Fallah A, Wang S. Optimal management of seizures associated with tuberous sclerosis complex: current and emerging options. *Neuropsychiatric Disease and Treatment*. Published online October 2014:2021. doi:<https://doi.org/10.2147/ndt.s51789>
10. Kidney Cancer. *NCCN Clinical Practice Guidelines in Oncology*. 2024; Version 3.2024. Accessed March 20, 2024. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf

5.0 Appendices:

See page 5.

6.0 Revision History:

Original Effective Date: 06/30/2016

Next Review Date: 05/01/2025

| Revision Date | Reason for Revision |
|---------------|---|
| 3/19 | Transfer to new format |
| 4/19 | Presented and approved at P & T Workgroup and Committee |
| 3/20 | Annual review; clarified verbiage regarding other therapies and criteria to meet, replaced abbreviations |
| 2/21 | Annual review; updated criteria instruction verbiage, added appropriate use section; approved at 4/28/21 P&T |
| 2/22 | Annual review; Referred to NCCN for other therapies; added compendium reference to appropriate medication use |
| 2/23 | Annual review; no change |
| 2/24 | Annual review; added references, removed Appendix 1: Patient Safety and Monitoring |