DRUG DETERMINATION POLICY

Title: DDP-14 Afinitor

Effective Date: 06/01/2021

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:

A. Neuroendocrine Tumors.
    1. Diagnosis and severity:
        a. Progressive, unresectable, locally advanced or metastatic disease [must meet one listed below]:
            i. Pancreatic neuroendocrine tumors (PNET).
            ii. Well-differentiated, nonfunctional GI or lung neuro-endocrine tumors.
    2. Other therapies: none.
    3. Dosage regimen: Afinitor (everolimus): 10mg once daily.
    4. Approval.
        a. Initial: six months.
        b. Re-approval: six months until disease progression or unacceptable toxicity.

B. Breast Cancer.
    1. Diagnosis and severity [must meet all listed below]:

a. Postmenopausal.

b. Advanced HR+ disease.

c. HER2-negative.

2. Other therapies: contraindication; inadequate response or significant adverse effects to both therapies listed below:

a. Femora (letrozole).

b. Arimidex (anastrozole).

3. Dosage regimen (everolimus).

a. 10mg once daily.

b. Combination with Aromasin (exemestane).

4. Approval.

a. Initial: six months.

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

C. Renal Cell Carcinoma (RCC), Advanced.

1. Diagnosis and severity:

a. Advanced RCC with predominant clear cell histology.

b. Relapsed or medically unresectable RCC with non-clear cell histology.

2. Other therapies: contraindication; inadequate response, or significant adverse effects to one category listed below:

a. Listed in the Food and Drug Administration (FDA) approved indication: Sutent (sunitinib) or Nexavar (sorafenib); OR

b. Not listed in indication: Votrient (pazopanib) or Inlyta (axltinib).

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

4. Approval.

a. Initial: six months.

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

D. Tuberous Sclerosis Complex-Associated Partial Onset Seizures.

1. Age: at least two years

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

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

4. Dosage regimen (everolimus): 5mg per m^2 once daily.

5. Approval.

a. Initial: six months.

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

E. Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma (AML).

1. Diagnosis and severity [must meet one listed below]:

a. Tuberous sclerosis complex (TSC); AND

b. AML.

2. Other therapies: contraindication or inadequate response to one category listed below depending on the parameters noted:

    a. Surgery: AMLs above four centimeters; symptoms refractory to conservative measures; high suspicion of malignancy.

    b. Radiofrequency ablation and cryo-ablation: AMLs below four centimeters.
3. Dosage regimen for Afinitor (everolimus): 10mg once daily.
4. Approval.
    a. Initial: six months.
    b. Re-approval: six months until disease progression or unacceptable toxicity.

F. Tuberous Sclerosis Complex-Associated Sub-ependymal Giant Cell Astrocytoma (SEGA).
1. Diagnosis and severity [must meet both diagnoses and severity listed below]:
    a. Tuberous sclerosis complex (TSC); AND
    b. SGCT needs intervention and not curably resectable or symptomatic/growing after surgery.
2. Other therapies: surgery if advisable.
3. Dosage regimen:
    a. Initial: Afinitor (everolimus): 4.5mg per m^2 once daily.
    b. 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).
4. Approval.
    a. Initial: six months.
    b. Re-approval: six months until disease progression or unacceptable toxicity.

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

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

2. FDA approval status [must meet one listed below]:

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

    b. Off-label use: at least two supporting studies from major peer-reviewed medical journals that support the off-label use as safe and effective.

3. 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 March 2021.
2. Metastatic well-differentiated pancreatic neuroendocrine tumors: Systemic therapy options to control tumor growth and symptoms of hormone hypersecretion. UpToDate [internet] Accessed April 2016.
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.

5.0 Appendices:

See page 5.

6.0 Revision History:

Original Effective Date: 06/30/2016

Next Review Date: 03/24/2022

Revision Date	Reason for Revision
March 2019	Transfer to new format
April 2019	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

Appendix I: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Afinitor everolimus	• Cardiovascular: edema (13-39%), hypertension (4-13%) • Central Nervous System: malaise (≤45%), fatigue (14-44%), headache (19-29%), migraine (≤30%), behavioral problems (21%), insomnia (6-14%), dizziness (7-12%) • Dermatology: skin rash (21-59%), cellulitis (29%), acne (10-22%), nail dx (5-22%), pruritus 13-20%), xeroderma (13%) • Endocrine/Metabolism: increased cholesterol (81-85%), decreased bicarb (56%), increased tri-glycerides (27-52%), increased phosphate (9-49%), decreased calcium (37%), decreased albumin (13-33%), increased glucose (14-25%), amenorrhea (15-17%) • Gastrointestinal: stomatitis (62-78%), diarrhea (14-50%), abdominal pain (9-36%), decreased appetite (6-30%), nausea/vomiting (15-29%), weight loss (9-28%), anorexia (25%), dysgeusia 5-22%), mucositis • Genitourinary: UTI (5-16%), irregular menses (10-11%) • Hematology/Oncology: increased bleeding time, anemia (41-61%), decreased lymphocytes (45-54%), decreased platelets (45-54%), neutropenia (46%), leukopenia (37%) • Hepatic: increased liver function tests. (23-74%) • Musculoskeletal: weakness (13-33%), arthralgia (13-20%), back/limb pain (8-15%) • Respiratory: respiratory tract infection. (31%), cough (20-30%), rhinitis (25%), nasopharyngitis (6-25%), upper respiratory infection (5-11%), dyspnea (20-24%), epistaxis (5-22%), pneumonitis (1-19%), oral pain (11%) • Miscellaneous: fever (15-31%), infection (37-50%) • Pregnancy Category: C	• Labs (prior and during): CBC with differential; liver function tests, creatinine, urinary protein and BUN; serum glucose and lipid profile. • Hematology oncology: monitor for signs and symptoms of malignancy • Infection: monitor for signs and symptoms • Respiratory: monitor signs and symptoms of non-infectious pneumonitis	None Needed