BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 3/17/2016**
SECTION: DRUGS	**LAST REVIEW DATE: 2/17/2022**
	LAST CRITERIA REVISION DATE: 2/17/2022
	ARCHIVE DATE:

AFINITOR® (everolimus) tablet
AFINITOR® DISPERZ (everolimus) tablet for suspension
Everolimus tablet
Everolimus tablet for suspension

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the

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form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

Criteria:

- **Criteria for initial therapy:** Afinitor (everolimus), Afinitor Disperz (everolimus), everolimus tablet, or everolimus tablet for suspension is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist, Nephrologist, Gastroenterologist, Neurologist, or Gynecologist depending upon indication or use

2. A confirmed diagnosis of **ONE** of the following:
    a. **For Afinitor:**
        i. Postmenopausal woman with advanced hormone receptor positive, HER2-negative breast cancer used in combination with exemestane, after failure of treatment with letrozole or anastrozole.
        ii. Individual 18 years of age or older with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease
        iii. Individual 18 years of age or older with progressive, well-differentiated, nonfunctional NET of gastrointestinal (GI) or lung origin with unresectable, locally advanced or metastatic disease
        iv. Individual 18 years of age or older with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib
        v. Individual 18 years of age or older with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery
        vi. Individual 18 years of age or older with TSC who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected
        vii. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

    b. **For Afinitor Disperz:**
        i. Individual 1 year of age or older with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected
        ii. Individual 2 years of age or older who have partial-onset seizures associated with TSC used as adjuvant treatment

iii. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

3. Individual does not have functional carcinoid tumors

4. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
    a. Lipid profile
    b. Negative pregnancy test is a woman of childbearing potential

5. There are **NO** FDA-label contraindications, such as:
    a. Hypersensitivity to other rapamycin derivatives (e.g., Torisel (temsirolimus), Rapamune (sirolimus))

6. Afinitor or everolimus tablet and Afinitor Disperz or everolimus tablet for suspension will not be used in combination

7. There are no significant interacting drugs

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Afinitor (everolimus), Afinitor Disperz (everolimus), everolimus tablet or everolimus tablet for suspension is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist, Nephrologist, Gastroenterologist, Neurologist, or Gynecologist depending upon indication or use

2. Individual's condition has responded while on therapy
    a. Response is defined as:
        i. Documented evidence of efficacy, disease stability and/or improvement
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:

i. Life-threatening non-infectious pneumonitis that has not recovered or has recurred and is in need of urgent intervention
ii. Invasive fungal infection needing antifungal treatment
iii. Life-threatening stomatitis needing urgent intervention
iv. Life-threatening febrile neutropenia needing urgent intervention
v. Life-threatening hyperglycemia or dyslipidemia
vi. Life-threatening non-hematologic toxicity or serious non-hematologic toxicity that recurs after dose reduction
vii. Clinically significant hypersensitivity reactions
viii. Angioedema

5. Afinitor or everolimus tablet and Afinitor Disperz or everolimus tablet for suspension will not be used in combination

6. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Everolimus is indicated for the treatment of postmenopausal women with advanced hormone receptor positive, HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane, after failure of treatment with letrozole or anastrozole; for the treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease and treatment of adult patients with progressive, well-differentiated, nonfunctional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin with unresectable, locally advanced or metastatic disease (everolimus is not indicated for the treatment of patients with functional carcinoid tumors); for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib; and for the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.

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Everolimus tab and everolimus tab for suspension are indicated for the treatment of pediatric (1 year of age or older) and adult patients with tuberous sclerosis complex (TSC) for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.
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. Everolimus binds to an intracellular protein, FKBP-12, resulting in an inhibitory complex formation with mTOR complex 1 (mTORC1) and thus inhibition of mTOR kinase activity. Inhibition of mTOR by everolimus has been shown to reduce cell proliferation, angiogenesis, and glucose uptake in *in vitro* and/or *in vivo* studies.

Resources:

Afinitor (everolimus) tablet and Afinitor Disperz (everolimus) tablet for oral suspension product information, revised by Novartis Pharmaceuticals Corporation 04-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 25, 2021.

Everolimus tablet product information, revised by Breckenridge Pharmaceuticals Inc. 01-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 25, 2021.

Everolimus tablet for oral suspension product information, revised by Mylan Pharmaceuticals Inc. 04-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 25, 2021.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.