BlueCross BlueShield of Arizona
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| **PHARMACY COVERAGE GUIDELINES** | **ORIGINAL EFFECTIVE DATE: 3/17/16** |
| **SECTION: DRUGS** | **LAST REVIEW DATE: 3/15/18** |
| | **LAST CRITERIA REVISION DATE: 3/15/18** |
| | **ARCHIVE DATE:** |

# AFINITOR® (everolimus) oral tablet
# AFINITOR® DISPERZ (everolimus) oral 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 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.**

## AFINITOR® (everolimus) oral tablet
## AFINITOR® DISPERZ (everolimus) oral tablet for suspension (cont.)

**Description:**

Afinitor (everolimus) tab 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.

Afinitor (everolimus) tab and Afinitor (everolimus) Disperz 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.

Afinitor (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.

# Afinitor (everolimus)
# Afinitor Disperz (everolimus)

**Medication class:**
Antineoplastic Agent, mTOR Kinase Inhibitor

**FDA-approved indication(s):**

- Afinitor
  - Treatment of postmenopausal women with advanced hormone receptor positive (HR+), human epidermal growth factor receptor-2 (HER2)-negative breast cancer in combination with exemestane, after failure of treatment with letrozole or anastrozole
  - Treatment of adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic disease
  - 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
    - It is not indicated for the treatment of patients with functional carcinoid tumors
  - Treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib

## AFINITOR® (everolimus) oral tablet
## AFINITOR® DISPERZ (everolimus) oral tablet for suspension (cont.)

- Treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery
- Treatment of pediatric (1 year of age or older) and adult patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected

- Afinitor Disperz
  - Treatment of pediatric (1 year of age or older) and adult patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected
    - Safety and effectiveness have not been established in pediatric patients with renal angiomyolipoma with TSC in the absence of SEGA

**Recommended Dose:**
- Breast cancer, neuroendocrine tumors, RCC, renal angiomyolipoma with TSC:
  - 10 mg once daily
- SEGA with TSC:
  - 4.5 mg/m$^2$ once daily, adjust dose to maintain a whole blood trough level between 5-15 mg/mL
    - When possible, use the same assay and laboratory

***Maximum dosage***
- Not stated

**Available Dosage Forms:**
- Afinitor: 2.5 mg, 5 mg, 7.5 mg, & 10 mg tabs
- Afinitor Disperz: 2 mg, 3 mg, & 5 mg tabs for oral suspension

**Warnings, Precautions, and other Clinical Information:**
- Safety and effectiveness of AFINITOR in patients with locally advanced or metastatic functional carcinoid tumors have not been demonstrated
- Starting doses should be reduce in patients with hepatic impairment
- If moderate inhibitors of CYP3A4/PgP inhibitors are used, Afinitor and Afinitor Disperz dosing should be reduced
- Avoid simultaneous use with strong CYP3A4/PgP inhibitors such as ketoconazole, itraconazole, clarithromycin, atazanavir, nefazodone, saquinavir, telithromycin, ritonavir, indinavir, nelfinavir, voriconazole
- If strong inducers of CYP3A4/PgP inhibitors are used, Afinitor and Afinitor Disperz dosing should be increased
- Avoid simultaneous use with live vaccines such as intranasal influenza, measles, mumps, rubella, oral polio, BCG, yellow fever, varicella, and TY21a typhoid vaccines
- Discontinue if non-infectious pneumonitis fails to recover within 4 weeks of corticosteroid treatment and dose adjustment or if it recurs
- Discontinue if invasive systemic fungal infection is diagnosed and treat with antifungal therapy
- Discontinue for stomatitis that is life-threatening
- Discontinue for life-threatening febrile neutropenia
- Avoid simultaneous use of St. John's wort (*hypericum perforatum*), grapefruit, grapefruit juice

## AFINITOR® (everolimus) oral tablet
## AFINITOR® DISPERZ (everolimus) oral tablet for suspension (cont.)

- Do not combine the two dosage forms (Afinitor tablets with Afinitor Disperz) to achieve desired total dose
- Woman of child bearing potential should use effective contraception
- Woman who is breast feeding an infant or child should stop breast feeding
- Woman of child bearing potential should be warned against becoming pregnant
- Males with female partners of reproductive potential should use effective contraception

**Criteria:**

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

1. Prescriber is an Oncologist

2. A confirmed diagnosis of **ONE** of the following:

   **For Afinitor:**
   - Individual is a postmenopausal woman with
     - Advanced hormone receptor-positive **and**
     - HER2-negative breast cancer in combination with exemestane (Aromasin) **and**
     - After failure of treatment with letrozole or anastrozole
   - Individual is an adult with progressive neuroendocrine tumors of pancreatic origin (PNET) with unresectable, locally advanced or metastatic
   - Individual is an adult with progressive, well differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic disease; it is not indicated for the treatment of individuals with functional carcinoid tumors
   - Individual is an adult with advanced renal cell carcinoma (RCC) who has failed treatment with sunitinib (Sutent) or sorafenib (Nexavar)
   - Individual is an adult with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery

   **For Afinitor and Afinitor Disperz:**
   - Individual (pediatric or adult) with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected

3. **ALL** of the following baseline tests have been completed before initiation of treatment:
   - Comprehensive metabolic panel
   - Lipid profile
   - Complete blood count

## AFINITOR® (everolimus) oral tablet
## AFINITOR® DISPERZ (everolimus) oral tablet for suspension (cont.)

4. There are **NO** contraindications
    - Contraindications include:
        - Hypersensitivity to everolimus, to other rapamycin derivatives, or to any of the excipients

**Initial approval duration**: 6 months

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

1. Individual continues to be seen by an Oncologist

2. Individual's cancer has not progressed while on therapy
    - For renal angiomyolipoma with tuberous sclerosis complex
        - Response is defined as **ONE** of the following:
            - Reduction in angiomyolipoma volume
            - Absence of new angiomyolipoma lesions
            - No angiomyolipoma related bleeding
    - For subependymal giant cell astrocytoma with tuberous sclerosis complex
        - Response is defined as **ONE** of the following:
            - Reduction in subependymal giant cell astrocytoma volume
            - Absence of new subependymal giant cell astrocytoma lesions
            - No new or worsening hydrocephalus

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    - Contraindications as listed in the criteria for initial therapy section
    - Significant adverse effect such as:
        - Life-threatening non-infectious pneumonitis that has not recovered or has recurred and is in need of urgent intervention
        - Invasive fungal infection needing antifungal treatment
        - Life-threatening stomatitis needing urgent intervention
        - Life-threatening febrile neutropenia needing urgent intervention

5. There are no significant interacting drugs

**Renewal duration**: 6 months

## AFINITOR® (everolimus) oral tablet
## AFINITOR® DISPERZ (everolimus) oral tablet for suspension (cont.)

**Resources:**

Afinitor and Afinitor Disperz. Package Insert. Revised by manufacturer 9/2017. Accessed 02-26-2018.

Afinitor and Afinitor Disperz. Package Insert. Revised by manufacturer 6/2016. Accessed 02-14-2017.

Afinitor and Afinitor Disperz. Package Insert. Revised by manufacturer 2/2016. Accessed 03-17-2016.

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.

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**Fax completed prior authorization request form to 602-864-3126** or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

# Pharmacy Prior Authorization Request Form

**Do not copy for future use. Forms are updated frequently.**
**REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.**

## Member Information

| Member Name (first & last): | Date of Birth: | Gender: | BCBSAZ ID#: |
|---|---|---|---|
| Address: | City: | State: | Zip Code: |

## Prescribing Provider Information

| Provider Name (first & last): | Specialty: | NPI#: | DEA#: |
|---|---|---|---|
| Office Address: | City: | State: | Zip Code: |
| Office Contact: | Office Phone: | Office Fax: | |

## Dispensing Pharmacy Information

| Pharmacy Name: | Pharmacy Phone: | Pharmacy Fax: |
|---|---|---|

## Requested Medication Information

| Medication Name: | Strength: | Dosage Form: |
|---|---|---|
| Directions for Use: | Quantity: / Refills: | Duration of Therapy/Use: |

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

## Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

## Clinical Information

1. **What is the diagnosis? Please specify below.**

   **ICD-10 Code:** _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

| Medication Name, Strength, Frequency | Dates started and stopped or Approximate Duration | Describe response, reason for failure, or allergy |
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5. **Are there any supporting labs or test results? Please specify below.**

| Date | Test | Value |
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# Pharmacy Prior Authorization Request Form

**6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.**
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

**Signature affirms that information given on this form is true and accurate and reflects office notes**

Prescribing Provider's Signature: Date:

**Please note**: Some medications may require completion of a drug-specific request form.

**Incomplete forms or forms without the chart notes will be returned.**

Office notes, labs, and medical testing relevant to the request that show medical justification are required.