

PHARMACY COVERAGE GUIDELINE

AFINITOR® (everolimus) tablet

AFINITOR® DISPERZ (everolimus) tablet for suspension

Everolimus tablet

Everolimus tablet for suspension

TORPENZ™ (everolimus) tablet

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for **EVEROLIMUS PRODUCTS**

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by or in consultation with an Oncologist, Nephrologist, Gastroenterologist, Neurologist, or Gynecologist depending on indication

PHARMACY COVERAGE GUIDELINE

AFINITOR® (everolimus) tablet **AFINITOR® DISPERZ (everolimus) tablet for suspension** **Everolimus tablet** **Everolimus tablet for suspension** **TORPENZ™ (everolimus) tablet**

Indication

- **For Afinitor tablet / everolimus tablet ONE** of the following:
 - Advanced HR+ HER2 negative breast cancer, used with exemestane after failure of letrozole or anastrozole in a postmenopausal woman
 - Progressive neuroendocrine tumors of pancreatic origin (PNET), unresectable, locally advanced or metastatic (not functional carcinoid)
 - Progressive, well differentiated, nonfunctional NET of GI or lung origin, unresectable, locally advanced or metastatic (not functional carcinoid)
 - Advanced renal cell carcinoma (RCC) after failure of sunitinib or sorafenib
 - Renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery
 - TSC with subependymal giant cell astrocytoma (SEGA) requiring intervention but cannot be curatively resected
 - Other oncologic use listed in NCCN Guidelines (Category 1 or 2A)
- **For Afinitor Disperz / everolimus tablet for suspension ONE** of the following:
 - TSC with subependymal giant cell astrocytoma (SEGA) requiring intervention but cannot be curatively resected
 - TSC associated partial onset seizures (adjuvant treatment)
 - Other oncologic use listed in NCCN Guidelines (Category 1 or 2A)
- **For Torpenz tablet ONE** of the following:
 - Advanced HR+ HER2 negative breast cancer, used with exemestane after failure of letrozole or anastrozole in a postmenopausal woman
 - Renal angiomyolipoma and TSC, not requiring immediate surgery
 - TSC with subependymal giant cell astrocytoma (SEGA) requiring intervention but cannot be curatively resected
 - Other oncologic use listed in NCCN Guidelines (Category 1 or 2A)

Age Requirement

- 18 years of age or older for **ANY** of the following:
 - Advanced HR+ HER2 negative breast cancer
 - Progressive neuroendocrine tumors of pancreatic origin (PNET)
 - Progressive, well differentiated, nonfunctional NET of gastrointestinal (GI) or lung origin
 - Advanced renal cell carcinoma (RCC)
 - Renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring surgery
- 2 years of age or older for TSC associated partial onset seizures (Afinitor Disperz / Everolimus tablet for suspension only)
- 1 year of age or older for TSC with subependymal giant cell astrocytoma (SEGA) requiring intervention

Baseline Clinical Evaluation

- Lipid profile
- Fasting serum glucose
- Negative pregnancy test in a woman of childbearing potential
- ECOG Performance Status 0 to 2

ORIGINAL EFFECTIVE DATE: 03/17/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/20/2025

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

PHARMACY COVERAGE GUIDELINE

AFINITOR® (everolimus) tablet

AFINITOR® DISPERZ (everolimus) tablet for suspension

Everolimus tablet

Everolimus tablet for suspension

TORPENZ™ (everolimus) tablet

Brand Specific Criteria

- Failure (adequate trial), contraindication, intolerance, or is not a candidate:
 - **For Afinitor** and **generic Torpenz**: Generic everolimus tablet
 - **For Afinitor Disperz**: Generic everolimus tablet for suspension
(**Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section))

Safety

- There is **NONE** of the following:
 - Hypersensitivity to rapamycin derivatives (e.g., temsirolimus, sirolimus)
 - Concomitant use with:
 1. Live vaccines
 2. P gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin)
 3. ACE inhibitors (e.g., enalapril, lisinopril)

Additional Requirements

- Tablet and suspension formulations will not be used together or interchangeably

Documentation Requirements

- Completed request form
- Chart notes
- Lab results
- Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification

- Continues under care of or is in consultation with appropriate specialist

Clinical Response

- No evidence of disease progression or unacceptable toxicity

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Failure (adequate trial), contraindication, intolerance, or is not a candidate:

PHARMACY COVERAGE GUIDELINE

AFINITOR® (everolimus) tablet

AFINITOR® DISPERZ (everolimus) tablet for suspension

Everolimus tablet

Everolimus tablet for suspension

TORPENZ™ (everolimus) tablet

-
- **For Afinitor and generic Torpenz:** Generic everolimus tablet
 - **For Afinitor Disperz:** Generic everolimus tablet for suspension
(**Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section))

Safety

- There is **NONE** of the following:
 - Hypersensitivity to rapamycin derivatives (e.g., temsirolimus, sirolimus)
 - Concomitant use of:
 1. Live vaccines
 2. P gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin)
 3. ACE inhibitors (e.g., enalapril, lisinopril)
 - Severe adverse effects such as:
 1. Life threatening pneumonitis
 2. Invasive fungal infection
 3. Severe stomatitis
 4. Febrile neutropenia
 5. Myelosuppression
 6. Severe hyperglycemia/dyslipidemia
 7. Serious non hematologic toxicity
 8. Hypersensitivity
 9. Angioedema

Additional Requirements

- Tablet and suspension formulations will not be used together or interchangeably

Documentation Requirements

- Chart notes
- Lab values confirming safe use
- Evidence of clinical improvement

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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

PHARMACY COVERAGE GUIDELINE

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

Description:

Afinitor (everolimus) is indicated for the treatment of postmenopausal women with advanced hormone receptor positive, HER2-negative breast cancer (advanced HR+ BC) used 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 Disperz (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 tab for suspension is indicated for the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.

Torpenz (everolimus tab) is indicated for the treatment of postmenopausal women with advanced hormone receptor positive, HER2-negative breast cancer (advanced HR+ BC) used in combination with exemestane, after failure of treatment with letrozole or anastrozole; for the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery; and 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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
[MedWatch Forms for FDA Safety Reporting | FDA](#)

ECOG Performance status: (also known as WHO performance status and Zubrod performance status)

| Eastern Co-operative Oncology Group (ECOG) Performance Status | |
|---|--|
| Grade | ECOG description |
| 0 | Fully active, able to carry on all pre-disease performance without restriction |

PHARMACY COVERAGE GUIDELINE

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

| | |
|---|--|
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work |
| 2 | Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours |
| 3 | Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours |
| 4 | Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair |
| 5 | Dead |
| Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982 | |

NCCN recommendation definitions:

Category 1:

Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:

Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:

Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:

Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Resources:

Afinitor (everolimus) tablet and Afinitor Disperz (everolimus) tablet for oral suspension product information, revised by Novartis Pharmaceuticals Corporation 02-2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 10, 2025.

Everolimus tablet and Everolimus tablet for oral suspension product information, revised by Breckenridge Pharmaceutical Inc. 09-2025. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 10, 2025.

Torpenz (everolimus) tablet product information, revised by Upsher-Smith Laboratories, LLC 03-2024. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 10, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Breast Cancer Version 5.2025 –Updated October 16, 2025. Available at <https://www.nccn.org>. Accessed December 30, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Central Nervous System Cancers Version 3.2025 –Updated December 05, 2025. Available at <https://www.nccn.org>. Accessed December 30, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer Version 1.2026 –Updated July 24, 2025. Available at <https://www.nccn.org>. Accessed December 30, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Neuroendocrine and Adrenal Tumors Version 3.2025 –Updated October 01, 2025. Available at <https://www.nccn.org>. Accessed December 30, 2025.

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.