ROCKY MOUNTAIN HEALTH PLANS®

UNIFORM PHARMACY PRIOR AUTHORIZATION REQUEST FORM

CONTAINS CONFIDENTIAL PATIENT INFORMATION

Complete this form in its entirety and send to Rocky Mountain Health Plans at 858-357-2538

☐ **Urgent**[1] ☐ **Non-Urgent**

Requested Drug Name: Afinitor & Afinitor Disperz (everolimus)

Patient Information:	**Prescribing Provider Information:**
Patient Name:	Prescriber Name:
Member/Subscriber Number:	Prescriber Fax:
Policy/Group Number:	Prescriber Phone:
Patient Date of Birth (MM/DD/YYYY):	Prescriber Pager:
Patient Address:	Prescriber Address:
Patient Phone:	Prescriber Office Contact:
Patient Email Address:	Prescriber NPI:
	Prescriber DEA:
Prescription Date:	Prescriber Tax ID:
	Specialty/Facility Name (If applicable):
	Prescriber Email Address:

Prior Authorization Request for Drug Benefit: ☐ New Request ☐ Reauthorization

Patient Diagnosis and ICD Diagnostic Code(s):

Drug(s) Requested (with J-Code, if applicable):

Strength/Route/Frequency:

Unit/Volume of Named Drug(s):

Start Date and Length of Therapy:

Location of Treatment: (e.g. provider office, facility, home health, etc.) including name, Type 2 NPI (if applicable), address and tax ID:

Clinical Criteria for Approval, Including other Pertinent Information to Support the Request, other Medications Tried, Their Name(s), Duration, and Patient Response:

Afinitor® & Afinitor Disperz (everolimus)

Diagnosis (documentation supportive of diagnosis is required)

AFINITOR ONLY

☐ Advanced renal cell carcinoma (RCC)

☐ Progressive neuroendocrine tumor of pancreatic origin (PNET) that is unresectable, locally advanced, or metastatic

☐ Progressive, well-differentiated, non-functional neuroendocrine tumor (NET) of gastrointestinal (GI) or lung origin that is unresectable, locally advanced, or metastatic

☐ Renal angiomyolipoma and tuberous sclerosis complex (TSC) that does not require immediate surgery

☐ Advanced HR-positive, HER2-negative breast cancer in a postmenopausal woman

☐ Subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected

☐ Other (please state):_____

AFINITOR DISPERZ ONLY

☐ Subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected

☐ Other (please state):_____

Clinical Consideration (for approval, please indicate and provide documentation of the following):

ADVANCED RENAL CELL CARCINOMA (RCC)

☐ Patient has failed or is contraindicated to treatment with Sutent (sunitinib) **OR** Nexavar (sorafenib)

ADVANCED HR-POSITIVE, HER2-NEGATIVE BREAST CANCER

☐ Patient has failed or is contraindicated to treatment with letrozole (Femara) or anastrozole (Arimidex)

☐ Afinitor will be used in combination with exemestane (Aromasin)

Physician Specialty:

☐ Oncology

☐ Other (please state):_____

Coverage Policy:

Our guideline for **EVEROLIMUS (AFINITOR)** requires either a diagnosis of advanced renal cell carcinoma (RCC) after failure or contraindication to treatment with Sutent (sunitinib) or Nexavar (sorafenib) **OR** a diagnosis of progressive neuroendocrine tumor of pancreatic origin (PNET) that is unresectable, locally advanced, or metastatic **OR** a diagnosis of progressive, well-differentiated, non-functional neuroendocrine tumor of GI or lung origin that is unresectable, locally advanced, or metastatic **OR** renal angiomyolipoma and tuberous sclerosis complex (TSC) that does not require immediate surgery **OR** subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected **OR** advanced HR-positive, HER2-negative breast cancer in a postmenopausal woman in combination with exemestane after failure or contraindication to treatment with letrozole or anastrozole.

Our guideline for **EVEROLIMUS (AFINITOR DISPERZ)** requires a diagnosis of subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected.

When criteria are met, the duration of approval is 12 months.

☐ For use in clinical trial? (If yes, provide trial name and registration number):

Drug Name (Brand Name and Scientific Name)/Strength:

Dose:	Route:	Frequency:
Quantity:	Number of Refills:	

Product will be delivered to: ☐ Patient's Home ☐ Physician Office Other:

Prescriber or Authorized Signature: Date:

Dispensing Pharmacy Name and Phone Number:

☐ **Approved** ☐ **Denied**

If denied, provide reason for denial, and include other potential alternative medications, if applicable, that are found in the formulary of the carrier:

1. A request for prior authorization that if determined in the time allowed for non-urgent requests could seriously jeopardize the life or health of the covered person or the ability of the covered person to regain maximum function, or subject the person to severe pain that cannot be adequately managed without the drug benefit contained in the prior authorization request

RMHP Formulary Coverage Policy

THIS INFORMATION IS NOT ALL-INCLUSIVE AND IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY

Afinitor (everolimus)

CLASSIFICATION

- Antineoplastic

DESCRIPTION

- Inhibits mammalian target of rapamycin kinase activity which reduces the activity of S6 ribosomal protein kinase, eukaryotic elongation factor 4E-binding protein, inhibits the expression of hypoxia-inducible factor, and reduces vascular endothelial growth factor expression.
- Everolimus is an analogue of rapamycin (sirolimus) with immunosuppressive and antiproliferative activity. It was developed to improve upon the wide inter-individual variation in pharmacokinetic parameters observed with oral sirolimus in animal and human studies. Everolimus is not a prodrug of sirolimus; it exhibits metabolic stability in that hydrolytic cleavage of the side chain does not occur to a significant extent in vivo.
- In renal transplantation: Similar to sirolimus (rapamycin), everolimus has been studied for use with cyclosporine/steroids to prevent acute rejection episodes in renal transplant recipients. Everolimus is available under the brand name Zortress for this purpose.
- Everolimus was superior to placebo for progression-free survival (PFS) in 410 adults with **metastatic renal cell carcinoma** whose disease had progressed despite prior treatment with sunitinib, sorafenib, or both sequentially, according to a randomized, double-blind, phase 3 trial.
- Everolimus is indicated for the treatment of **subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis** in adults and children 1 year or older who are not candidates for curative surgical resection. Treatment with everolimus for 6 months resulted in a significant decrease in the volume of the primary subependymal giant cell astrocytoma compared with baseline in patients with tuberous sclerosis, according to a phase 1-2, prospective, open-label study (n=28). Clinical benefit such as improvement in disease related symptoms or increase in overall survival has not been demonstrated.
- Everolimus is indicated in adults with **progressive neuroendocrine tumors of pancreatic origin** (PNET) that is unresectable, locally advanced or metastatic. PFS was significantly improved with everolimus compared with placebo in a randomized, double-blind, multicenter study (n=410). Everolimus is also indicated for **progressive, well-differentiated, nonfunctional neuroendocrine tumors of GI or lung origin** in adults with unresectable, locally advanced, or metastatic disease. PFS was significantly improved with everolimus compared with placebo (11 vs 3.9 months) in the randomized RADIANT-4 study. There was no significant between group difference in an interim analysis of overall survival.
- Efficacy of everolimus in the treatment of patients with carcinoid tumors has not been established. In a randomized, double-blind, multicenter study (n=429) in patients with carcinoid tumors the overall survival interim analysis favored the placebo and depot octreotide group over the everolimus group.
- Everolimus is indicated in postmenopausal woman with **advanced hormone receptor positive, HER2-negative breast cancer** in combination with exemestane after failure of treatment with letrozole or anastrozole. In the Breast Cancer Trials of Oral Everolimus-2 (BOLERO-2) trial (n=724), progression-free survival was significantly improved with the addition of everolimus to treatment with exemestane in women with ER+ advanced breast cancer refractory to non-steroidal aromatase inhibitors in an interim and PFS remained significantly improved with the addition of everolimus to treatment with exemestane in the final analysis (7.8 vs 3.2 months).

- Everolimus is indicated for the treatment of adult patients with **renal angiomyolipoma and tuberous sclerosis complex (TSC)**, not requiring immediate surgery. Efficacy is based on an analysis of durable objective responses in patients treated for a median of 8.3 months. Further follow-up of patients is required to determine long-term outcomes.

FORMULARY COVERAGE

Prior authorization:	Required
Good Health Formulary:	Tier 3
Legacy Formulary:	Tier 3

COVERAGE CRITERIA

Afinitor (everolimus) meets the definition of medical necessity for the following:

- Advanced renal cell carcinoma (RCC) in adults
  - **Documentation required:** Failure or contraindication to treatment with Sutent (sunitinib) or Nexavar (sorafenib)
- Progressive neuroendocrine tumors of pancreatic origin (PNET) in adults with unresectable, locally advanced, or metastatic disease
- Progressive, well-differentiated, nonfunctional neuroendocrine tumors of GI or lung origin in adults with unresectable, locally advanced, or metastatic disease
- Renal angiomyolipoma and tuberous sclerosis complex (TSC) in adults who do not require immediate surgery
- Subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected in adults and children ≥ 1 year of age
- Advanced HR-positive, HER2-negative breast cancer in postmenopausal women
  - **Documentation required:**
    - Failure or contraindication to treatment with letrozole (Femara) or anastrozole (Arimidex)
    - Use in combination with exemestane (Aromasin)

Afinitor Disperz (everolimus tablets for oral suspension) meets the definition of medical necessity for the following:

- Subependymal giant cell astrocytoma (SEGA) with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected in adults and children ≥ 1 year of age

Afinitor and Afinitor Disperz (everolimus) are considered **experimental** for the following:
- Any condition or diagnosis not FDA approved or Compendia supported

Required Provider Specialty: None Required

APPROVAL DURATION
- 12 months

DOSAGE/ADMINISTRATION:

Advanced HR-positive, HER2-negative breast cancer, advanced NET, advanced RCC, and renal angiomyolipoma with TSC (<u>Adults only</u>; not indicated in pediatric patients):

- 10 mg once daily at the same time every day. Give consistently with food or consistently without food

- Continue until disease progression or unacceptable toxicity
- For patients with hepatic impairment, reduce the AFINITOR dose
- For patients requiring coadministration with moderate inhibitors of CYP3A4/P-glycoprotein (PgP), reduce the AFINITOR dose to 2.5 mg once daily; if tolerated, consider increasing to 5 mg once daily.
- For patients requiring coadministration with a strong inducers of CYP3A4, consider doubling the daily dose of AFINITOR using increments of 5 mg or less

SEGA with TSC (not indicated in pediatric patients <u>less than 1 year of age</u>):

- Do NOT combine tablets and tablets for oral suspension to achieve the desired dose; administer only 1 dosage form.
- 4.5 mg/m^2 once daily; adjust dose to attain trough concentrations of 5-15 ng/mL.
- Assess trough concentrations approximately 2 weeks after initiation of treatment, a change in dose, a change in co-administration of CYP3A4 and/or PgP inducers or inhibitors, a change in hepatic function, or a change in dosage form between AFINITOR tablets and AFINITOR DISPERZ.
- For patients with severe hepatic impairment, reduce the starting dose of AFINITOR tablets or AFINITOR DISPERZ.
- If concomitant use of moderate inhibitors of CYP3A4 and/or PgP is required, reduce the dose of AFINITOR tablets or AFINITOR DISPERZ by 50%.
- If concomitant use of strong inducers of CYP3A4 is required, double the dose of AFINITOR tablets or AFINITOR DISPERZ.

Full dose adjustment information: See prescribing information.

PRECAUTIONS:

- Adverse reactions, severe and/or intolerable; may require dose adjustment, interruption or withdrawal; risk greater in elderly 65 years of age and older
- Hematologic aberrations (decreases in hemoglobin, lymphocytes, neutrophils, platelets) have been reported; monitoring recommended
- Hepatic impairment, preexisting severe (Child-Pugh class C); use not recommended
- Hepatic impairment due to increased exposure to everolimus may require dose adjustment.
- Hyperglycemia, hyperlipidemia and hypertriglyceridemia have been reported; monitoring is recommended and dose reduction, interruption, or withdrawal may be required.
- Hypersensitivity reactions, including anaphylaxis and angioedema have been reported
- Localized or systemic opportunistic infections, sometimes severe including fatalities have been reported; monitoring recommended; interruption or discontinuation of therapy may be required
- Mouth ulcers, oral mucositis, and stomatitis have been reported and may require dose reduction, interruption, or withdrawal
- Noninfectious pneumonitis has been reported; monitoring and dose adjustments recommended; discontinuation of therapy may be required in severe cases
- Concomitant use with live vaccines or strong CYP3A4 inhibitors, including grapefruit, should be avoided; close contact with live vaccine recipients should also be avoided
- Fluid accumulation (peripheral edema, pericardial and pleural effusions) has been reported
- Impaired wound healing and wound complications may occur
- Male infertility may occur
- Nephrotoxicity, including serum creatinine elevations, proteinuria, and acute renal failure with fatalities, has been reported; increased risk with standard dose cyclosporine; monitoring recommended
- Angioedema: patients taking concomitant ACEIs may be at an increased risk

COST

- AWP (April 2010): Afinitor 10mg tablets (1): $247.58
- AWP (August 2012): Afinitor 10mg tablets (1): $320.86
- AWP (May 2013): Afinitor 10mg tablets (1): $336.56
- AWP (January 2015): Afinitor 10mg tablets (1): $451.61
- AWP (June 2016): Afinitor 10mg tablets (1): $516.08

COMMITTEE APPROVAL:

- January 26, 2011

GUIDELINE UPDATE INFORMATION:

April 2010	Policy created
December 2011	Updated with new indication (SEGA)
August 2012	Updated with Advanced HR+ BC and renal angiomyolipoma with TSC indications
May 2013	Updated with Afinitor Disperz prescribing information
December 2015	Coverage policy reviewed and updated
July 2016	Coverage policy reviewed and updated

REFERENCES:

- DRUGDEX®, accessed 04/06/2010, 08/06/2012, 5/8/2013, 12/2/15, 7/7/16
- Product Information: AFINITOR® (everolimus) tablets for oral administration, Afinitor Disperz® (everolimus tablets for oral suspension). Novartis Pharmaceutical Corporation, East Hanover, NJ, 2016.