DRUG QUANTITY MANAGEMENT POLICY – PER RX

POLICY: Oncology – Everolimus Drug Quantity Management Policy – Per Rx
- Afinitor® (everolimus tablets – Novartis, generic)
- Afinitor® Disperz (everolimus tablets for oral suspension – Novartis, generic)

REVIEW DATE: 08/03/2022

OVERVIEW

Everolimus (Afinitor, Afinitor Disperz, generic), a kinase inhibitor, is indicated for the following uses:[1]

- **Breast cancer**, treatment of postmenopausal women with advanced hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative disease in combination with exemestane, after failure of treatment with letrozole or anastrozole.
- **Neuroendocrine tumors (NET)**, treatment of adults with progressive disease of pancreatic origin and adults with progressive, well-differentiated, non-functional NET of gastrointestinal or lung origin that are unresectable, locally advanced, or metastatic. Limitation of Use: Afinitor (generic) is not indicated for the treatment of patients with functional carcinoid tumors.
- **Renal cell carcinoma**, treatment of adults with advanced disease after failure of treatment with Sutent® (sunitinib capsules) or Nexavar® (sorafenib tablets).
- **Tuberous sclerosis complex (TSC)-associated renal angiomyolipoma,** treatment of adults not requiring immediate surgery.
- **TSC-associated subependymal giant cell astrocytoma (SEGA)**, treatment of patients ≥ 1 year of age who require therapeutic intervention but cannot be curatively resected. Afinitor Disperz (generic) is also FDA-approved for this indication.
- **TSC-associated partial-onset seizures**, adjunctive treatment of patients ≥ 2 years of age. Afinitor Disperz (generic) is FDA-approved for this indication.

Of note, Zortress® (everolimus tablets) is indicated in combination with other drugs for prophylaxis of organ rejection in adults undergoing kidney or liver transplant.[2] The tablet strengths and dosing is different for Zortress than with Afinitor/Afinitor Disperz (generic). Zortress is not targeted in this policy.

Dosing

Dosing for Afinitor (generic) and Afinitor Disperz (generic) is outlined in Table 1 below.

Table 1. Dosing for Afinitor and Afinitor Disperz.[1]

Indication	Afinitor (generic) Dose	Afinitor Disperz (generic) Dose
Hormone Receptor-Positive, HER2-Negative Breast Cancer	10 mg QD	N/A
NET	10 mg QD	N/A
RCC	10 mg QD	N/A
TSC-Associated Renal Angiomyolipoma	10 mg QD	N/A
TSC-Associated SEGA	4.5 mg/m^2 QD. Titrate to maintain a trough of 5 ng/mL to 15 ng/mL.	4.5 mg/m^2 QD. Titrate to maintain a trough of 5 ng/mL to 15 ng/mL.
TSC-Associated Partial-Onset Seizures	N/A	5 mg/m^2 QD. Titrate to maintain a trough of 5 ng/mL to 15 ng/mL.

HER-2 – Human epidermal growth factor receptor-2; QD – Once daily; N/A – Not applicable; NET – Neuroendocrine tumor; RCC – Renal cell carcinoma; TSC – Tuberos sclerosis complex; SEGA – Subependymal Giant Cell Astrocytoma.

Dose interruption and/or dose reduction may be required in the event of various adverse events (50% of the original dose or increased dosing interval). Dose reductions ranging from one 2.5 mg, 5 mg, or 7.5 mg

tablet once daily (QD) are also recommended for hepatic impairment, co-administration with moderate cytochrome P450(CYP) 3A inhibitors, and/or co-administration with P-glycoprotein (PgP) inhibitors (Table 2). Concomitant use of St. John's Wort should be avoided. The dose of Afinitor (generic) and Afinitor Disperz (generic) should be increased in patients taking a concomitant P-gP and strong inducers of CYP3A4 (Table 3).

Table 2. Dose Modifications for Concurrent Use of Afinitor/Afinitor Disperz with a P-gP and Moderate CYP3A4 Inhibitor.[1]

Indication	Dose Modification for Afinitor/Afinitor Disperz
Breast Cancer, NET, RCC, TSC-Associated Renal Angiomyolipoma	• Reduce dose to 2.5 mg QD • May increase dose to 5 mg QD if tolerated • Resume dose administered prior to inhibitor initiation, once the inhibitor is discontinued for 3 days
TSC-Associated SEGA and TSC-Associated Partial Onset Seizures	• Reduce the daily dose by 50%. • Change to every other day dosing if the reduced dose is lower than the lowest available strength. • Resume the dose administered prior to inhibitor initiation, once the inhibitor is discontinued for 3 days. • Assess trough concentrations when initiating and discontinuing the inhibitor.

P-gP – P-glycoprotein; CYP – Cytochrome P450; NET – Neuroendocrine tumor; RCC – Renal cell carcinoma; TSC – Tuberos sclerosis complex; QD – Once daily; SEGA – Subependymal Giant Cell Astrocytoma.

Table 3. Dose Modifications for Concurrent Use of Afinitor/Afinitor Disperz with a P-gP and Strong CYP3A4 Inducer.[1]

Indication	Dose Modification for Afinitor/Afinitor Disperz
Breast Cancer, NET, RCC, TSC-Associated Renal Angiomyolipoma	• Avoid co-administration where alternatives exist. • If co-administration cannot be avoided, double the daily dose using increments of ≤ 5 mg. Multiple increments may be required. • Resume the dose administered prior to inducer initiation, once an inducer is discontinued for 5 days.
TSC-Associated SEGA and TSC-Associated Partial Onset Seizures	• Double the daily dose using increments using increments of ≥ 5 mg. Multiple increments may be required. • Addition of another strong CYP3A4 inducer may not require additional dosage modification. • Assess trough concentrations when initiating and discontinuing the inducer. • Resume the dose administered before starting any inducer, once all inducers are discontinued for 5 days.

P-gP – P-glycoprotein; CYP – Cytochrome P450; NET – Neuroendocrine tumor; RCC – Renal cell carcinoma; TSC – Tuberos sclerosis complex; SEGA – Subependymal Giant Cell Astrocytoma.

Availability

Afinitor tablets (generic) are available in the following strengths: 2.5 mg, 5 mg, 7.5 mg, and 10 mg.[1] Afinitor Disperz tablets for oral suspension (generic) are available in the following strengths: 2 mg, 3 mg, and 5 mg. Afinitor tablets (generic) and Afinitor Disperz tablets (generic) are supplied in a carton containing 28 tablets (4 blister cards of 7 tablets each).[1]

POLICY STATEMENT

This Drug Quantity Management program has been developed to promote dose consolidation of Afinitor (generic) and Afinitor Disperz (generic). If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration.

Automation: None.

Drug Quantity Limits

Product	Strength and Form	Retail Maximum Quantity per Rx	Home Delivery Maximum Quantity per Rx

Afinitor® (everolimus tablets, generic)	2.5 mg tablet	30 tablets	90 tablets
	5 mg tablet	30 tablets	90 tablets
	7.5 mg tablet	30 tablets	90 tablets
	10 mg tablet	30 tablets	90 tablets
Afinitor Disperz® (everolimus tablets for oral suspension, generic)	2 mg tablets for oral suspension	30 tablets	90 tablets
	3 mg tablets for oral suspension	30 tablets	90 tablets
	5 mg tablets for oral suspension	30 tablets	90 tablets

CRITERIA

Afinitor 2.5 mg tablets (generic)

1. If the patient has Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA) and needs to increase their dose to maintain blood trough concentrations between 5 ng/mL and 15 ng/mL, approve based on the daily dose (A or B):
   A) Patient's dose is 12.5 mg/day, approve 150 tablets per dispensing at retail or 450 tablets per dispensing at home delivery; OR
   B) Patients dose is 17.5 mg/day, approve 210 tablets per dispensing at retail or 630 tablets per dispensing at home delivery.

Afinitor 5 mg tablets (generic)

1. If the patient has Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA) and needs to increase their dose to maintain blood trough concentrations between 5 ng/mL and 15 ng/mL, approve based on the daily dose (A):
   A) Patient's dose is 25 mg/day, approve 150 mg tablets per dispensing at retail or 450 tablets per dispensing at home delivery.

Afinitor 7.5 mg tablets (generic)

1. If the patient is taking a strong CYP3A4 inducer (e.g., rifampin, carbamazepine, phenobarbital, phenytoin, rifabutin, rifapentine) at the same time as Afinitor (generic) and requires a dose of 15 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery.
2. If the patient has Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA) and needs to increase their dose to maintain blood trough concentrations between 5 ng/mL and 15 ng/mL, approve based on the daily dose (A or B):
   A) Patient's dose is 15 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
   B) Patient's dose is 22.5 mg/day, approve 90 tablets per dispensing at retail or 270 tablets per dispensing at home delivery.

Afinitor 10 mg tablets (generic)

1. If the patient is taking a strong CYP3A4 inducer (e.g., rifampin, carbamazepine, phenobarbital, phenytoin, rifabutin, rifapentine) at the same time as Afinitor (generic) and requires a dose of 20 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery.
2. If the patient has Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA), and who needs to increase their dose to maintain blood trough concentrations between 5 ng/mL and 15 ng/mL, approve based on the daily dose (A or B):
   A) Patient's dose is 20 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
   B) Patient's dose is 30 mg/day, approve 90 tablets per dispensing at retail or 270 tablets per dispensing at home delivery.

Afinitor Disperz 2 mg tablets (generic)

1. If the patient is taking a strong CYP3A4 inducer (e.g., rifampin, carbamazepine, phenobarbital, phenytoin, rifabutin, rifapentine) at the same time as Afinitor Disperz (generic) and requires a dose of 4 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery.
2. If the patient has Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA) or Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures, and needs to increase their dose to maintain blood trough concentrations between 5 ng/mL and 15 ng/mL, approve based on the daily dose (A, B, C, D, or E):
   - **A)** Patient's dose is 4 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
   - **B)** Patient's dose is 8 mg/day, approve 120 tablets per dispensing at retail or 360 tablets per dispensing at home delivery; OR
   - **C)** Patient's dose is 14 mg/day, approve 210 tablets per dispensing at retail or 630 tablets per dispensing at home delivery; OR
   - **D)** Patient's dose is 16 mg/day, approve 240 tablets per dispensing at retail or 720 tablets per dispensing at home delivery; OR
   - **E)** Patient's dose is 22 mg/day, approve 330 tablets per dispensing at retail or 990 tablets per dispensing at home delivery.

Afinitor Disperz 3 mg tablets (generic)

1. If the patient is taking a strong CYP3A4 inducer (e.g., rifampin, carbamazepine, phenobarbital, phenytoin, rifabutin, rifapentine) at the same time as Afinitor Disperz (generic) and requires a dose of 6 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery.
2. If the patient has Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA) or Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures, and needs to increase their dose to maintain blood trough concentrations between 5 ng/mL and 15 ng/mL, approve based on the daily dose (A, B, C, D, E, or F):
   - **A)** Patient's dose is 6 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
   - **B)** Patient's dose is 9 mg/day, approve 90 tablets per dispensing at retail or 270 tablets per dispensing at home delivery; OR
   - **C)** Patient's dose is 12 mg/day, approve 120 tablets per dispensing at retail or 360 tablets per dispensing at home delivery; OR
   - **D)** Patient's dose is 18 mg/day, approve 180 tablets per dispensing at retail or 540 tablets per dispensing at home delivery; OR
   - **E)** Patient's dose is 21 mg/day, approve 210 tablets per dispensing at retail or 630 tablets per dispensing at home delivery; OR
   - **F)** Patient's dose is 24 mg/day, approve 240 tablets per dispensing at retail or 720 tablets per dispensing at home delivery.

Afinitor Disperz 5 mg tablets (generic)

1. If the patient is taking a strong CYP3A4 inducer (e.g., rifampin, carbamazepine, phenobarbital, phenytoin, rifabutin, rifapentine) at the same time as Afinitor Disperz (generic) and requires a dose of 10 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery.
2. If the patient has Tuberous Sclerosis Complex (TSC)-Associated Subependymal Giant Cell Astrocytoma (SEGA) or Tuberous Sclerosis Complex (TSC)-Associated Partial-Onset Seizures, and needs to increase their dose to maintain blood trough concentrations between 5 ng/mL and 15 ng/mL, approve based on the daily dose (A, B, C, D, or E):
   - **A)** Patient's dose is 10 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
   - **B)** Patient's dose is 15 mg/day, approve 90 tablets per dispensing at retail or 270 tablets per dispensing at home delivery; OR

C) Patient's dose is 20 mg/day, approve 120 tablets per dispensing at retail or 360 tablets per dispensing at home delivery; OR
D) Patients dose is 25 mg/day, approve 150 tablets per dispensing at retail or 400 tablets per dispensing at home delivery; OR
E) Patients dose is 30 mg/day, approve 180 tablets per dispensing at retail or 540 tablets per dispensing at home delivery.

REFERENCES

1. Afinitor® tablets, Afinitor Disperz® tablets for oral suspension [prescribing information]. East Hanover, NJ: Novartis; December 2021.

Type of Revision	Summary of Changes	Review Date
New Policy	Reviewed and approved at TAC.	06/02/2021

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