



Drug Quantity Management – Per Rx Oncology – Everolimus

Table of Contents

National Formulary Medical Necessity	1
Conditions Not Covered.....	4
Background.....	4
References	5
Revision History.....	5

Product Identifier(s)

Effective 1/1/23 to 4/11/23: 110940

Effective 4/12/23: 94698

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

National Formulary Medical Necessity

Drugs Affected

- Afinitor® (everolimus tablets, generic)
- Afinitor® Disperz (tablets for oral suspension, generic)

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.

Drug Quantity Limits

Product	Strength and Form	Retail	Home Delivery
		Maximum Quantity per Rx	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

Cigna covers quantities as medically necessary when the following criteria are met:

Afinitor 2.5 mg tablets (generic)

1. If the individual 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) Individual's dose is 12.5 mg/day, approve 150 tablets per dispensing at retail or 450 tablets per dispensing at home delivery; OR
 - B) Individual's 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 individual 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):
 1. Individual'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 individual 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 individual 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) Individual's dose is 15 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
 - B) Individual'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 individual 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 individual 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) Individual's dose is 20 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
 - B) Individual'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 individual 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 individual 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) Individual's dose is 4 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
 - B) Individual's dose is 8 mg/day, approve 120 tablets per dispensing at retail or 360 tablets per dispensing at home delivery; OR
 - C) Individual's dose is 14 mg/day, approve 210 tablets per dispensing at retail or 630 tablets per dispensing at home delivery; OR
 - D) Individual's dose is 16 mg/day, approve 240 tablets per dispensing at retail or 720 tablets per dispensing at home delivery; OR
 - E) Individual'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 individual 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 individual 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) Individual's dose is 6 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
 - B) Individual's dose is 9 mg/day, approve 90 tablets per dispensing at retail or 270 tablets per dispensing at home delivery; OR
 - C) Individual's dose is 12 mg/day, approve 120 tablets per dispensing at retail or 360 tablets per dispensing at home delivery; OR
 - D) Individual's dose is 18 mg/day, approve 180 tablets per dispensing at retail or 540 tablets per dispensing at home delivery; OR
 - E) Individual's dose is 21 mg/day, approve 210 tablets per dispensing at retail or 630 tablets per dispensing at home delivery; OR
 - F) Individual'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 individual 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 individual 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) Individual's dose is 10 mg/day, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery; OR
 - B) Individual's dose is 15 mg/day, approve 90 tablets per dispensing at retail or 270 tablets per dispensing at home delivery; OR
 - C) Individual's dose is 20 mg/day, approve 120 tablets per dispensing at retail or 360 tablets per dispensing at home delivery; OR
 - D) Individuals dose is 25 mg/day, approve 150 tablets per dispensing at retail or 400 tablets per dispensing at home delivery; OR

- E) Individuals dose is 30 mg/day, approve 180 tablets per dispensing at retail or 540 tablets per dispensing at home delivery.

Conditions Not Covered

Any other exception is considered not medically necessary.

Background

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 – Tuberous 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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

References

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

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	<p>Generics to Afinitor 10 mg tablets were added to the clinical policy (already rolled in to the targeting).</p> <p>Generics to all strengths of Afinitor Disperz were added to the clinical policy (already rolled in to the targeting).</p> <p>Home delivery maximum quantities per Rx were added to the quantity limits for all products at a maximum of 90 tablets per Rx.</p>	08/03/2022

	<p>Afinitor 2.5 mg tablets (generic): Override quantities for patients with Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma were updated to include home delivery override quantities of 450 tablets per Rx (for patients with a dose 12.5 mg/day) and 630 tablets per Rx for patients with a dose of 17.5 mg/day.</p> <p>Afinitor 5 mg tablets (generic): The override quantity for patients with Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma were updated to include a home delivery override quantity of 450 tablets per Rx (for patients with a dose 25 mg/day).</p> <p>Afinitor 7.5 mg tablets (generic): The override quantity for patients taking a strong CYP3A4 inducer requiring a dose of 15 mg/day was updated to include the home delivery override quantity of 180 tablets per Rx.</p> <p>Override quantities for patients with Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma were updated to include home delivery override quantities of 180 tablets per Rx (for patients with a dose 15 mg/day) and 270 tablets per Rx (for patients with a dose of 22.5 mg/day).</p> <p>Afinitor 10 mg tablets (generic): The override quantity for patients taking a strong CYP3A4 inducer requiring a dose of 20 mg/day was updated to include the home delivery override quantity of 180 tablets per Rx.</p> <p>Override quantities for patients with Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma were updated to include home delivery override quantities of 180 tablets per Rx (for patients with a dose 20 mg/day) and 270 tablets per Rx (for patients with a dose of 30 mg/day).</p> <p>Afinitor Disperz 2 mg tablets (generic): A new override quantity for patients taking a strong CYP3A4 inducer requiring a dose of 4 mg/day was added to approve 60 tablets per Rx at retail and 180 tablets per Rx at home delivery.</p> <p>Override quantities for patients with Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma or Tuberous Sclerosis Complex Associated Partial-Onset Seizures were updated to include home delivery override quantities of 180 tablets per Rx (for patients with a dose 4 mg/day), 360 tablets per Rx (for patients with a dose of 8 mg/day), 630 tablets per Rx (for patients with a dose of 14 mg/day), 720 tablets per Rx (for patients with a dose of 16 mg/day), and 990 tablets per Rx (for patients with a dose of 22 mg/day).</p> <p>Afinitor Disperz 3 mg tablets (generic): A new override quantity for patients taking a strong CYP3A4 inducer requiring a dose of 6 mg/day was added to approve 60 tablets per Rx at retail and 180 tablets per Rx at home delivery.</p> <p>Override quantities for patients with Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma or Tuberous Sclerosis Complex Associated Partial-Onset Seizures were updated to include home delivery override quantities of 180 tablets per Rx (for patients with a dose 6 mg/day), 270 tablets per Rx (for patients with a dose of 9 mg/day), 360 tablets per Rx (for patients with a dose of 12 mg/day), 540 tablets per Rx (for patients with a dose of 18 mg/day), 630 tablets per Rx (for patients with a dose of 21 mg/day), and 720 tablets per Rx (for patients with a dose of 24 mg/day).</p> <p>Afinitor Disperz 5 mg tablets (generic): A new override quantity for patients taking a strong CYP3A4 inducer requiring a dose of 10 mg/day was added to approve 60 tablets per Rx at retail and 180 tablets per Rx at home delivery.</p> <p>Override quantities for patients with Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma or Tuberous Sclerosis Complex Associated Partial-Onset Seizures were updated to include home delivery override quantities of 180 tablets per Rx (for patients with a dose 10 mg/day), 270 tablets per Rx (for patients with a dose of 15 mg/day), 360 tablets per Rx (for patients with a dose of 20 mg/day), 400 tablets per Rx (for patients with a dose of 25 mg/day), and 540 tablets per Rx (for patients with a dose of 30 mg/day).</p>	
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