

**Clinical Policy: Everolimus (Afinitor, Afinitor Disperz, Zortress)**

Reference Number: CP.PHAR.63

Effective Date: 06.01.11

Last Review Date: 02.24

Line of Business: Commercial, HIM\*, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Everolimus (Afinitor<sup>®</sup>, Afinitor Disperz<sup>®</sup>, Zortress<sup>®</sup>) is an mTOR kinase inhibitor.

*\*For Health Insurance Marketplace (HIM), Afinitor Disperz is non-formulary and should not be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

**FDA Approved Indication(s)**

Indication	Afinitor	Afinitor Disperz	Zortress
<i>Labeled uses (and recommended NCCN uses by product as indicated)</i>			
Breast cancer	X - adults	X - adults per NCCN	---
PNET (pancreas)	X - adults	X - adults per NCCN	---
NET (GI, lung, [thymic-off-label])	X - adults	X - adults per NCCN	---
RCC	X - adults	X - adults per NCCN	---
TSC-AML (renal)	X - adults	X - adults per NCCN	---
TSC-SEGA	X - 1 year and older	X - 1 year and older	---
TSC-seizures	---	X - 2 years and older	---
Prophylaxis of organ rejection	---	---	X - adults
<i>Recommended NCCN uses (adults)</i>			
Meningioma	X	X	---
HL	X	X	---
STS-GIST	X	X	---
STS-PEComa, angiomyolipoma, lymphangiomyomatosis	X	X	---
Thymoma/thymic carcinoma	X	X	---
DTC	X	X	---
WM/LPL	X	X	---
Endometrial carcinoma	X	X	---
Histiocytic neoplasms	X	X	---

*Abbreviations: DTC (differentiated thyroid carcinoma), GI (gastrointestinal), HL (Hodgkin lymphoma), PNET (pancreatic neuroendocrine tumor), NET (neuroendocrine tumors), RCC (renal cell carcinoma), STS-GIST (soft tissue sarcoma-gastrointestinal stromal tumor), STS-PEComa (soft tissue sarcoma-perivascular epithelioid cell tumor), TSC-AML (tuberous sclerosis complex- angiomyolipoma), TSC-SEGA (tuberous sclerosis complex-subependymal giant cell astrocytoma), TSC-seizures (tuberous sclerosis complex-seizures). WM/LPL (Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma)*

Afinitor is indicated for the treatment of:

- Postmenopausal women with advanced hormone receptor (HR)-positive, human epidermal growth factor receptor-2 (HER2)-negative breast cancer (advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole or anastrozole.
- Adult patients with progressive neuroendocrine tumors of pancreatic origin (PNET) and adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic.\*
- Adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.
- Adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.

Afinitor and Afinitor Disperz are indicated for the treatment of adult and pediatric patients aged 1 year and older with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

Afinitor Disperz is indicated for the adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.

Zortress is indicated for the prophylaxis of organ rejection in adult patients:†

- Kidney transplant: at low-moderate immunologic risk. Use in combination with basiliximab, cyclosporine (reduced doses) and corticosteroids.
- Liver transplant: administer no earlier than 30 days post-transplant. Use in combination with tacrolimus (reduced doses) and corticosteroids.

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\* *Limitation(s) of use: Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.*

† *Limitation(s) of use: Safety and efficacy of Zortress have not been established in the following:*

- *Kidney transplant patients at high immunologic risk*
- *Recipients of transplanted organs other than kidney or liver*
- *Pediatric patients (less than 18 years)*

### **Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that everolimus are **medically necessary** when the following criteria are met:

#### **I. Initial Approval Criteria**

##### **A. Breast Cancer (must meet all):**

1. Request is for Afinitor or Afinitor Disperz;
2. Diagnosis of recurrent or metastatic breast cancer;
3. Prescribed by or in consultation with an oncologist;
4. Age  $\geq$  18 years;

5. Disease is HR-positive and HER2-negative;
6. History of endocrine therapy (*see Appendix B*) unless contraindicated or clinically significant adverse effects are experienced;
7. For Afinitor or Afinitor Disperz requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Prescribed in combination with exemestane, fulvestrant or tamoxifen;
9. Request meets one of the following (a or b):\*
  - a. Dose does not exceed all of the following (i, ii, and iii):
    - i. 20 mg per day;
    - ii. Afinitor: 2 tablets per day;
    - iii. Afinitor Disperz: 4 tablets per day;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

\*Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval duration:**

**Medicaid** – 6 months

**HIM** – 6 months (*refer to HIM.PA.103 for Afinitor Disperz*)

**Commercial** – 12 months or duration of request, whichever is less

**B. Neuroendocrine Tumor** (must meet all):

1. Request is for Afinitor or Afinitor Disperz;
2. Diagnosis of NET of one of the following origins (a, b, c, d, or e):
  - a. Pancreatic;
  - b. GI tract;
  - c. Lung;
  - d. Bronchopulmonary (off-label);
  - e. Thymus (off-label);
3. Disease is unresectable, locally advanced or metastatic;
4. Prescribed by or in consultation with an oncologist;
5. Age  $\geq$  18 years;
6. For Afinitor or Afinitor Disperz requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed all of the following (i, ii, and iii):
    - i. 20 mg per day;
    - ii. Afinitor: 2 tablets per day;
    - iii. Afinitor Disperz: 4 tablets per day;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

\*Prescribed regimen must be FDA-approved or recommended by NCCN

**Approval duration:**

**Medicaid** – 6 months

**HIM** – 6 months (*refer to HIM.PA.103 for Afinitor Disperz*)

**Commercial** – 12 months or duration of request, whichever is less

**C. Renal Cell Carcinoma (must meet all):**

1. Request is for Afinitor or Afinitor Disperz;
2. Diagnosis of relapsed or stage IV (unresectable or metastatic) RCC;
3. Prescribed by or in consultation with an oncologist;
4. Age  $\geq$  18 years;
5. For Afinitor or Afinitor Disperz requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. If clear cell histology, failure of a prior therapy (*see Appendix B*) unless contraindicated or clinically significant adverse effects are experienced;  
*\*Prior authorization may be required for prior therapies*
7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed all of the following (i, ii, and iii):
    - i. 20 mg per day;
    - ii. Afinitor: 2 tablets per day;
    - iii. Afinitor Disperz: 4 tablets per day;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).  
*\*Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration:**

**Medicaid** – 6 months

**HIM** – 6 months (*refer to HIM.PA.103 for Afinitor Disperz*)

**Commercial** – 12 months or duration of request, whichever is less

**D. Renal Angiomyolipoma with Tuberous Sclerosis Complex (must meet all):**

1. Request is for Afinitor or Afinitor Disperz;
2. Diagnosis of renal angiomyolipoma associated with TSC, not requiring immediate surgery;
3. Prescribed by or in consultation with an oncologist;
4. Age  $\geq$  18 years;
5. For Afinitor or Afinitor Disperz requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):\*
  - a. Dose does not exceed all of the following (i, ii, and iii):
    - i. 20 mg per day;
    - ii. Afinitor: 2 tablets per day;
    - iii. Afinitor Disperz: 4 tablets per day;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).  
*\*Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration:**

**Medicaid** – 6 months

**HIM** – 6 months (*refer to HIM.PA.103 for Afinitor Disperz*)

**Commercial** – 12 months or duration of request, whichever is less

**E. Tuberous Sclerosis Complex with Subependymal Giant Cell Astrocytoma (must meet all):**

1. Request is for Afinitor or Afinitor Disperz;
2. Diagnosis of SEGA associated with TSC;
3. Prescribed by or in consultation with an oncologist;
4. Age  $\geq$  1 year;
5. Member is not a candidate for curative surgical resection.
6. For Afinitor or Afinitor Disperz requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced;

**Approval duration:**

**Medicaid** – 6 months

**HIM** – 6 months (*refer to HIM.PA.103 for Afinitor Disperz*)

**Commercial** – 12 months or duration of request, whichever is less

**F. Tuberous Sclerosis Complex-Associated Partial-Onset Seizures (must meet all):**

1. Request is for Afinitor Disperz;
2. Diagnosis of partial-onset seizures associated with TSC;
3. Prescribed by or in consultation with an oncologist or neurologist;
4. Age  $\geq$  2 years;
5. Afinitor Disperz will be used as adjunctive therapy;
6. For Afinitor Disperz requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced.

**Approval duration:**

**Medicaid** – 6 months

**HIM** – *refer to HIM.PA.103*

**Commercial** – 12 months or duration of request, whichever is less

**G. Prophylaxis of Organ Rejection (must meet all):**

1. Request is for Zortress;
2. Member has received or is scheduled for a kidney or liver transplant;
3. Prescribed by or in consultation with a nephrologist, hepatologist, or transplant specialist;
4. Age  $\geq$  18 years;
5. For kidney transplant, failure of tacrolimus unless contraindicated or clinically significant adverse effects are experienced;
6. For Zortress requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Prescribed in combination with one of the following (a or b):
  - a. For kidney transplant: Simulect<sup>®</sup>, cyclosporine, and corticosteroids;
  - b. For liver transplant: tacrolimus and corticosteroids.

**Approval duration:**

**Medicaid/HIM** – 6 months

**Commercial** – 12 months or duration of request, whichever is less

**H. NCCN Compendium Indications (off-label) (must meet all):**

1. Request is for Afinitor or Afinitor Disperz;
2. Diagnosis of one of the following (a, b, c, or d):
  - a. Afinitor or Afinitor Disperz is prescribed as single-agent therapy:
    - i. HL, WM/LPL, thymoma, or thymic carcinoma (refractory, recurrent, progressive, unresectable, or metastatic disease, or disease not responding to previous therapy);
    - ii. PEComa, recurrent angiomyolipoma, or lymphangiomyomatosis;
    - iii. Histiocytic neoplasms (i.e., Erdheim-Chester disease, Langerhans cell histiocytosis, Rosai-Dorfman disease)
  - b. Endometrial carcinoma, prescribed in combination with letrozole;
  - c. GIST, prescribed in combination with imatinib, Sutent<sup>®</sup>, or Stivarga<sup>®</sup> for disease progression after therapy with imatinib, Sutent, and Stivarga;\*
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. For Afinitor or Afinitor Disperz requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).\*

*\*Prior authorization may be required for imatinib, Sutent, and Stivarga*  
*\*Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration:**

**Medicaid** – 6 months

**HIM** – 6 months (*refer to HIM.PA.103 for Afinitor Disperz*)

**Commercial** – 12 months or duration of request, whichever is less

**I. Other diagnoses/indications (must meet 1 or 2):**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

### A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Afinitor, Afinitor Disperz, or Zortress for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Afinitor, Afinitor Disperz, Zortress requests, member must use generic everolimus, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. For all indications, except partial-onset seizures associated with TSC, SEGA associated with TSC, and organ rejection prophylaxis, if request is for a dose increase, request meets one of the following (a or b):\*
  - a. New dose does not exceed all of the following (i, ii, and iii):
    - i. 20 mg per day;
    - ii. Afinitor: 2 tablets per day;
    - iii. Afinitor Disperz: 4 tablets per day;
  - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

\*Prescribed regimen must be FDA-approved or recommended by NCCN.

### Approval duration:

**Medicaid** – 12 months

**HIM** – 12 months (*refer to HIM.PA.103 for Afinitor Disperz*)

**Commercial** – 12 months or duration of request, whichever is less

### B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

AML: angiomyolipoma	PEComa: perivascular epithelioid cell tumor
ER: estrogen receptor	PNET: pancreatic neuroendocrine tumor
DTC: differentiated thyroid cancer	RCC: renal cell carcinoma
FDA: Food and Drug Administration	SEGA: subependymal giant cell astrocytoma
GI: gastrointestinal	STS: soft tissue sarcoma
GIST: gastrointestinal stromal tumor	TSC: tuberous sclerosis complex
HER-2: human epidermal growth factor receptor-2	WM/LPL: Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma
HL: Hodgkin lymphoma	
HR: hormone receptor	
NET: neuroendocrine tumor	

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
<i>Breast cancer: Examples of endocrine therapies per NCCN</i>		
<ul style="list-style-type: none"> <li>• Nonsteroidal aromatase inhibitors (anastrozole and letrozole);</li> <li>• Steroidal aromatase inhibitors (exemestane)</li> <li>• Serum estrogen receptor (ER) modulators (tamoxifen, toremifene)</li> <li>• ER down-regulators (fulvestrant)</li> <li>• Progestin (megestrol acetate)</li> <li>• Androgens (flouxymesterone)</li> <li>• High-dose estrogen (ethinyl estradiol)</li> </ul>	Varies	Varies
<i>RCC: Examples of first and second-line therapies for relapsed or stage IV disease with clear cell histology per NCCN</i>		
<ul style="list-style-type: none"> <li>• Votrient<sup>®</sup> (pazopanib)</li> <li>• Sutent<sup>®</sup> (sunitinib)</li> <li>• Opdivo<sup>®</sup> (nivolumab) ± Yervoy<sup>®</sup> (ipilimumab)</li> <li>• Proleukin<sup>®</sup> (aldesleukin)</li> <li>• Cabometyx<sup>®</sup> (cabozantinib)</li> <li>• Torisel<sup>®</sup> (temsirolimus)</li> <li>• Inlyta<sup>®</sup> (axitinib)</li> <li>• Afinitor/Afinitor Disperz (everolimus) ± Lenvima (lenvatinib)</li> <li>• Nexavar (sorafenib)</li> </ul>	Varies	Varies



Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• Tarceva <sup>®</sup> (erlotinib)		
<i>GIST</i>		
imatinib (Gleevec <sup>®</sup> )	400 mg PO QD or BID	800 mg/day
Sutent (sunitinib)	50 mg PO QD	50 mg/day
Stivarga (regorafenib)	160 mg PO QD	160 mg/day
<i>DTC</i>		
Lenvima (lenvatinib)	24 mg PO QD	24 mg/day
Nexavar (sorafenib)	400 mg PO QD	400 mg/day

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Afinitor and Afinitor Disperz: clinically significant hypersensitivity to everolimus or to other rapamycin derivatives
  - Zortress: known hypersensitivity to everolimus, sirolimus, or to components of the drug product
- Boxed warning(s) for Zortress: malignancies and serious infections, kidney graft thrombosis, nephrotoxicity, and mortality in heart transplantation when used in de novo patients within the first three months post-transplantation

*Appendix D: General Information*

- Heart transplant: Although the off-label use of Zortress in heart transplant is not supported by the Micromedex DrugDex compendium, it does have both literature and guideline support. Individual risk-benefit ratios must be considered prior to such use because of safety concerns (see Appendix C – boxed warnings). Examples of patient-specific scenarios where use may be appropriate include, but are not limited to: patient already established on therapy, refractory or recurrent rejection, renal insufficiency, cardiac allograft vasculopathy (CAV), history of malignancies, calcineurin inhibitor (CNI) toxicity.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Breast cancer, PNET (pancreas), NET (GI, lung), RCC, TSC-AML (renal)	Afinitor 10 mg PO QD	20 mg/day
TSA-SEGA	Afinitor/Afinitor Disperz 4.5 mg/m <sup>2</sup> PO QD; adjust dose to attain trough concentrations of 5-15 ng/mL	Based on trough concentrations
TSC-associated partial-onset seizures	Afinitor Disperz 5 mg/m <sup>2</sup> PO QD; adjust dose to attain trough concentrations of 5-15 ng/mL	
Kidney transplant rejection prophylaxis	Zortress	

Indication	Dosing Regimen	Maximum Dose
	0.75 mg PO BID; adjust dose to attain trough concentrations of 3 to 8 ng/mL	
Liver transplant rejection prophylaxis	Zortress 1 mg PO BID; adjust dose to attain trough concentrations of 3 to 8 ng/mL	

## VI. Product Availability

Drug Name	Availability
Everolimus (Afinitor)	Tablets: 2.5 mg, 5 mg, 7.5 mg, 10 mg
Everolimus (Afinitor Disperz)	Tablets for oral suspension: 2 mg, 3 mg, 5 mg
Everolimus (Zortress)	Tablets: 0.25 mg, 0.5 mg, 0.75 mg, 1 mg

## VII. References

1. Afinitor/Afinitor Disperz Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2022. Available at: <https://www.novartis.us/sites/www.novartis.us/files/afinitor.pdf>. Accessed October 16, 2023.
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3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed November 15, 2023.
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### Kidney and Liver Transplantation

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10. Breda A, Budde K, Figueiredo KA, et al. Renal Transplantation Guidelines 2019. European Association of Urology (EAU). Available at: <http://www.uroweb.org/guideline/renal-transplantation/>.

11. Lucey MR, Terrault N, Ojo L, et al. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver Transplantation* 2013;19:3-26.
12. Costanzo MR, Dipchand A, Ross H, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *Journal of Heart and Lung Transplantation*. 2020; 29(8): 914-956.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7527	Everolimus, oral, 0.25mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: added new dosage form of Zortress 1 mg.	06.21.19	
1Q 2020 annual review: TSC association seizures - neurologist added; meningioma removed NCCN 2B; NET bronchopulmonary disease added NCCN 2A; specified max dose requirement in continued therapy applies to all diagnoses except partial-onset seizures associated with TSC and organ rejection prophylaxis; references reviewed and updated.	11.19.19	02.20
Added Appendix D with information regarding off-label use of Zortress in heart transplant; updated Appendix C to clarify Zortress’s boxed warning in heart transplant.	07.01.20	
1Q 2021 annual review: oral oncology generic redirection language added; for HL, WM//LPL, thymoma, or thymic carcinoma, unresectable or disease not responding to previous therapy added; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.14.20	02.21
1Q 2022 annual review: added histiocytic neoplasms indication per NCCN; added legacy WellCare auth durations (WCG.CP.PHAR.63 to retire); clarified oral oncology generic redirection language to “must use”; references reviewed and updated.	11.13.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
Template changes applied to other diagnoses/indications.	10.12.22	
1Q 2023 annual review: added age requirement for TSA-SEGA and TSC-seizures; For TSC-seizures, added Afinitor Disperz will be used as adjunctive therapy per PI; Legacy WellCare approval durations consolidated to 6 months; references reviewed updated.	11.11.22	02.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
COC applied to Zortress in continued therapy section II.A.	07.10.23	
1Q 2024 annual review: clarified oral oncology redirection language to “generic” everolimus; for DTC, removed requirement of prior therapy per NCCN; for HL, WM/LPL, thymoma, thymic carcinoma, histiocytic neoplasms, PEComa, recurrent angiomyolipoma, and lymphangiomyomatosis, added prescribed as single agent per NCCN; references reviewed and updated.	10.16.23	02.24

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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