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

Reference Number: CP.PHAR.63
Effective Date: 06.01.11
Last Review Date: 11.18 Coding Implications
Line of Business: Commercial, HIM*, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Everolimus (Afinitor®, Afinitor Disperz®, Zortress®) is an mTOR kinase inhibitor.

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

FDA Approved Indication(s)

Afinitor is indicated for the treatment of:

- Adult patients with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.
- 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 renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.
- 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.

Afinitor and Afinitor Disperz are indicated for the treatment of pediatric and adult patients 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.

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

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.

Limitaiton(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® that Afinitor, Afinitor Disperz, and Zortress are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of breast cancer;
2. Request is for Afinitor;
3. Prescribed by or in consultation with an oncologist;
4. Disease is HR-positive and HER2-negative;
5. Disease is recurrent or metastatic;
6. Failure of a nonsteroidal aromatase inhibitor (e.g., anastrozole or letrozole) at up to maximally indicated doses. unless contraindicated or clinically significant adverse effects are experienced;
7. Prescribed in combination with exemestane;
8. Dose does not exceed 10 mg/day (1 tablet/day).

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

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

1. Diagnosis of NET of one of the following origins (a – d):
   a. Pancreatic;
   b. GI tract;
   c. Lung;
   d. Thymus (off-label);
2. Request is for Afinitor;
3. Prescribed by or in consultation with an oncologist;
4. Disease is unresectable, locally advanced or metastatic;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/day (1 tablet/day);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

C. Prophylaxis of Organ Rejection (must meet all):

1. Member has received or is scheduled for a kidney or liver transplant;
2. Request is for Zortress;

3. Prescribed by or in consultation with a nephrologist, hepatologist, or transplant specialist;
4. Age ≥ 18 years;
5. For kidney transplant, failure of tacrolimus unless contraindicated or clinically significant adverse effects are experienced;
6. Prescribed in combination with one of the following (a or b):
   a. For kidney transplant: Simulect®, cyclosporine, and corticosteroids;
   b. For liver transplant: tacrolimus and corticosteroids.

Approval duration: 6 months

D. Renal Cell Carcinoma (must meet all):
1. Diagnosis of advanced (relapsed or surgically unresectable stage IV disease) RCC;
2. Request is for Afinitor;
3. Prescribed by or in consultation with an oncologist;
4. Meets one of the following (a or b):
   a. For RCC with predominant clear cell histology both of the following (i and ii):
      i. Failure of one of the following, unless contraindicated or clinically significant adverse effects are experienced: Sutent®, Votrient®, Inlyta®, Avastin® in combination with Intron®-A, Proleukin®, Cabometyx®, or Torisel®;
      ii. Failure of a trial of Opdivo® or Cabometyx® (if not previously used as first-line therapy), unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for all of the above agents*
   b. RCC with non-clear cell histology (off-label);
5. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/day (1 tablet/day);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

E. Renal Angiomyolipoma with Tuberous Sclerosis Complex (must meet all)**:**
1. Diagnosis of renal angiomyolipoma and TSC, not requiring immediate surgery;
2. Request is for Afinitor;
3. Prescribed by or in consultation with an oncologist;
4. Dose does not exceed 10 mg/day (1 tablet/day).

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

F. Tuberous Sclerosis Complex with Subependymal Giant Cell Astrocytoma (must meet all)**:**
1. Diagnosis of SEGA associated with tuberous sclerosis;
2. Request is for Afinitor or Afinitor Disperz;
3. Prescribed by or in consultation with an oncologist;

4. Member is not a candidate for curative surgical resection;
5. Dose does not exceed 10 mg/day (1 tablet/day).

Approval duration:
Medicaid – 6 months
HIM – 6 months Afinitor (*refer to HIM.PA.103 for Afinitor Disperz*)
Commercial – Length of Benefit

G. Tuberous Sclerosis Complex-Associated Partial-Onset Seizures (must meet all):
1. Diagnosis of tuberous sclerosis complex-associated partial-onset seizures;
2. Request is for Afinitor Disperz;
3. Prescribed by or in consultation with an oncologist.

Approval duration:

Medicaid – 6 months
HIM – Not applicable (*refer to HIM.PA.103 for Afinitor Disperz*)
Commercial – Length of Benefit

H. NCCN Compendium Indications (off-label) (must meet all)**:**
1. Confirmed diagnosis of one of the following (a – g):
   a. Hodgkin Lymphoma;
   b. Soft Tissue Sarcoma (i or ii):
      i. Gastrointestinal Stromal Tumors (GIST): Prescribed in combination with either imatinib, Sutent®, or Stivarga® for disease progression after single-agent therapy with imatinib, Sutent, and Stivarga;
      **Prior authorization may be required for these agents*
      ii. PEComa/recurrent angiomyolipoma/lymphangioleiomyomatosis;
   c. Thymomas and thymic Carcinomas (second line therapy as a single agent);
   d. Thyroid carcinoma – follicular carcinoma, Hurthle cell carcinoma, papillary carcinoma;
   e. Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma (for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease);
   f. Osteosarcoma (second-line in combination with Nexavar®);
   g. Endometrial carcinoma (in combination with letrozole);
2. Prescribed by or in consultation with an oncologist;
3. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/day (1 tablet/day);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid – 6 months
HIM – 6 months Afinitor (*refer to HIM.PA.103 for Afinitor Disperz*)
Commercial – Length of Benefit

I. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following:
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Afinitor or Afinitor Disperz for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase of Afinitor or Afinitor Disperz, request meets one of the following (a or b):
   a. New dose does not exceed 10 mg/day (1 tablet/day);
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid – 12 months
HIM – 6 months Afinitor (*refer to HIM.PA.103 for Afinitor Disperz*)
Commercial – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial 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 and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: angiomyolipoma
FDA: Food and Drug Administration
GI: gastrointestinal
GIST: gastrointestinal stromal tumor
HER-2: human epidermal growth factor receptor-2
HR: hormone receptor
NCCN: National Comprehensive Cancer Network
NET: neuroendocrine tumors
PEComa: perivascular epithelioid cell tumor
PNET: progressive neuroendocrine tumors

RCC: renal cell carcinoma
SEGA: subepndymal giant cell astrocytoma
TSC: tuberous sclerosis complex

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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
letrozole (Femara®)	**Breast Cancer** 2.5 mg PO QD	2.5 mg/day
anastrozole (Arimidex®)	**Breast Cancer** 1 mg PO QD	1 mg/day
Sutent® (sunitinib)	**Advanced RCC** 50 mg PO QD for 4 weeks followed by 2 weeks off. **Advanced PNET** 37.5 mg PO QD Dose increase or reduction of 12.5 mg increments is recommended based on individual safety and tolerability.	Advanced RCC: 87.5 mg/day Advanced PNET: 62.5 mg/day Treatment continues until no longer clinically beneficial or unacceptable toxicity occurs.
Votrient® (pazopanib)	**Advanced RCC** 800 mg PO QD	Advanced RCC: 800 mg/day Treatment continues until no longer clinically beneficial or until unacceptable toxicity occurs.
Inlyta® (axitinib)	**Advanced RCC** 5 mg PO BID	Advanced RCC: 10 mg PO BID Treatment continues until no longer clinically beneficial or unacceptable toxicity occurs.
Torisel® (temsirolimus)	**Advanced RCC** 25 mg IV infused over 30-60 minutes once a week.	Advanced RCC: 50 mg/week Treatment continues until no longer clinically beneficial or unacceptable toxicity occurs.
Avastin®	**Advanced RCC** 10 mg/kg IV infused over 60-90 minutes every 2 weeks in combination with	Advanced RCC: 15 mg/kg every 3 weeks or 10 mg/kg every 2

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(bevacizumab) in combination with Intron A® (interferon alfa-2b)	interferon alfa 3 million IU SC/IM 5 times per week up to 36 million IU SC/IM 3 times per week	weeks in combination with interferon alfa 20 million IU/m^2/day IV; 35 million IU/m^2/dose SC/IM
Proleukin® (aldesleukin, rIL-2)	**Advanced RCC** 600,000 IU/kg IV Q8 hrs for 14 doses, repeat after a rest period of 9 days	Advanced RCC: 600,000 IU/kg IV Q8 hrs; 18 million IU/m^2/day IV has been used off-label for RCC
Cabometyx® (cabozantinib)	**Advanced RCC** 60 mg PO QD	Advanced RCC: 80 mg/day
Opdivo® (nivolumab)	**Advanced RCC** 240 mg IV every 2 weeks	Advanced RCC: 240 mg IV every 2 weeks
Simulect® (basiliximab)	**Kidney transplant rejection prophylaxis** 20 mg IV within 2 hours prior to transplantation surgery, followed by 20 mg IV 4 days after transplantation	20 mg/dose
tacrolimus (Prograf®)	**Liver transplant rejection prophylaxis** 0.1 to 0.15 mg/kg/day PO in 2 divided doses q12h	varies based on trough concentrations
cyclosporine (Sandimmune®)	**Kidney transplant rejection prophylaxis** 15 mg/kg PO as a single dose 4 to 12 hours before transplantation	varies based on trough concentrations
corticosteroids	**Kidney or liver transplant rejection prophylaxis** varies	varies

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

Appendix C: Contraindications/Boxed Warnings

- Afinitor and Afinitor Disperz are contraindicated in patients with clinically significant hypersensitivity to everolimus or to other rapamycin derivatives.
- Zortress is contraindicated in patients with known hypersensitivity to everolimus, sirolimus, or to components of the drug product.
- Boxed warning(s) for Zortress: malignancies and serious infections, kidney graft thrombosis, nephrotoxicitym and mortality in heart transplantation.

Appendix D: General Information

- Advanced renal cell carcinoma includes relapsed disease or Stage IV and medically or surgically unresectable disease.

- Use in metastatic breast cancer in combination with Aromasin (a steroidal aromatase inactivator) after failure of a nonsteroidal aromatase inhibitor (such as Arimidex or Femara) is a category 2A recommendation per NCCN compendium.
- Hodgkin Lymphoma, Soft Tissue Sarcoma - Gastrointestinal Stromal Tumors (GIST), PEComa/Recurrent Angiomyolipoma/Lymphangioleiomyomatosis, Thymomas and Thymic Carcinomas (second line therapy as a single agent), Waldenstrom's Macroglobulinemia/Lymphoplasmacytic lymphoma (for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease), Osteosarcoma (second-line in combination with sorafenib), and Endometrial carcinoma (in combination with letrozole) are category 2A recommendations per NCCN compendium.
- NCCN recommends patients should receive Opdivo (nivolumab) and Cabometyx (cabozantinib) over Afinitor for subsequent therapy in renal cell carcinoma, predominant clear cell histology as clinical trial evidence demonstrated increased overall survival (OS) over Afinitor (median OS 21.4 vs. 16.5 months [Cabometyx vs Afinitor, HR. 0.66; 95% CI, 0.53, 0.83]; 25.0 vs 19.6 months [Opdivo vs. Afinitor, HR 0.73, p=0.002]).
- The Symphony Study, a large multicenter clinical trial, showed that the combination of low-dose tracolimus, mycophenolate mofetil, and steroids with daclizumab induction provided superior efficacy without the negative impact on renal function compared with cyclosporine or a calcineurin inhibitor-free regimen of low-dose sirolimus. The KDOQI US commentary on the 2009 KDIGO guidelines state that sirolimus and everolimus delay wound healing, prolong delayed graft function, and are no longer used in the early posttransplant period.

V. Dosage and Administration

Drug Nam	Indication	Dosing Regimen	Maximum Dose
Afinitor	PNET, NET, RCC, breast cancer, renal angiomyolipoma, Hodgkins lymphoma, soft tissue sarcoma, thymomas and thymic carcinomas, Waldenstrom's macroglobulinemia/ lymphoplasmacytic lymphoma, osteosarcoma, endometrial carcinoma	10 mg PO QD If strong inducers of CYP3A4 are required, increase dose in 5 mg increments to a maximum of 20 mg PO QD.	20 mg/day
Afinitor, Afinitor Disperz	TSA-SEGA	4.5 mg/m^2 PO QD; adjust dose to attain trough concentrations of 5-15 ng/mL	Based on trough concentrations

Drug Nam	Indication	Dosing Regimen	Maximum Dose
		If strong inducers of CYP3A4 are required, double the Afinitor dose.	
Afinitor Disperz	TSC-associated partial-onset seizures	5 mg/m^2 PO QD; adjust dose to attain trough concentrations of 5 to 15 ng/mL	Based on trough concentrations
Zortress	Kidney transplant rejection prophylaxis	0.75 mg PO BID; adjust dose to attain trough concentrations of 3 to 8 ng/mL	Based on trough concentrations
Zortress	Liver transplant rejection prophylaxis	1 mg PO BID; adjust dose to attain trough concentrations of 3 to 8 ng/mL	Based on trough concentrations

VI. Product Availability

Drug Name	Availability
Everolimus (Afinitor)	Tablets: 2.5 mg, 5 mg, 7.5 mg and 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

VII. References

1. Afinitor Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2018. Available at: https://www.pharma.us.novartis.com/files/afinitor.pdf. Accessed April 12, 2018.
2. Zortress Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2018. Available at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/zortress.pdf. Accessed August 16, 2018.
3. National Comprehensive Cancer Network. Kidney Cancer Version 1.2018. Available at: http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed November 9, 2017.
4. National Comprehensive Cancer Network. Neuroendocrine Tumors Version 3.2017. Available at: http://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed November 9, 2017.
5. National Comprehensive Cancer Network. Breast Cancer Version 2.2017. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November, 9, 2017.
6. Everolimus. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 9, 2017.
7. Yao, JC, Fazio N, Singh S, et al. Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised,

placebo-controlled, phase 3 study. Lancet. 2015 Dec 15. pii: S0140-6736(15)00817-X. doi: 10.1016/S0140-6736(15)00817-X. [Epub ahead of print].
8. Kidney Disease Improving Global Outcomes. KDIGO clinical practice guideline for the care of kidney transplant recipients. American Journal of Transplantation 2009; 9 (Suppl 3): Si-S155. doi: 10.1111/j.1600-6143.2009.02834.x
9. Bia M, Adey DB, Bloon RD, Chan L, Kulkarni S, and Tomlanovich S. KDOQI US Commentary on the 2009 KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Kidneys Dis 2010;56:189-218.
10. 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.

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
Added efficacy data; corrected algorithm to match FDA indication for MBC, PNET, and SEGA. Removed Votrient from RCC failure question.	06.14	07.14
Edited FDA indications Edited algorithm to include both Afinitor and Afinitor Disperz, and the pediatric population for SEGA. Also changed initial approval periods from 6 months to 3 months for initial auths. Edited background & safety	05.15	05.15
Policy converted to new template; Added maximum dose and contraindications per PI; For breast cancer: added definition for advanced breast cancer; added that Afinitor may be used in after previous treatment with tamoxifen to comply with NCCN recommendation for use; For RCC, added definition for advanced RCC References updated	04.16	05.16
NCCN and FDA uses separated in criteria sets; dosing removed if NCCN uses added. NET: "Non-functional" designation removed for NET of GI and lung origin; the term "locally advanced" is incorporated into recurrent, unresectable or metastatic. RCC: The term "advanced" RCC is restated as recurrent, unresectable or metastatic. The term "unless contraindicated" is removed from "failed sunitinib	04.17	05.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
or sorafenib treatment." Safety information removed. Approval durations lengthened to 6 and 12 months.		
Added thyroid carcinoma as an NCCN compendium supported use.	06.14.17	11.17
1Q18 annual review: Combined Medicaid and Commercial policies; removed dose form requirement by indication, no clinical difference expected (dosing is equivalent for SEGA indication); for RCC, included list of first line therapies per NCCN guidelines; for breast cancer, removed compendium supported use after tamoxifen as this was removed from the 1.2017 NCCN guideline update; added the following off-label NCCN compendium supported uses: GIST, lymphoplasmacytic lymphoma, osteosarcoma, endometrial carcinoma; references reviewed and updated.	11.09.17	02.18
Criteria added for new FDA indication: TSC-associated partial-onset seizures; references reviewed and updated.	05.22.18	08.18
Zortress added to the policy; added HIM line of business; added that requested agent is for each FDA-approved agent for that indication; references reviewed and updated.	09.04.18	11.18

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.