# Clinical Policy: Sacubitril/Valsartan (Entresto)

Reference Number: CP.PMN.67
Effective Date: 11.01.15
Last Review Date: 02.18
Line of Business: Commercial, Health Insurance Marketplace, Medicaid Revision Log

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

## Description

Sacubitril/valsartan (Entresto®) is a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin II receptor blocker (ARB).

## FDA Approved Indication(s)

Entresto is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (New York Heart Association [NYHA] Class II-IV) and reduced ejection fraction.

Entresto is usually administered in conjunction with other heart failure therapies, in place of an angiotensin-converting enzyme (ACE) inhibitor or other ARB.

## Policy/Criteria

*Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria*

It is the policy of health plans affiliated with Centene Corporation® that Entresto is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Heart Failure** (must meet all)**:**

1. Diagnosis of chronic heart failure of NYHA Class II, III, or IV;
2. Prescribed by or in consultation with a cardiologist;
3. Age ≥ 18 years;
4. Left ventricular ejection fraction (LVEF) is ≤ 35%;
5. At the time of request, member has none of the following contraindications:
   a. Concomitant use with ACE inhibitors;
   b. If member has a diagnosis of diabetes, concomitant use with aliskiren;
6. Dose does not exceed sacubitril/valsartan 97/103 mg twice daily (2 tablets per day).

**Approval duration:**
**Medicaid/Health Insurance Marketplace –** 12 months
**Commercial –** Length of Benefit

**B. 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, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

**A. Heart Failure** (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Entresto for heart failure 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, new dose does not exceed sacubitril/valsartan 97/103 mg twice daily (2 tablets per day).

**Approval duration:**
**Medicaid/Health Insurance Marketplace –** 12 months
**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 12 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, HIM.PHAR.21 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.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

ACE: angiotensin-converting enzyme
ARB: angiotensin II receptor blocker
FDA: Food and Drug Administration
NYHA: New York Heart Association

*Appendix B: Therapeutic Alternatives*

N/A

*Appendix C: General Information*

- Concomitant use of Entresto with an ACE inhibitor is contraindicated because of the increased risk of angioedema
- Concomitant use of Entresto and ARB should be avoided since Entresto contains an ARB.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Heart failure | The recommended starting dose is 49/51 mg (sacubitril/valsartan) PO BID. Double the dose after 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) BID, as tolerated by the patient.<br><br>Therapy may be initiated at 24/26 mg (sacubitril/valsartan) PO BID for:<br>• patients not currently taking an ACE inhibitor or an ARB or previously taking a low dose of these agents<br>• patients with severe renal impairment<br>• patients with moderate hepatic impairment<br>Double the dose every 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) BID, as tolerated by the patient. | 97/103 mg BID (sacubitril/valsartan) |

## VI. Product Availability

Film-coated tablets (sacubitril/valsartan): 24/26 mg, 49/51 mg, 97/103 mg

## VII. References

1. Entresto Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2015. Available at: https://www.entrestohcp.com/. Accessed November 1, 2017.
2. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Colvin MM, Drazner MH, Filippatos GS, Fonarow GC, Givertz MM, Hollenberg SM, Lindenfeld J, Masoudi FA,
3. McBride PE, Peterson PN, Stevenson LW, Westlake C. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology /American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Am Coll Cardiol. 2017.
4. Yancy CW, Jessup M, Bozkurt B, Butler J,Casey DE Jr, Colvin MM, Drazner MH, Filippatos G, Fonarow GC, Givertz MM, Hollenberg SM, Lindenfeld J, Masoudi FA,McBride PE, Peterson PN, Stevenson LW, Westlake C. 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2016;134: 000-000.
5. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation. 2013 Oct 15;128(16):e240-327.
6. McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014;371:993-1004.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| New guideline created | 09.15 | 11.15 |
| Converted to new integrated template.<br>Removed age requirement since not referenced in indications section in PI.<br>Modified specific max quantity limit to FDA max recommended dose and health plan approved QL statement.<br>Increased initial approval duration to 12 months.<br>Removed "For renewal request below the target dose of sacubitril/valsartan 97/103mg twice daily, provider must provide a clinical rationale for continued treatment at a sub-therapeutic dose" as dose is dependent on patient tolerability per PI and provider's clinical judgment.<br>Updated continuation criteria to include continuity of care<br>Updated references to reflect current literature search | 08.16 | 11.16 |
| Converted to new template. Added age restriction and contraindications related to DDI per PI/safety approach. Modified max dose requirement to include specific quantity limit. Updated references. | 08.07.17 | 11.17 |
| 1Q18 annual review.<br>- Policies combined for Centene Medicaid, Marketplace and Commercial lines of business.<br>- No significant change from previous corporate approved policy.<br>- Commercial: added age restriction as safety and effectiveness in pediatric patients have not been established; modified LVEF from < 40% to ≤ 35% per PARADIGM-HF clinical trial; added contraindications related to DDI per PI; updated re-auth to allow COC for heart failure. Added requirement for positive response to therapy.<br>- Marketplace and Medicaid: added age restriction and contraindications related to DDI per PI (Marketplace only); removed "previously tolerated an ACEI or ARB at therapeutic doses for ≥ 30 days" since specialist is involved in care<br>- References reviewed and updated. | 11.01.17 | 02.18 |

**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.



**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.

**For Health Insurance Marketplace members**, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.