Clinical Policy: Sacubitril-Valsartan (Entresto)

Reference Number: PA.CP.PMN.67
Effective Date: 01/18
Last Review Date: 04/18

Coding Implications
Revision Log

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

FDA approved indication
- 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 (including office chart notes and lab results) supporting that member has met all approval criteria **

It is the policy of Pennsylvania Health and Wellness® 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 with NYHA Class II, III, or IV;
2. Age ≥ 18 years;
3. Left ventricular ejection fraction (LVEF) is ≤41%;
4. 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;
5. Request does not exceed sacubitril/valsartan 97 mg/103 mg twice daily, and health plan approved daily quantity limit.

Approval duration: 12 months

B. Other diagnoses/indications – Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. Heart Failure (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit, or documentation supports that member is currently receiving Entresto for heart failure, has received this medication, and is responding positively to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed sacubitril/valsartan 97 mg/103 mg twice daily and health plan approved daily quantity limit.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53 if requested indication is NOT listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

Approval duration: 12 months

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 policy – PA.CP.PMN.53 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation key
ACE: angiotensin-converting enzyme
ARB: angiotensin II receptor blocker
LVEF: left ventricular ejection fraction
NYHA: New York Heart Association

V. Dosage and administration

- The recommended starting dose of Entresto is 49/51 mg (sacubitril/valsartan) twice-daily. Double the dose of Entresto after 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) twice-daily, as tolerated by the patient.
- Reduce the starting dose to 24/26 mg (sacubitril/valsartan) twice-daily for:
  - patients not currently taking an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) or previously taking a low dose of these agents
  - patients with severe renal impairment
  - patients with moderate hepatic impairment

  Double the dose of Entresto every 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) twice-daily, as tolerated by the patient.

VI. Product Availability

Entresto is supplied as unscored, film-coated tablets (sacubitril/valsartan) in the following strengths: 24/26 mg; 49/51 mg; and 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 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.

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	Approval Date
2Q18 annual review: Removed prescriber requirement; 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 requirement for positive response to therapy;removed "previously tolerated an ACEI or ARB at therapeutic doses for ≥ 30 days"; references reviewed and updated.	03.04.18	