Clinical Policy Title:	sacubitril/valsartan
Policy Number:	RxA.368
Drug(s) Applied:	Entresto®
Original Policy Date:	03/06/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Sacubitril/valsartan (Entresto®) is a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin II receptor blocker (ARB). It 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. It is usually administered in conjunction with other heart failure therapies, in place of an angiotensin-converting enzyme (ACE) inhibitor or other ARB.
- For the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients one year of age and older. It reduces NT-proBNP and is expected to improve cardiovascular outcomes.

Dosing Information

Drug Name	Indication	Titration Step Dose (twice daily)		
		Starting	Second	Final
sacubitril/ valsartan (Entresto®)	Adult heart failure	49/51 mg	97/103 mg	
	Pediatric heart failure (Patients less than 40 kg)	1.6 mg/kg	2.3 mg/kg	3.1 mg/kg
	Pediatric heart failure (Patients at least 40 kg but less than 50 kg)	24/26 mg	49/51 mg	72/78 mg
	Pediatric heart failure (Patients 50 kg or more)	49/51 mg	72/78 mg	97/103 mg

- Adjust adult doses every 2 to 4 weeks and pediatric doses every 2 weeks to the target maintenance dose, as tolerated by the patient.
- Reduce starting dose to half the usually recommended starting dosage for:
  - Patients not currently taking an ACE inhibitor or ARB or previously taking a low dose of these agents;
  - Patients with severe renal impairment; and
  - Patients with moderate hepatic impairment.

Dosage Forms

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

Clinical Policy

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

I. Initial Approval Criteria

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

1. Member has a diagnosis of chronic heart failure of NYHA Class II, III, or IV;
2. Prescribed by or in consultation with a cardiologist or a provider with expertise in cardiac care;
3. Member is 1 year of age or older;
4. Member has a documented left ventricular ejection fraction (LVEF) of 40% or less;
5. At the time of request, member does not have the following contraindications:
   a. Concomitant use with ACE inhibitors; and
   b. If member has a diagnosis of diabetes, concomitant use with aliskiren;
6. Dose does not exceed sacubitril 194 mg/valsartan 206 mg (2 tablets) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (e.g., improvement in signs or symptoms of chronic heart failure);
3. If request is for a dose increase, new dose does not exceed sacubitril 194 mg/valsartan 206 mg (2 tablets) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ACE: Angiotensin Converting Enzyme
ARB: Angiotensin II Receptor Blocker
FDA: Food and Drug Administration
NYHA: New York Heart Association
LVEF: Left Ventricular Ejection Fraction

APPENDIX B: Therapeutic Alternatives
Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to any component;
  - History of angioedema related to previous ACE inhibitor or ARB therapy;
  - Concomitant use of sacubitril/valsartan with an ACE inhibitor; and
  - Concomitant use of sacubitril/valsartan with aliskiren in patients with diabetes.

- Boxed Warning(s):
  - When pregnancy is detected, discontinue sacubitril/valsartan as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

APPENDIX D: General Information

- Avoid concomitant use with aliskiren in patients with eGFR less than 60 mL/min/1.72 m^2.
- Use of potassium-sparing diuretics may lead to increased serum potassium.

References

1. Entresto Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2019. Available at: https://www.novartis.us/sites/www.novartis.us/files/entresto.pdf. Accessed February 3, 2021.
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, 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. Accessed February 3, 2021.
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4. 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. Accessed February 3, 2021.
5. McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014; 371:993-1004. Accessed February 3, 2021.
6. Sacubitril/valsartan. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, November 23. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed February 3, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy reviewed and updated: 1. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…" 2. FDA approved indication in Background was updated 3. Dosing information was updated to include pediatric dosing 4. Criteria I.A.2 was updated to age ≥ 1 year 5. Criteria I.A.3 was updated to LVEF ≤ 40%;	05/2020	05/2020
Policy reviewed and updated: 1. Clinical policy title and lines of business updated. 2. Initial criteria for approval updated. 3. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…". 4. References updated.	02/03/2021	03/09/2021