Neprilysin Inhibitor (Entresto™) Prior Authorization with Quantity Limit Criteria Program Summary

This prior authorization applies to Commercial, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Neprilysin Inhibitor Prior Authorization (PA) and Quantity Limit (QL) program is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and according to dosing recommended in product labeling. Neprilysin inhibitors will be approved for use in patients with New York Heart Association (NYHA) Stage II-IV chronic heart failure; who have a reduced baseline or current ejection fraction ≤40%; and patients who are on a beta blocker or who have a documented intolerance, FDA labeled contraindication, or hypersensitivity to a beta blocker. The program will not allow approval for patients who have an FDA labeled contraindication to the requested agent, or for patients who are pregnant, or for patients who will use the requested agent concomitantly with another ACEI or ARB. The program will approve for doses within the set limit. Doses above the set limit will be approved if the requested quantity is below the FDA limit and cannot be dose optimized or when the quantity is above the FDA limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis. Requests will be reviewed when patient specific documentation is provided.

TARGET AGENT

Entresto™ (sacubitril/valsartan)

Brand (generic)	GPI	Multisource Code	Quantity Limit Per Day
Entresto (sacubitril/valsartan)			
24/26 mg tablets	40992002600320	M, N, O, Y	2 tablets
49/51 mg tablets	40992002600330	M, N, O, Y	2 tablets
97/103 mg tablets	40992002600340	M, N, O, Y	2 tablets

PRIOR AUTHORIZATION AND QUANTITY LIMIT CRITERIA FOR APPROVAL

Neprilysin Inhibitor will be approved when ALL of the following are met:

1. The patient has a diagnosis of chronic heart failure NYHA Class II, III, or IV
   AND
2. The patient has a baseline OR current left ventricular ejection fraction of ≤40%
   AND
3. ONE of the following:
   a. The patient is currently taking a beta blocker (e.g. atenolol, bisoprolol, carvedilol, metoprolol)
      OR
   b. The patient has a history of a documented intolerance, FDA labeled contraindication, or hypersensitivity to a beta blocker
   AND
4. ONE of the following:
   a. The patient is not currently taking another ACE Inhibitor or ARB
      OR

b. The patient will discontinue the other current ACE Inhibitor or ARB before starting the requested agent

AND

5. The patient does NOT have any FDA labeled contraindication(s) to the requested agent

AND

6. The patient is NOT pregnant

AND

7. ONE Of the following:
    a. The requested quantity (dose) is NOT greater than the program quantity limit

    OR

    b. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit

        AND

        ii. The requested quantity (dose) is less than or equal to the FDA labeled dose

        AND

        iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

    OR

    c. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit

        AND

        ii. The requested quantity (dose) is greater than the FDA labeled dose

        AND

        iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

FDA APPROVED INDICATIONS AND DOSAGE[1]

	Indication	Dosage & Administration
Entresto™ (sacubitril/valsartan)	Reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction. Sacubitril/valsartan is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB.	The recommended starting dose of sacubitril/valsartan is 49/51 mg twice-daily. Double the dose of sacubitril/valsartan after 2 to 4 weeks to the target maintenance dose of 97/103 mg twice-daily, as tolerated by the patient. Reduce the starting dose to 24/26 mg twice-daily for: • Patients not currently taking an ACEi or an ARB or previously taking a low dose of these agents • Patients with severe renal impairment • Patients with moderate hepatic impairment Double the dose of sacubitril/valsartan every 2 to 4 weeks to the target maintenance dose of 97/103 mg twice-daily, as tolerated by the patient.

CLINICAL RATIONALE

Guidelines

The ACCF/AHA guideline classifies heart failure by the following in relation to New York Heart Association (NYHA) Functional Classification: [2]

ACCF/AHA Stages of HF	ACCF/AHA Stage Description	NYHA Functional Classification	NYHA Functional Classification Description
A	At high risk for HF but without structural heart disease or symptoms of HF	None	None
B	Structural heart disease but without signs or symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF
C	Structural heart disease with prior or current symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF

ACCF/AHA Stages of HF	ACCF/AHA Stage Description	NYHA Functional Classification	NYHA Functional Classification Description
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest
D	Refractory HF requiring specialized interventions	IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest

The ACCF/AHA guideline recommends the following algorithm for the treatment of heart failure with reduced ejection fraction (≤40%) ACCF/AHA Class C and NYHA Class I-IV: [2]

- All patients should receive an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) in addition to a beta blocker
- For volume overloaded NYHA Class II-IV patients, a loop diuretic should be added
- For persistently symptomatic African American NYHA class III-IV patients, hydralazine and isosorbide dinitrate should be added
- For NYHA Class II-IV patients with estimated creatinine >30 mL/min and potassium <5.0 mEq/dL, an aldosterone antagonist should be added

ACC/AHA/HFSA recommends an angiotensin receptor/neprilysin inhibitor (ARNI) combination, as an alternative to ACEI or ARB, in conjunction with evidence-based beta blockers, and aldosterone antagonists in select patients with chronic Heart Failure with reduced Ejection Fraction (HFrEF) to reduce morbidity and mortality. ACC/AHA/HFSA also states that in patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEI or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.[3]

Safety[1]

Sacubitril/valsartan carries a black box warning that drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus and when pregnancy is detected, sacubitril/valsartan should be discontinued as soon as possible.

Sacubitril/valsarta is contraindicated in the following:

- In patients with hypersensitivity to any component

- In patients with a history of angioedema related to previous ACE inhibitor or ARB therapy
- With concomitant use of ACE inhibitors. Do not administer within 36 hours of switching from or to an ACE inhibitor
- With concomitant use of aliskiren in patients with diabetes

REFERENCES

1. Entresto prescribing information. Novartis Pharmaceuticals Inc. July 2015.
2. 2013 ACCF/AHA Guideline for the Management of Heart Failure. Accessed on 5/23/2016. http://circ.ahajournals.org/.
3. 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/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America Developed in Collaboration With the International Society of Heart and Lung Transplantation. Accessed on 5/23/2016. http://circ.ahajournals.org/