EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Entresto™ (sacubitril and valsartan tablets – Novartis)

TAC APPROVAL DATE: 07/08/2015; selected revision 09/09/2015

LAY CRITERIA EFFECTIVE DATE: 09/16/2015

OVERVIEW

Entresto, a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin II receptor blocker (ARB) is indicated to reduce the risk of cardiovascular (CV) death and hospitalization for heart failure (HF) in patients with chronic heart failure (New York Heart Association [NYHA] class II to IV) and reduced ejection fraction (EF).[1] Entresto is usually given with other HF therapies, in place of an angiotensin converting enzyme (ACE) inhibitor or an ARB. The recommended starting dose of Entresto is 49/51 mg (sacubitril/valsartan) twice daily (BID). Contraindications to Entresto use include hypersensitivity to any component; history of angioedema related to previous ACE inhibitor or ARB therapy; concomitant use with ACE inhibitors; and concomitant use with Tekturna® (aliskiren tablets) in patients with diabetes.

The efficacy of Entresto was established in a multinational, randomized, double-blind trial called PARADIGM-HF (Prospective Comparison of ARNI [angiotensin receptor-neprilysin inhibitor] with ACEI [angiotensin converting-enzyme inhibitor] to Determine Impact on Global Mortality and morbidity in Heart Failure Trial) which compared therapy with Entresto and enalapril, in addition to other recommended therapies, in patients with HF and reduced EF [n = 8,442].[1-2] Patients had symptomatic chronic HF (NYHA class II to IV) and systolic dysfunction (left ventricular ejection fraction [LVEF] ≤ 40%). Prior to entry, patients were on an ACE inhibitor or an ARB for at least 4 weeks and were also receiving maximally tolerated doses of beta blockers. Upon trial entry, patients discontinued their existing ACE inhibitor or ARB therapy. The primary endpoint was the first event in the composite of CV death or hospitalization for HF. The median duration of follow-up was 27 months and received therapy for up to 4.3 years. Entresto was superior to enalapril in reducing the risk of the combined endpoint of CV death or hospitalization for HF (21.8% with Entresto vs. 26.5% with enalapril; P < 0.0001). Entresto also improved overall survival (P = 0.0009), a finding driven by a lower incidence of CV mortality among patients given Entresto.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Entresto. Because of the specialized skills required for evaluation and diagnosis of patients treated with Entresto, as well as the monitoring required for adverse events and long-term efficacy, approval requires Entresto to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 1 year in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Entresto is recommended in those who meet the following criteria:

1. **Chronic Heart Failure.** Approve for 1 year if the patient meets the following criteria (A and B):
   A) The patient has a left ventricular ejection fraction (LVEF) ≤ 40% prior to initiation of Entresto therapy; AND
   B) The agent is prescribed by, or in consultation with, a cardiologist; AND

   Entresto is indicated to reduce the risk of CV death and hospitalization for HF in patients with chronic HF (NYHA class II to IV) and a reduced EF. Entresto is usually given with other HF therapies, in place or an ACE inhibitor or an ARB.[1] In the pivotal PARADIGM-HF trial, patients had systolic dysfunction (LVEF ≤ 40%).[1-2] In this trial, Entresto was superior to enalapril in reducing the risk of the combined endpoint of CV death or hospitalization for HF (21.8% with Entresto vs. 26.5% with enalapril; P < 0.0001). Entresto also improved overall survival (P = 0.0009), a finding driven by a lower incidence of CV mortality among patients given Entresto.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Entresto has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below.

1. **Use of Entresto with an Angiotensin Converting Enzyme (ACE) Inhibitor or an ACE Inhibitor-Containing Product.** Use of Entresto concomitantly with ACE inhibitors is contraindicated.[1]

2. **Use of Entresto with an Angiotensin II Receptor Blocker (ARB) or an ARB-Containing Product.** One of the components of Entresto is an ARB, valsartan. Avoid use of Entresto with an ARB.[1]

3. **Use of Entresto with Tekturna® (aliskiren tablets) or a Tekturna-Containing Product in patients with diabetes.** Use of Entresto with Tekturna in patients with diabetes is contraindicated.[1]

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Entresto™ tablets [prescribing information]. East Hanover, NJ: Novartis; August 2015.
2. McMurray JJV, Packer M, Desai AS, et al, for the PARADIGM-HF Investigators and Committees. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med*. 2014;371(11):993-1004.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date	Lay Criteria Effective Date
New Policy	--	07/08/2015	07/09/2015
Selected revision.	For the approval criteria in chronic HF, removed criteria that the patient has tried one ACE inhibitor for HF or has a contraindication to one. Also, criteria was removed that the patient has tried or is currently receiving one beta blocker for HF, and/or Corlanor, or has a contraindication for use of beta blocker therapy.	09/09/2015	09/16/2015

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; ACE – Angiotensin converting enzyme.