Entresto

Description

Entresto (sacubitril / valsartan)

Background
Entresto is a combination of a neprilysin inhibitor (sacubitril) and an angiotensin II receptor blocker (valsartan) used to reduce the risk of hospitalization in people with certain types of long-lasting (chronic) heart failure. Entresto is used with other heart failure therapies other than an angiotensin converting enzyme (ACE) inhibitor or other angiotensin II receptor blocker (ARB) therapy (1).

Regulatory Status
FDA-approved indication: Entresto is a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin II receptor blocker, indicated: (1)

- to 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.
- Entresto is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB.
- for the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older. Entresto reduces NT-proBNP and is expected to improve cardiovascular outcomes.

Entresto has a boxed warning that fetal harm can occur when administered to a pregnant woman. Use of drugs that act directly on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function. When pregnancy is detected, discontinue Entresto as soon as possible (1).
Entresto is contraindicated in patients with a history of angioedema related to previous ACE inhibitor or ARB therapy. Entresto is also contraindicated with concomitant use of an angiotensin-converting enzyme (ACE) inhibitor. If switching from an ACE inhibitor to Entresto allow a washout period of 36 hours between administrations of the two drugs (1).

Eligibility requirements in the PARADIGM-HF trial at screening included an age of at least 18 years, New York Heart Association (NYHA) class II, III, or IV symptoms, and an ejection fraction of 40% or less (which was changed to 35% or less by an amendment to the protocol on December 15, 2010) (2).

The safety and efficacy of Entresto has not been established in pediatric patients less than 1 year of age (1).

Related policies
Corlanor

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Entresto may be considered medically necessary in patients with heart failure and if the conditions indicated below are met.

Entresto is considered investigational for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis
Patient must have the following:

Chronic heart failure

AND ALL of the following:
1. NYHA activity class II – IV
2. Systolic dysfunction with left ventricular ejection fraction ≤ 40%
3. NO history of angioedema related to previous ACE inhibitor or ARB therapy
4. Documented 4 week prior treatment with an ACE or ARB
5. Used in combination with beta blocker or diuretic as tolerated
6. Prescribed by or recommended by cardiologist
7. **NO** severe hepatic impairment (Child-Pugh Class C)
8. **NOT** to be used in combination with an ACE or ARB
9. Prescriber agrees to start patient on Entresto 24mg/26mg in patients with a eGFR <30 mL/min

**Age**

1 to 17 years of age

**Diagnosis**

Patient must have the following:

Symptomatic heart failure

AND ALL of the following:
1. NYHA activity class II – IV
2. Systemic left ventricular systolic dysfunction with left ventricular ejection fraction ≤ 40%
3. **NO** history of angioedema related to previous ACE inhibitor or ARB therapy
4. Prescribed by or recommended by cardiologist
5. **NO** severe hepatic impairment (Child-Pugh Class C)
6. **NOT** to be used in combination with an ACE or ARB

**Prior – Approval Renewal Requirements**

**Age**

18 years of age or older

**Diagnosis**

Patient must have the following:

Chronic heart failure

AND ALL of the following:
1. Symptoms have improved or stabilized
2. Used in combination with beta blocker or diuretic as tolerated
3. **NO** severe hepatic impairment (Child-Pugh Class C)

**Age**

1 to 17 years of age
**Diagnosis**

Patient must have the following:

- Heart failure

AND ALL of the following:
  1. Symptoms have improved or stabilized
  2. NO severe hepatic impairment (Child-Pugh Class C)

**Policy Guidelines**

**Pre - PA Allowance**

None

**Prior - Approval Limits**

Duration 2 years

**Prior – Approval Renewal Limits**

Same as above

**Rationale**

**Summary**

Entresto is a prescription medicine used to reduce the risk of death and hospitalization in people with certain types of heart failure. Entresto is usually used with other heart failure therapies, in place of an ACE inhibitor or other ARB therapy. Entresto can cause fetal harm when administered to a pregnant woman. Female patients of childbearing age should be advised about the consequences of exposure to Entresto during pregnancy. Entresto is not recommended in patients with severe hepatic impairment or concomitant use with aliskiren in diabetic patients (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Entresto while maintaining optimal therapeutic outcomes.

**References**


### Policy History

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<tr>
<th>Date</th>
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<tr>
<td>August 2015</td>
<td>Addition of Entresto to PA</td>
</tr>
<tr>
<td>September 2015</td>
<td>Annual review and addition of ARB in combination with beta blocker</td>
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<tr>
<td>December 2015</td>
<td>Annual review and reference update</td>
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<tr>
<td>March 2016</td>
<td>Removal of the ACE in combination with calcium channel blocker requirement and change the left ventricular ejection fraction ≤ 35% to 40% Policy number change from 5.16.07 to 5.40.07</td>
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<tr>
<td>May 2016</td>
<td>Removal of the word intolerance and the addition of a wash-out period.</td>
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<tr>
<td>June 2016</td>
<td>Annual review</td>
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<td></td>
<td>Change from inadequate treatment response or contraindication to ACE or ARB in combination beta blocker or diuretic to prior treatment with one of those combinations per SME</td>
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<td>August 2016</td>
<td>Addition of prescriber agrees to start patient on Entresto 24mg/26mg in patients with an eGFR &lt;30 mL/min and documented 4 week prior treatment with an ACE or ARB. Also the addition of as tolerated to use in combination with beta blocker or diuretic per SME</td>
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<td>December 2016</td>
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<td>September 2017</td>
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<td>August 2018</td>
<td>Removal of requirements of no dual therapy with Tekturna and prescriber agreement to 36 hour washout period of ACE/ARB therapy</td>
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<tr>
<td>September 2018</td>
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<td>September 2019</td>
<td>Annual editorial review and reference update. Changed approval duration from lifetime to 2 years</td>
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<td>October 2019</td>
<td>Addition of indication: symptomatic heart failure in pediatric patients 1 to 17 years of age</td>
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### Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective January 1, 2020.