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Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Cardiovascular Agent	**Original Policy Date:**	August 14, 2015
Subject:	Entresto	**Page:**	1 of 5

Last Review Date: June 16, 2022

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 adult patients with certain types of chronic heart failure, and for the treatment of symptomatic heart failure in pediatric patients. 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 indications: Entresto is indicated: (1)

- to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure. Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal.
- 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 indicating 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 aliskiren in

patients with diabetes, and 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).

The use of Entresto in patients with severe hepatic impairment (Child-Pugh C classification) is not recommended, as no studies have been conducted in these patients (1).

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

Related policies
Corlanor, Verquvo

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 may be 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. **NO** history of angioedema related to previous ACE inhibitor or ARB therapy
2. **NO** severe hepatic impairment (Child-Pugh Class C)
3. **NOT** to be used in combination with an ACE inhibitor
4. 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. Systemic left ventricular systolic dysfunction
2. **NO** history of angioedema related to previous ACE inhibitor or ARB therapy
3. **NO** severe hepatic impairment (Child-Pugh Class C)
4. **NOT** to be used in combination with an ACE inhibitor

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. **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 used to reduce the risk of death and hospitalization in adult patients with certain types of chronic heart failure, and for the treatment of symptomatic heart failure in pediatric patients. 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 reproductive potential 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 patients with diabetes. The safety and efficacy of Entresto have not been established in pediatric patients less than 1 year of age (1).

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

References

1. Entresto [package insert]. East Hanover, NJ: Novartis Inc; February 2021.

Policy History

Date	Action
August 2015	Addition of Entresto to PA
September 2015	Annual review and addition of ARB in combination with beta blocker

December 2015	Annual review and reference update
March 2016	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
May 2016	Removal of the word intolerance and the addition of a wash-out period.
June 2016	Annual review Change from inadequate treatment response or contraindication to ACE or ARB in combination with beta blocker or diuretic to prior treatment with one of those combinations per SME
August 2016	Addition of prescriber agrees to start patient on Entresto 24mg/ 26mg in patients with an eGFR <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
December 2016	Annual review
September 2017	Annual editorial review and reference update
August 2018	Removal of requirements of no dual therapy with Tekturna and prescriber agreement to 36 hour washout period of ACE/ARB therapy
September 2018	Annual editorial review and reference update
September 2019	Annual editorial review and reference update. Changed approval duration from lifetime to 2 years
October 2019	Addition of indication: symptomatic heart failure in pediatric patients 1 to 17 years of age
December 2019	Annual review
September 2020	Annual review
February 2021	Removed initiation requirement to have “documented 4 week prior treatment with ACE or ARB” per FEP. Removed requirements for chronic heart failure in adults: NYHA class II-IV and LVEF ≤40%
March 2021	Annual review
June 2021	Annual review
December 2021	Annual review. Removed requirements per FEP: prescribed or recommended by a cardiologist; used in combo with beta blocker or diuretic; NYHA Class; LVEF ≤ 40%; not to be used in combination with an ARB
March 2022	Annual review
June 2022	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.