Pharmacy Policy Bulletin: J-1396 Entresto Sprinkle (sacubitril/valsartan) – Commercial and Healthcare Reform	
Number: J-1396	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1396-001	**Original Date:** 08/07/2024
Effective Date: 09/18/2024	**Review Date:** 08/07/2024

Drugs Product(s):	• Entresto sprinkle (sacubitril/valsartan)
FDA-Approved Indication(s):	• Reduce the risk of cardiovascular (CV) death and hospitalization for heart failure (HF) in adult patients with chronic heart failure (CHF). Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal. • Treat symptomatic HF with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older. Entresto reduces NT-proBNP and is expected to improve CV outcomes.

Background:	• Entresto inhibits neprilysin via the active metabolite of the prodrug sacubitril. The CV and renal effects Entresto in HF patients are due to the increased levels of peptides degraded by neprilysin, such as natriuretic peptides, and the simultaneous inhibition angiotensin II and angiotensin II-dependent aldosterone release by valsartan. This both decreases blood pressure and provides cardioprotective benefits through the release of natriuretic peptides. • In 2017, approximately one million patients in the United States (US) were diagnosed with HF and these patients constituted 1.2 million HF hospitalizations. In 2014, over 300,000 deaths were caused by HF. Hypertension, diabetes, obesity, and atherosclerotic CV disease are all known risk factors of HF. Symptoms of HF include shortness of breath, fluid retention, fatigue, and irregular heartbeat. • In pediatric patients, HF is most commonly caused by congenital heart defects. There are approximately 1-2 cases of HF caused by congenital heart defects per 1000 live births. Cardiomyopathy is another cause of pediatric HF; these patients have poorer outcomes and have a 5-year risk of death or heart transplantation of 50%. • Entresto is available in both tablet and sprinkle forms. Table 1. Entresto sprinkle dosing

Patient Weight (kg)	Dose
13 to < 19 kg	24/24 mg (four 6/6 mg capsules) twice daily

19 to < 26 kg	30/32 mg (two 15/16 mg capsules) twice daily
26 to < 34 kg	45/48 mg (three 15/16 mg capsules) twice daily
34 to < 50 kg	60/64 mg (four 15/16 mg capsules) twice daily

- Prescribing Considerations:
  - Entresto sprinkles are recommended in pediatric patients < 50 kg. They are pellets contained in a capsule that are opened and sprinkled over soft food; the capsules should not be swallowed whole or crushed.
  - Entresto tablets can be used in patients who weigh at least 40 kg without any additional compounding.
  - Entresto sprinkles are not intended for adult use.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Entresto sprinkles may be approved when all of the following criteria are met **(A. through D.)**:

A. The member is less than 18 years of age.
B. The member has a diagnosis of heart failure (ICD-10: I50.9) that is symptomatic.
C. The member has left ventricular systolic dysfunction.
D. The member meets one (1) of the following criteria **(1. or 2.)**:
  1. The member weighs < 40 kg.
  2. The member weighs ≥ 40 kg but < 50 kg and meets one (1) of the following criteria **(a. or b.)**:
    a. The member has experienced therapeutic failure or intolerance to Entresto tablets.
    b. The member is unable to swallow tablets.

II. Reauthorization

When a benefit, reauthorization of Entresto sprinkles may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member is less than 18 years of age.
B. The member meets one (1) of the following criteria **(1. or 2.)**:
  1. The member weighs < 40 kg.
  2. The member weighs ≥ 40 kg but < 50 kg and meets one (1) of the following criteria **(a. or b.)**:
    a. The member has experienced therapeutic failure or intolerance to Entresto tablets.
    b. The member is unable to swallow tablets.
C. The prescriber attests that the member has experienced positive clinical response to therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Entresto [package insert]. East Hanover, NJ: Novartis; April 2024.
2. Jayaprasad N. Heart Failure in Children. *Heart Views*. 2016 Jul-Sep;17(3):92-99.
3. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Published April 1, 2022. Accessed April 24, 2024.
4. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2024.