

Entresto® (sacubitril/valsartan) - New indication

- On October 2, 2019, <u>Novartis announced</u> the <u>FDA approval</u> of <u>Entresto (sacubitril/valsartan)</u>, for the
 treatment of symptomatic heart failure (HF) with systemic left ventricular systolic dysfunction in pediatric
 patients aged one year and older. Entresto reduces N-terminal pro-B-type natriuretic peptide (NTproBNP) and is expected to improve cardiovascular (CV) outcomes.
- Entresto is also approved to reduce the risk of CV death and hospitalization for HF in adult patients with chronic HF (NYHA Class II-IV) and reduced ejection fraction.
- HF is a chronic and progressive condition where the heart cannot pump enough blood to support the body's need for blood and oxygen. Children diagnosed with systolic HF face a poor prognosis. It has been estimated that half require a heart transplant before the age of five, and almost one-third die or require a transplant within one year.
- The approval of the new indication for Entresto was based on the PANORAMA-HF study enrolling 110 pediatric patients 1 to <18 years old with HF (NYHA/Ross Class II-IV) due to systemic left ventricular systolic dysfunction (LVEF ≤ 40%). Patients received Entresto or enalapril. The endpoint was the between-group difference in the change in plasma NT-proBNP from baseline to 12 weeks.
 - The reduction from baseline in NT-proBNP was 44% and 33% in the Entresto and enalapril groups, respectively.
 - While the between-group difference was not statistically significant, the reductions for Entresto and enalapril were similar to or larger than what was seen in adults.
 - Because Entresto improved outcomes and reduced NT-proBNP in adults in the PARADIGM-HF study, the effect on NT-proBNP was considered a reasonable basis to infer improved CV outcomes in pediatric patients.
- Entresto carries a boxed warning for fetal toxicity.
- The recommended dose of Entresto for pediatric patients aged one year and older is based on body weight and given orally twice daily. Adjust pediatric patient doses every 2 weeks, as tolerated by the patient as follows:

	Titration Step Dose (twice daily)		
	Starting	Second	Final
Pediatric patients less than 40 kg [†]	1.6 mg/kg	2.3 mg/kg	3.1 mg/kg
Pediatric patients at least 40 kg, less than 50 kg	24/26 mg	49/51 mg	72/78 mg [‡]
Pediatric patients at least 50 kg	49/51 mg	72/78 mg [‡]	97/103 mg

[†] Use of the oral suspension recommended in these patients. Recommended mg/kg doses are of the combined amount of both sacubitril and valsartan.

 Consult the Entresto drug label for adult dosing recommendations and for instructions on compounding the oral suspension using the 49/51 mg tablets.



optumrx.com

OptumRx® specializes in the delivery, clinical management and affordability of prescription medications and consumer health products. We are an Optum® company — a leading provider of integrated health services. Learn more at **optum.com**.

All Optum[®] trademarks and logos are owned by Optum, Inc. All other brand or product names are trademarks or registered marks of their respective owners.

This document contains information that is considered proprietary to OptumRx and should not be reproduced without the express written consent of OptumRx.

RxNews® is published by the OptumRx Clinical Services Department.

©2019 Optum, Inc. All rights reserved.

[‡] Doses of 72/78 mg can be achieved using three 24/26 mg tablets.