Sacubitril/Valsartan (Entresto™)

Goal(s):

- Restrict use of sacubitril/valsartan in populations and at doses in which the drug has demonstrated efficacy.
- Encourage use of beta-blockers with demonstrated evidence of mortality reduction in heart failure with reduced ejection fraction.

Length of Authorization:

- 60 days to 12 months

Requires PA:

- Sacubitril/valsartan (Entresto™)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. Is this a request for continuation of therapy previously approved by the FFS program?	**Yes:** Go to Renewal Criteria	**No:** Go to #2
2. What diagnosis is being treated?	Record ICD10 code.	
3. Does the patient have stable New York Heart Association Class II or III heart failure with reduced ejection fraction less than 40% (LVEF <40%)?	**Yes:** Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
4. Has the patient tolerated a minimum daily dose an ACE-inhibitor or ARB listed in Table 1 for at least 30 days?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness
5. Is the patient currently on a maximally tolerated dose of carvedilol, sustained-release metoprolol succinate, or bisoprolol; and if not, is there a documented intolerance or contraindication to each of these beta-blockers? *Note: the above listed beta-blockers have evidence for mortality reduction in chronic heart failure at target doses and are recommended by national and international heart failure guidelines.[1,2] Carvedilol and metoprolol succinate are preferred agents on the PDL.*	**Yes:** Approve for up to 60 days	**No:** Pass to RPh. Deny; medical appropriateness

Renewal Criteria		
1. Is the patient currently taking sacubitril/valsartan at the target dose of 97/103 mg 2-times daily?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh and go to #2
2. What is the clinical reason the drug has not been titrated to the target dose of 97/103 mg 2-times daily?	Document rationale and approve for up to 60 days. Prior authorization required every 60 days until target dose achieved.	

Table 1. Minimum Daily Doses of ACE-inhibitors or ARBs Required.[1,2]

ACE-inhibitor		Angiotensin-2 Receptor Blocker (ARB)	
Captopril	50 mg TID	Candesartan	32 mg QDay
Enalapril	10 mg BID	Losartan	150 mg QDay
Lisinopril	20 mg QDay	Valsartan	160 mg BID
Ramipril	5 mg BID		
Trandolapril	4 mg QDay		

Abbreviations: BID = twice daily; QDay = once daily; mg = milligrams; TID = three times daily.

Notes:

- Patients must achieve a minimum daily dose of one of the drugs listed for at least 30 days in order to improve chances of tolerability to the target maintenance dose of sacubitril/valsartan 97/103 mg 2-times daily.[3]
- Valsartan formulated in the target maintenance dose of sacubitril valsartan 97/103 mg 2-times daily is bioequivalent to valsartan 160 mg 2-times daily.[4]
- ACE-inhibitors and ARBs listed have demonstrated efficacy in heart failure with or without myocardial infarction.[1,2]
- Target daily doses of other ACE-inhibitors and ARBs for heart failure have not been established.[1,2]
- It is advised that patients previously on an ACE-inhibitor have a 36-hour washout period before initiation of sacubitril/valsartan to reduce risk of angioedema.[3,4]

References:

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;62(16):e147-239. doi: 10.1016/j.jacc.2013.05.019.
2. McMurray J, Adamopoulos S, Anker S, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. European Journal of Heart Failure. 2012;14:803-869. doi:10.1093/eurjhf/hfs105.
3. McMurray J, Packer M, Desai A, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Eng J Med*. 2014;371:993-1004. doi:10.1056/NEJMoa1409077.
4. ENTRESTO (sacubitril and valsartan) [Prescribing Information]. East Hanover, NJ: Novartis Pharmaceuticals, July 2015.

P&T / DUR Review: *05/17(DM), 09/15*
Implementation: *10/13/16; 10/1/15*