# Initiation, Titration and Monitoring Recommendations for Sacubitril/Valsartan (ENTRESTO™) Usage in British Columbia

**Patient must meet all the British Columbia eligibility criteria prior to initiating Sacubitril/Valsartan**

***Sacubitril/Valsartan is NOT to be used as first line therapy for HFrEF- (≤ 40%),***

***Consider initiating Sacubitril/Valsartan ONLY AFTER patient established on guideline-directed triple medical therapy for HF-rEF including Angiotensin Converting Enzyme Inhibitor (ACE-I), Angiotensin II Receptor Blocker (ARB), Beta Blocker (BB), Mineralocorticoid Receptor Antagonist (MRA) for a minimum of 3 months (based on the potential for improvement on standard medical therapy)***

## Prescribing tips

Sacubitril/Valsartan may be considered *instead* of an ACE-I or ARB in patients with:

- ✓ NYHA II-III functional status.
- ✓ LVEF ≤ 40% (preferably measured within the last year) despite a trial of optimally tolerated doses of guideline driven heart failure therapy including ACE-I/ARB, BB and MRA for a minimum of three months,(based on the potential for improvement on standard medical therapy).
- ✓ Elevated BNP > 150 pg/mL or NT-proBNP ≥600 pg/mL at time of decision to switch or/and a heart failure hospitalization within the last year.

- Consider decreasing the patient's diuretic dose for 3-4 days when initiating Sacubitril/Valsartan to reduce the risk of hypotension and kidney injury.
- NT-pro BNP is the biomarker of choice to be used once Sacubitril/Valsartan has been started, as BNP measurements will be inaccurate.
- Consider starting at the lowest dose of Sacubitril/Valsartan (24.3 mg sacubitril / 25.7 mg valsartan) in patients who have risk factors for hypotension or low baseline systolic blood pressure and in patients' ≥ 75 years of age.
- Patients with moderate hepatic impairment (Child-Pugh B classification) should be initiated on the lowest dose of Sacubitril/Valsartan.
- Sacubitril/Valsartan doses lower than 97.2/102. 8mg po BID have not yet been shown to reduce morbidity and mortality. Every effort should be made to reach target dose.

## Prescribing CAUTIONS:

**When converting from ACE-I, a 36 hour wash out period is required before Sacubitril/Valsartan can be started**

- Sacubitril/Valsartan can cause hypotension, potassium and renal abnormalities.
- Sacubitril/Valsartan may increase statin levels (especially simvastatin & atorvastatin). Careful monitoring for statin toxicity is recommended.
- Concomitant use of Sacubitril/Valsartan with aliskiren (Rasilez™) containing drugs should be avoided.
- Theoretically patients on Sacubitril/Valsartan could be at risk of Alzheimer's disease as amyloid β is a substrate for neprilysin. This will be addressed in ongoing cognitive studies.
- DO NOT use during pregnancy or if breast feeding.

## Ordering sacubitril/valsartan (Entresto™):

| sacubitril/valsartan must be ordered using available strengths as below: | Actual Content (Sacubitril/Valsartan) | Referred to in clinical studies as: | Equivalent Diovan™ dose: |
|---|---|---|---|
| sacubitril/valsartan 24/26 BID (White pill) | 24.3mg / 25.7mg | 50mg BID | 40mg BID |
| sacubitril/valsartan 49/51 BID (yellow pill) | 48.6 mg / 51.4 mg | 100mg BID | 80mg BID |
| sacubitril/valsartan 97/103 BID (pink pill) | 97.3 mg / 102.8mg | 200mg BID | 160mg BID |

# Titration Algorithm

## Assess

- ☐ Eligibility Checklist Completed
- ☐ Patient on guideline directed ACE-I or ARB at optimally tolerated dose
  - o if not, titrate to optimally tolerated dose and reassess eligibility for sacubitril/valsartan in 3 months

## Washout

**If on ACE-I, STOP for 36 hours to reduce the risk of angioedema**

*Do not need to stop ARB 36 hours prior to starting sacubitril/valsartan*

## Initiate

**Initiate *sacubitril/valsartan 49/51mg BID*** -if patient at target ACE-I or ARB* dose
**Initiate *sacubitril/valsartan 24/26mg BID-*** if patient on less than target dose ACE ARB,* older than 75 years old, at risk for hypotension, have moderate hepatic impairment or clinician concern about drug intolerability

## Titrate

**Increase to next highest dose every 2-4 weeks to a target dose of 97/103mg BID**

sacubitril/valsartan 24/26 mg po BID
sacubitril/valsartan 49/51 mg po BID
sacubitril/valsartan 97/103mg po BID

## Monitor

**SCr, $K^+$ and blood pressure**

1 week after initiation, after each dose increase and with each practitioner visit
Consider assessment of LV Function only if it will alter treatment or if otherwise clinically indicated

## Reassess

**Consider decreasing or stopping sacubitril/valsartan if:**

- SCr increases by > 30%
- $K^+$ is greater than 5.4 mmol/L
- Symptomatic hypotension ( < 95 mmHg)

* 36 hour washout of sacubitril/valsartan is required if switching back to ACE-I*

| Target Daily Dose | |
|---|---|
| ACE-I | ARB |
| captopril 150mg | valsartan 320mg |
| enalapril 20mg | candesartan 32mg |
| perindopril 8mg | |
| ramipril 10mg | |
| trandolapril 4mg | |