

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 HF_rEF- (≤ 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 mg sacubitril / 26 mg valsartan) in patients who have risk factors for hypotension or low baseline systolic blood pressure and in patient's ≥ 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 97/103mg po BID have not yet been shown to reduce morbidity and mortality. Every effort should be made to reach target dose.

Prescribing CAUTIONS:

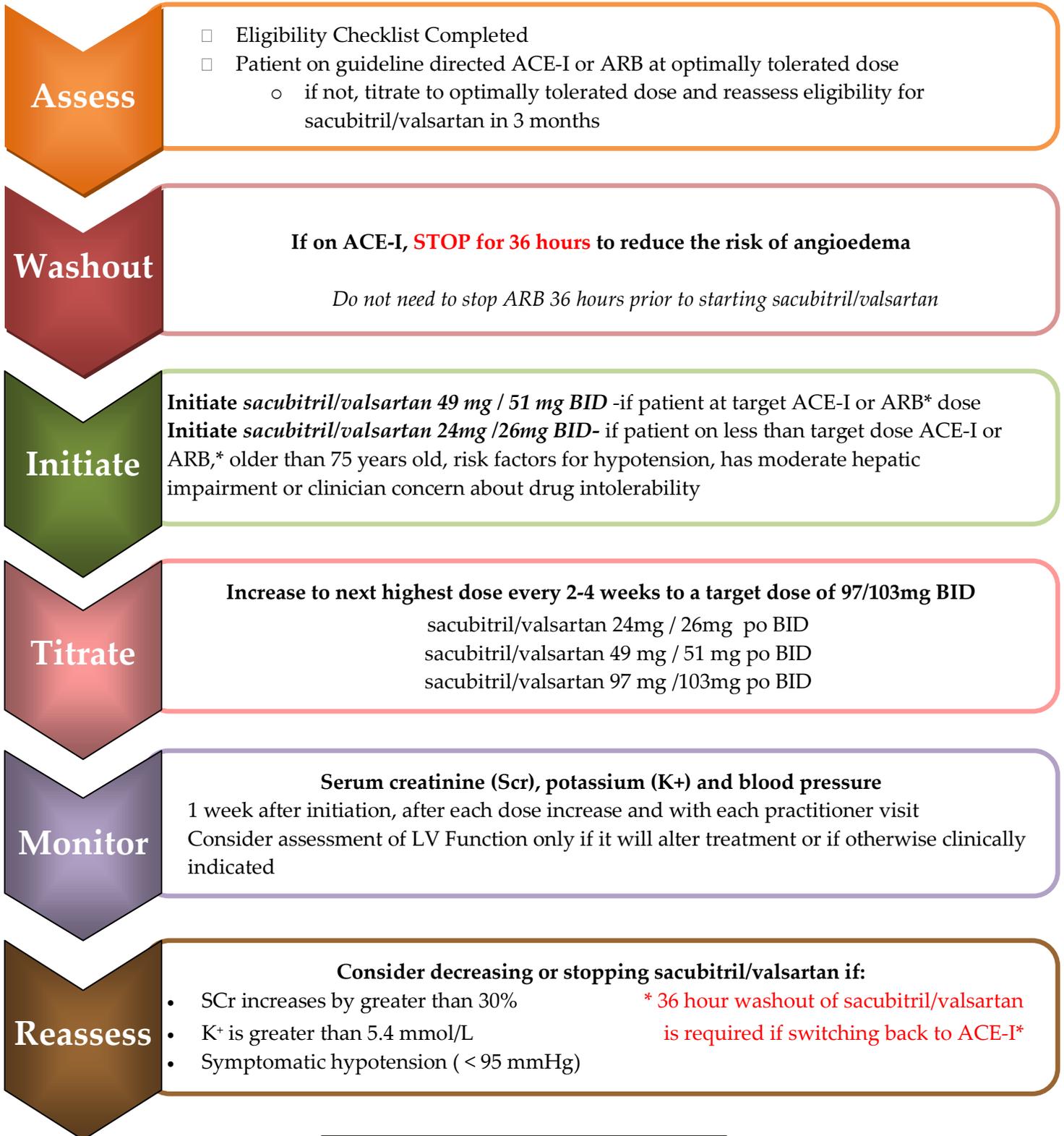
When converting from ACE-I, a 36 hour wash out period is required before Sacubitril/Valsartan can be started

- 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)	24mg / 26mg	50mg BID	40mg BID
sacubitril/valsartan 49/51 BID (yellow pill)	49 mg / 51 mg	100mg BID	80mg BID
sacubitril/valsartan 97/103 BID (pink pill)	97 mg / 103mg	200mg BID	160mg BID

Titration Algorithm



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