Angiotensin Converting Enzyme Inhibitors (ACEI) / Angiotensin Receptor Blockers (ARBS)*
Heart Failure Medication Initiation and Titration

Initiation

Symptomatic HF or LVEF < 40%

- **Bilateral renal artery stenosis**
- **Moderate/Severe aortic stenosis**
- **Hyperkalemia:** K+ > 5.2 mmol/L
- **Renal Dysfunction:** Serum creatinine >220 µmol/L
- **Hypotension:** SBP < 90 mmHg or symptoms
- **Allergy:** angioedema, hives, rash
- **Intolerance:** cough (ACEi)

NO → **Considerations:**
- Baseline cough (ACEi)
- K+ supplements
- K+ sparing diuretics
- MRA
- NSAIDS/COX2 inhibitors

→ **See dosing**

→ **See monitoring section**

YES → **Refer to Physician**

Titration

Titrate every 1-3 weeks, depending on tolerance

Goal: Target dose(see dosing) or maximum tolerated dose

Hypotension SBP<90mmHg with symptoms*
* Watch for trends

→ **Fluid Assessment**

- **Volume deplete** → Reduce/hold diuretic x 2-3 days → No improvement, hold/reduce ACEI/ARB x 1-2 wks & reassess
- **Euvolemic** → Reassess diuretic dose/other non-essential BP lowering meds Consider staggering doses
- **Volume overload** → Reduce/hold dose of other vasodilators +/- ACEI/ARB x 1-2 weeks → **See Diuretic algorithm** → Reassess 1-2 wks

Assess

- BP
- K +
- Scr

Hyperkalemia K+ > 5.2 mmol/L*
* Watch for trends

Considerations:
- Dietary K+
- K+ supplements
- K+ sparing diuretics
- MRA
- Renal dysfunction

- **K+ 5.2-5.5** → Stop K+ supplements, reduce/ hold MRA (if applicable) → Serum K+ in 3-5 days, Reassess ACEI/ARB dose
- **K+ 5.6-6.0** → Stop K+ supplements, MRA. hold ACEI/ARB → Serum K+ in 2-3 days, Reassess ACEI/ARB dose
- **K+ > 6.0** → Treat hyperkalemia Refer to MD/NP +/- send to ED

Renal dysfunction >30% in serum creatinine*
* Watch for trends

Considerations:
- Addition of nephro-toxic drugs: NSAIDS/COX2
- Worsening HF
- Co-morbidity: DM, dehydration, CKD

→ **Fluid Assessment**

- **Volume deplete** → Reduce/hold diuretic x 2-3 days → Scr in 5-7 days
- **Euvolemic** → Hold ACEI/ARB → Scr in 5-7 days → **Rechallenge at lower dose**
- **Volume overload** → Increase diuretic per Diuretic algorithm; reduce/hold of ACEI/ARB → Scr in 2-3 days

Monitoring **

Initiation of ACEI/ARB
- Baseline Scr / GFR
- Baseline K+
- Baseline blood pressure

Blood Pressure
- Every visit
  - Siting
  - Standing
  - +/- lying

Serum Creatinine

One week after:
1. initiation
2. dosage increase*
3. > 30% ↑ in Scr

Serum Potassium

One week after:
1. initiation
2. dosage increase*

* Obtain baseline value prior to any up-titration or change in symptom status
If stable: Q 3-6 months

Other Considerations:

Angioedema:
- Stop ACEI/ARB contact physician; refer to ED
- Do not rechallenge
- Caution when substituting ARB for ACEI

Cough:
- Assess at baseline as may be due to worsening HF
- If intractable cough secondary to ACEI consider:
  - Trial of another ACEI or lower dose
  - Switch to ARB
- Reassess in 2 weeks and document

* This algorithm is intended for single agent (ACEI or ARB)
** This is a guide to monitoring; increase monitoring may be required given patient's status and co-morbidities (ie. renal insufficiency)

December 2018

Beta - Blockers
Heart Failure Medication Initiation and Titration

Initiation

LVEF < 40%

- **Bifascicular block, PR interval prolongation (>0.24 msec)**
- **Bradycardia:** HR< 60 bpm or symptomatic
- **2nd or 3rd degree AV block without a pacemaker**
- **Hypotension:** SBP < 90 mmhg or symptoms
- **Asthma**
- **Acute decompensated heart failure**
- **Intolerance or allergy**

NO → **Considerations:**
- COPD with reversible component
- Other rate controlling drugs:
  - verapamil, diltiazem
  - amiodarone
  - sotalol
  - digoxin
  - ivabradine

→ **See dosing**

→ **See monitoring section**

YES → **Refer to Physician**

Titration

Titrate every 2-4 weeks, depending on tolerance

Goal: Target dose (see dosing) or maximum tolerated dose

Hypotension SBP<90mmHg with symptoms →

Considerations:
- Other BP lowering drugs:
  - vasodilators (nitrates, hydralazine, CCB)
  - ACEI/ARB/ARNI
  - diuretics

→ **Volume deplete** → Reduce/hold diuretic x 2-3 days

→ **Euvolemic** → Reassess diuretic dose, other BP lowering drugs. Consider staggering doses → No improvement, hold/reduce BB x 1-2 wks reassess

→ **Volume overload** → See below (volume overload)

Assess

- **BP**
- **Heart Rate**
- **Fluid Status**

Bradycardia HR < 55 bpm with symptoms →

Considerations:
- Other rate controlling drugs:
  - diltiazem, verapamil
  - sotalol
  - amiodarone
  - digoxin
  - Ivabradine

→ **Conduction Abnormality:**
- Bifascicular block
- PR interval prolongation
- 2nd or 3rd degree AV block in the absence of PPM

NO → Consider decreasing BB dose. Reassess in 1-2 weeks

YES → Stop BB. Consider referral to Cardiologist

Volume overload →

Considerations:
- Other precipitants of fluid retention:
  - NSAIDS/COX2, glitazones
  - Salt/fluid intake
  - Non adherence
  - Co-morbidity
  - Worsening HF

→ **Mild symptoms**
- Maintain BB dose
- Increase diuretic
- Sodium/fluid restriction

→ **see diuretic algorithm**

→ **Moderate to severe symptoms**
- Consider reducing BB dose
- Increase diuretic
- Sodium/fluid restriction

Monitoring **

Initiation Beta-Blocker
- Baseline ECG
- Baseline heart rate
- Baseline blood pressure

Blood Pressure
- Every visit
  - Siting
  - Standing
  - +/- lying

Heart Rate
- Every visit
- ECG as clinically indicated:
  - after each up-titration
  - Δ in symptom status

Fluids/ Weight Status
- Every visit
- Patient should be instructed to perform daily weights

Other
- Extreme limiting fatigue (other causes ruled out):
  - could consider decreasing dose of BB, review in 1-2 weeks

*verapamil and diltiazem are contraindicated in systolic heart failure (EF < 40%)

**This is a guide to monitoring; increase monitoring may be required given patient's status and co-morbidities

December 2018

Mineralocorticoid Receptor Antagonists (MRA)
Heart Failure Medication Initiation and Titration

Initiation

Symptomatic heart failure (NYHA II-IV) on ACEI/ARB or ARNI + BB and LVEF < 40%

- **Hyperkalemia:** K+ > 5.2 mmol/L
- **Renal Dysfunction:** Serum creatinine > 220 µmol/L or a creatinine clearance < 30 ml/min
- **Intolerance or allergy**

NO → **Considerations:**
- K+supplements
- K+sparing diuretics
- NSAIDS/COX2 inhibitors
- ACEI/ARB or ARNI

→ **See dosing**

→ **See monitoring section**

YES → **Refer to Physician**

Titration

Titrate monthly depending on tolerance

Goal: Target dose (see dosing below) or maximum tolerated dose

Hyperkalemia
K+ >5.2 mmol/L
*** Watch for trends**

Considerations:
- K+ supplements
- K+ sparing diuretics
- Dietary K+
- ACEI/ARB or ARNI
- Renal dysfunction

→ **K+ 5.2-5.5** → Stop K+ supplements, dietitian consult. If no major changes in K+ dietary intake, then reduce/hold MRA → Serum K+ in 3-5 days

→ **K+ >5.5** → Stop K+ supplements, Hold MRA, Reduce/hold ACE/ARB or ARNI, Refer to physician/NP, Treat hyperkalemia as required → Serum K+ in 2-3 days

Assess

- **K+**
- **SCr**

Renal Dysfunction
> 30 % ↑ in SCr
*** Watch for trends**

Considerations:
- Addition of nephrotoxic drugs: NSAIDS/COX2
- ACEI/ARB or ARNI
- GI loss

→ **Fluid Assessment**

- **Volume deplete** → Reduce/hold diuretic x 2-3 days → Scr in 5-7 days
- **Euvolemic** → Reduce/hold MRA → Scr in 5-7 days → Consider re-challenge at lower dose
- **Volume overload** → Reduce/hold MRA, Refer to diuretic algorithm → Scr in 2-3 days

Monitoring **

Initiation of MRA
- Baseline Scr / GFR
- Baseline K+

Serum Creatinine / Serum Potassium
- After initiation: 3 days, 1 week, 4 weeks, then monthly x 3
- Prior to up-titration of MRA
- 1 week post up-titration of MRA
- With dehydration, illness, change in symptom status or change in other medications affecting potassium/serum creatinine

Other

Dosing:

The usual dose is 25 mg daily, however, those with poor renal function and/or a history of hyperkalemia should be initiated on 12.5 mg daily and titrated as tolerated. Some patients may have their dose increased to 50mg with close monitoring.

Other considerations:

Gynecomastia (4-5% of males) with spironolactone. Consider switching to Eplerenone.

** This is a guide to monitoring; increase monitoring may be required given patient's status and co-morbidities (ie. renal insufficiency)

December 2018

ARNI (Angiotensin Receptor blocker / Neprilysin Inhibitors [Sacubutril/Valsartan])
Heart Failure Medication Initiation and Titration

Initiation

Symptomatic HF despite ACEI/ARB and B-blocker therapy

LVEF < 40%

- **Bilateral renal artery stenosis**
- **Moderate/Severe aortic stenosis**
- **Hyperkalemia:** K+ > 5.2 mmol/L
- **Renal Dysfunction:** GFR < 30 ml/min
- **Hypotension:** SBP < 90 mmhg or symptoms
- **Allergy:** angioedema, hives, rash

NO → **Considerations:**
- K+ supplements
- K+ sparing diuretics
- MRA
- NSAIDS/COX2 inhibitors
- **Stop ACEI x 36hr prior to start**
- **Stop ARB and start following day**

→ **See dosing**

→ **See monitoring section**

YES → **Refer to Physician**

Titration

Titrate every 3-6 weeks, depending on tolerance

Goal: Target dose(see dosing) or maximum tolerated dose

Hypotension SBP<90mmHg with symptoms
* Watch for trends

→ **Fluid Assessment**

- **Volume deplete** → Reduce/hold diuretic x 2-3 days → No improvement, hold/reduce ARNI x 1-2 wks & reassess
- **Euvolemic** → Reassess diuretic dose/vasodilator
- **Volume overload** → Reduce/hold dose of other vasodilators +/- ARNI x 1-2 weeks → **See Diuretic algorithm** → Reassess 1-2 wks

Assess

- **BP**
- **K +**
- **Scr**

Hyperkalemia K+ > 5.2 mmol/L
* Watch for trends

Considerations:
- Dietary K+
- K+ supplements
- K+ sparing diuretics
- MRA
- Renal Dysfunction

- **K+ 5.2-5.5** → Stop K+ supplements, reduce/hold MRA → Serum K+ in 3-5 days, Reassess ARNI dose
- **K+ 5.6-6.0** → Stop K+ supplements, MRA, hold ARNI → Serum K+ in 2-3 days, Reassess ARNI dose
- **K+ > 6.0** → Treat hyperkalemia, Refer to Physician, +/- ED

Renal dysfunction >30% in serum creatinine
* Watch for trends

Considerations:
- Addition of nephro-toxic drugs (NSAIDS/ COX2)
- Worsening HF
- Co-morbidity

→ **Fluid Assessment**

- **Volume deplete** → Reduce/hold diuretic x 2-3 days → Scr in 5-7 days
- **Euvolemic** → Hold ARNI → Scr in 5-7 days → **Rechallenge at lower dose**
- **Volume overload** → Increase diuretic; reduce/hold of ARNI → Scr in 2-3 days

Monitoring **

Initiation ARNI
- Baseline Scr / GFR
- Baseline K+
- Baseline blood pressure

Blood Pressure
- Every visit

Serum Creatinine
One week after:
1. initiation
2. dosage increase*
3. > 30% ↑ in Scr

Serum Potassium
One week after:
1. initiation
2. dosage increase*

Other Considerations:

Angioedema:
- Stop ARNI, contact physician, refer to ED
- Do not re-challenge

* Obtain baseline value prior to any up-titration or change in symptom status
If stable: Q 3-6 months

** This is a guide to monitoring; increase monitoring may be required given patient's status and co-morbidities (ie. renal insufficiency)

December 2018

Ivabradine (IVA)
Heart Failure Medication Initiation and Titration

Initiation

LVEF < 40% + HF symptoms

HR ≥ 70 bpm on maximally tolerate BB

Normal sinus rhythm

- **2°or 3° AV block, SSS, SA block**
- **Pacemaker dependence**
- **Atrial arrhythmia**
- **Ventricular arrhythmia**
- **Prolonged QT**
- **Intolerance or allergy**

NO →

YES → **Refer to Physician**

Considerations:

Other rate controlling drugs:
- CCB*: verapamil, diltiazem
- amiodarone
- sotalol
- beta-blockers
- digoxin

Caution:
- in combo with QT prolonging drugs
- 1°AV block

- Drug interactions: 3A4 substrate

→ **See dosing**

→ **See monitoring section**

Titration

Titrate every 2-4 weeks, depending on tolerance

Goal: Heart rate 50 - 60bpm

Assess

Heart Rate →

Bradycardia HR < 50 bpm with symptoms →

Considerations:
- Other rate controlling drugs:
  - diltiazem, verapamil
  - sotalol
  - amiodarone
  - digoxin

Note: IVA dose should be ↓ over beta-blocker dose.

→ **Conduction Abnormality ?**
- Bi-fascicular block
- 2° or 3° degree AV block

NO → Consider decreasing IVA dose
Reassess in two weeks

YES → Stop IVA
Consider referral to Cardiologist

Monitoring **

Initiation of IVA
- Baseline ECG
- Baseline heart rate

Heart Rate
- Every visit
- ECG as clinically indicated:
  - after each up-titration
  - Δ in symptom status

Other
- Transient visual changes
- May ↑ risk of atrial fibrillation

*verapamil and diltiazem are contraindicated in systolic heart failure (EF < 40%), these drug also increase IVA levels through CYP3A inhibition

**This is a guide to monitoring; increase monitoring may be required given patient's status and co-morbidities

December 2018

Diuretics
Heart Failure Medication Initiation and Titration

Initiation

Heart failure with signs and symptoms of fluid overload

Fluid Assessment	
Worsening / new SOB	Orthopnea/PND
Worsening SOBOE	Sacral edema / Ascites
Recent weight gain**	JVP assessment-JVD
Peripheral pitting edema	Hepatojugular reflex
Pulmonary edema: rales, crackles, CXR	

Considerations:

- Fluid restriction
- Sodium restriction (<2gm/d)
- Underlying renal dysfunction
- History of past diuretic use
- Non-adherence
- Other precipitants: NSAIDs,COX2 glitazones, increase BB dose
- Sodium load
- Worsening HF/ Co-morbidity

→ **See dosing**

→ **See monitoring section**

Titration

Titrate **up, down or maintain** according to symptoms

Goal: Minimum dose to achieve euvolemia

dose should be reassessed each visit

Hypotension SBP<90mmHg with symptoms

→ **Fluid Assessment**

- **Volume deplete** → Reduce/hold diuretic x 2-3 days & reassess maintenance dose in 3-7 days
- **Euvolemic** → Reassess diuretic dose/vasodilators
  Decrease diuretics/stagger dose of other medications affecting BP
- **Volume overload** → Reduce/hold dose of other vasodilators +/- ACEI/ARB/ARNI x 1-2 wks, ↑ diuretic dose as tolerated

Assess

- Fluid Status
- Blood Pressure
- K+
- SCr

Hypokalemia K+<3.5 mmol/L*

*** Watch for trends**

Considerations:

- K+ supplementation
- Addition of ACEI/ARB/ARNI
- MRA
- Renal function
- GI loss

→ **Consider K+ Supplementation**

→ **Fluid Assessment**

→ Reassess diuretic dose

Renal dysfunction >30 % ↑ in serum creatinine

*** Watch for trends**

Considerations:

- Additionof ACEI/ARB/ARNI
- MRA
- Nephrotoxic drugs: NSAIDS, COX2
- Worsening HF
- GI losses

→ **Fluid Assessment**

- **Volume deplete** → Reduce/hold diuretic x 2-3 days → Scr in 5-7 days
- **Euvolemic** → Reassess diuretic dose
- **Volume overload** → Consider reduce/hold dose MRA first; then ACEI/ARB/ARNI, ↑ diuretic dose as tolerated → Scr in 2-3 days

Monitoring **

Initiation of Diuretic

- Baseline Scr / GFR
- Baseline K+
- Baseline blood pressure

Fluid/Weight Assessment

- Every visit
- Patient should be instructed to perform daily weights

Serum Creatinine

One week after:
1. initiation
2. dosage increase**
3. 30 % ↑ in SCr

Serum Potassium

One week after:
1. initiation
2. dosage increase**

Blood Pressure

- Every visit
  - Siting
  - Standing
  - +/- lying

** Obtain baseline value prior to any up-titration or Δ in symptom status

** Weight gain: 2-3 lbs in 1-2 days or 5 lbs in 1 week

** This is a guide to monitoring; increased monitoring may be required given patient's status and co-morbidities

December 2018