Angiotensin Converting Enzyme Inhibitors (ACEIs) / 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+ > 5.5 mmol/L
Renal Dysfunction: Serum Creatinine > 220 µmol/L
Hypotension: SBP < 90 mmhg or symptoms
Allergy: angioedema, hives, rash
Intolerance: cough (ACE)

- NO → **Considerations:**
  - Baseline cough
  - K+ supplements
  - K+ sparing diuretics
  - Spironolactone
  - NSAIDs/COX2 inhibitors
  - Combination ACEI/ARB
  - → **See dosing section (reverse)**
  - → **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 < 90 mmHg 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/vasodilator
- **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
- Spironolactone
- Combo ACEI/ARB
- Renal Dysfunction

- **K+ 5.2-5.5** → Stop K+ supplements, reduce/hold spironolactone → Serum K+ in 3-5 days, Reassess ACEI/ARB dose
- **K+ 5.6-6.0** → Stop K+ supplements, spironolactone, hold ACEI/ARB → Serum K+ in 2-3 days, Reassess ACEI/ARB dose
- **K+ > 6.0** → **Refer to Physician**

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

Considerations:
- Addition of nephrotoxic drugs (NSAIDS/COX2)
- Worsening HF
- Co-morbidity interplay

→ **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 → **Re-challenge at lower dose**
- **Volume overload** → Increase diuretic; reduce/hold of ACEI/ARB → Scr in 2-3 days

Monitoring **

Initiation of ACEI/ARB	Blood Pressure	Serum Creatinine	Serum Potassium
• Baseline Scr / GFR • Baseline K+ • Baseline blood pressure	Every Visit	1 week after: 1) initiation 2) dosage increase* 3) > 30% ↑ in Scr	1 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
- Do not rechallenge
- Caution when substituting ARB for ACEI

Cough:
- Assess cough at baseline or if due to worsening HF
- If intractable cough secondary to ACEI consider:
- Trial of another ACEI
- 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; increased monitoring may be required given patient's status and co-morbidities (i.e. renal insufficiency)

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Drug	Initial Dose	Target Dose[1]	Dosage forms (mg)
ACEIs[2]			
Captopril[3] (generic)	**12.5mg tid**	**50mg tid**	**12.5, 25, 50, 100**
Cilazapril (Inhibace®, generic)	**2.5mg qd**	**10mg qd**	**1, 2.5, 5**
Enalapril (Vasotec®, generic)	**2.5mg bid**	**10mg bid**	**2.5, 5, 10, 20**
Fosinopril (Monopril®, generic)	**10mg qd**	**40mg qd**	**10, 20**
Lisinopril (Prinivil®, Zestril®, generic)	**2.5mg qd**	**30-40mg qd**	**5, 10, 20**
Perindopril (Coversyl®)	**2mg qd**	**4-8mg qd**	**2, 4, 8**
Quinapril (Accupril®)	**5-10mg qd**	**40mg qd**	**5, 10, 20, 40**
Ramipril (Altace®, generic)	**1.25-2.5mg bid**	**5mg bid**	**1.25, 2.5, 5, 10**
Trandolapril (Mavik®)	**0.5-1mg qd**	**4mg qd**	**0.5, 1, 2, 4**
ARBs[4]			
Candesartan (Atacand®)	**4mg qd**	**32mg**	**8, 16**
Valsartan (Diovan®)	**40mg bid**	**160mg bid**	**80, 160**

[1]Target doses based on clinical trials, but are limited to patient tolerance
[2]ACEIs are first line agents
[3]Limited use due to TID dosing
[4]ARBs are second line. Agents listed have been used and studied in clinical trials

Key points:

-ACEIs are first line treatment for NYHA Class I-IV

-ARBs are considered second line agents when an ACEI is not tolerated secondary to a **cough** and rarely **angioedema**

-Cough should be assessed and clearly documented **prior to** initiation of ACEI

-If cough is determined to be secondary to ACEI use (e.g. resolves upon discontinuation or recurs on re-challenge), and is bothersome enough to warrant reassessment of therapy, it should be documented

-If titration of dose is limited by **hypotension**:

- -reassess diuretic use
- -consider staggering dosing with other vasoactive agents or dosing at bedtime

-Compliance is increased with once daily dosing strategy

-Given that the main side effects of ACEIs and ARBs are **renal dysfunction** and **hyperkalemia**, assessment of other medications and factors that precipitate these effects are warranted:

1) Renal dysfunction: NSAIDs and COX2 inhibitors
2) Hyperkalemia: combination therapy, spironolactone, potassium supplements, potassium-sparing diuretics (triazide, Dyazide, triamterene, amiloride), salt substitutes (No Salt, Half Salt), dietary K+

•Goal is to keep patient at target or maximally tolerated dose of evidence based medications
•Clinical course of HF is variable—frequent reassessment of medication regime required
•Complete and thorough history and physical assessment essential with each dose adjustment
•Titrate one medication at a time—small dose changes may result in significant clinical ones (ie. symptoms, BW)

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