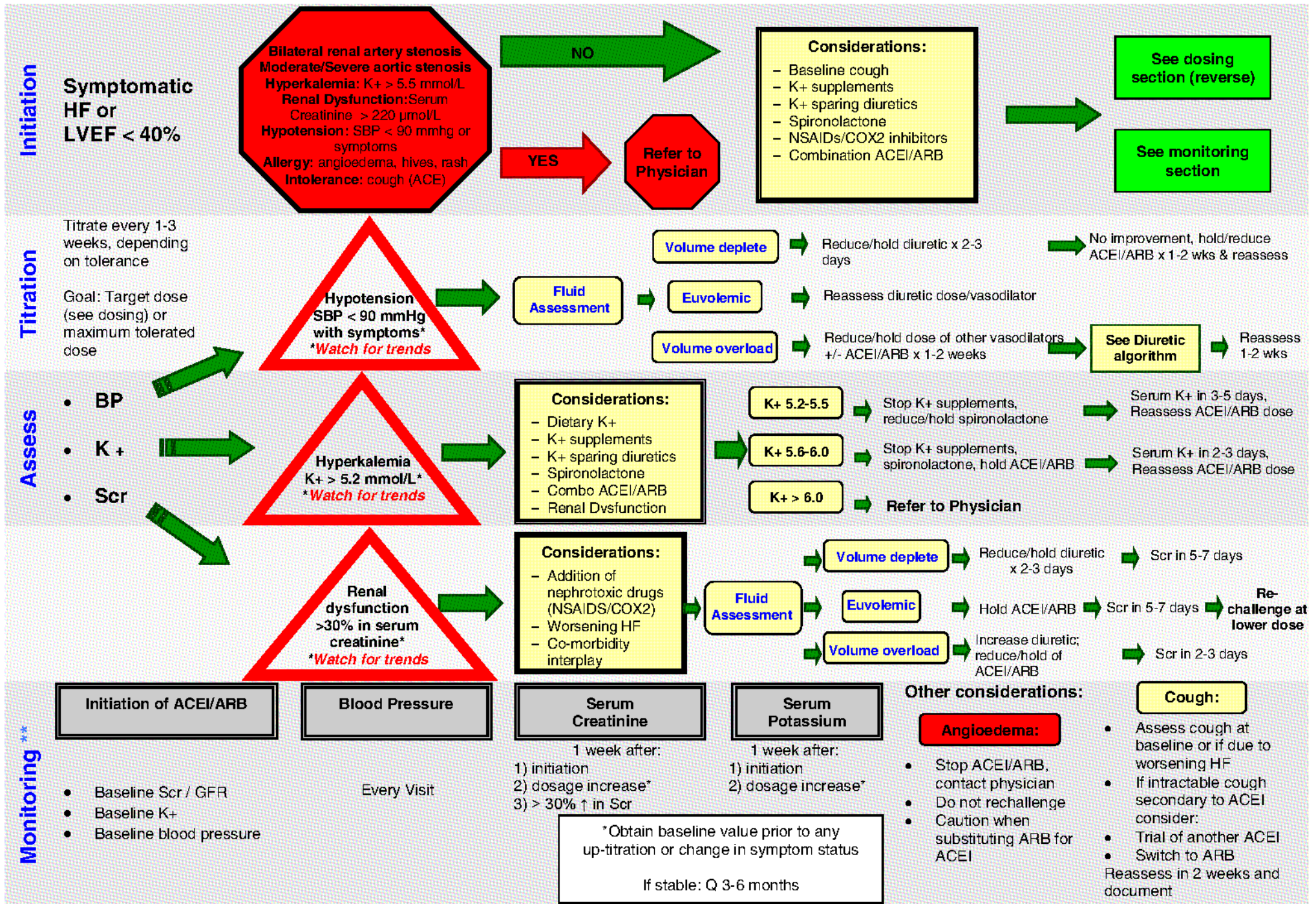


Angiotensin Converting Enzyme Inhibitors (ACEIs) / Angiotensin Receptor Blockers (ARBs)*

Heart Failure Medication Initiation and Titration



*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)

Drug	Initial Dose	Target Dose ¹	Dosage forms (mg)
ACEIs²			
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
ARBs⁴			
Candesartan (Atacand®)	4mg qd	32mg	8, 16
Valsartan (Diovan®)	40mg bid	160mg bid	80, 160

¹Target doses based on clinical trials, but are limited to patient tolerance

²ACEIs are first line agents

³Limited use due to TID dosing

⁴ARBs 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

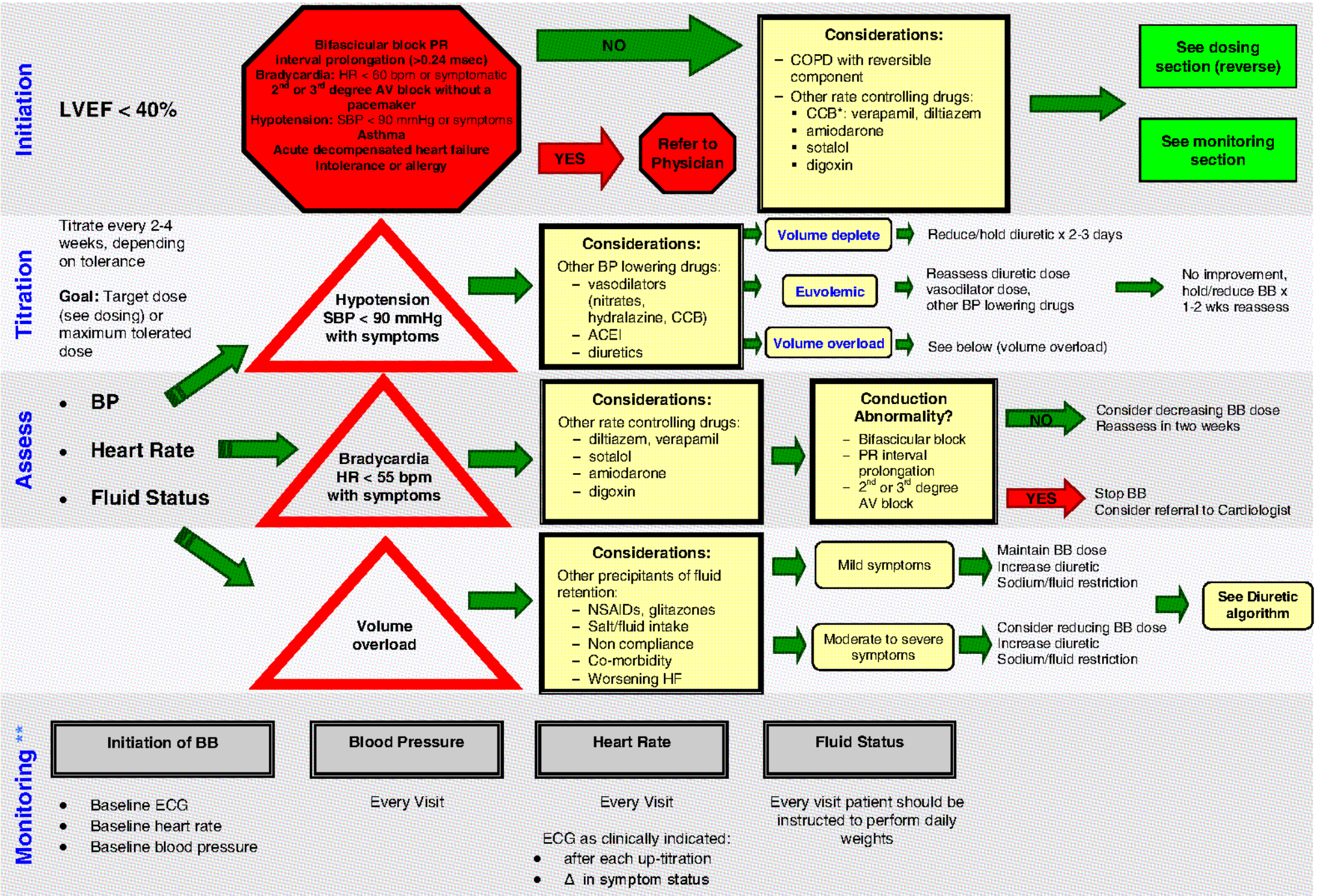
•Clinical course of HF is variable—frequent reassessment of medication regime required

•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)

Beta - Blockers

Heart Failure Medication Initiation and Titration



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

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

Drug	Initial Dose	Target Dose ¹	Dosage forms (mg)
BetaBlockers²			
Bisoprolol* (Monacor®, generic)	1.25mg daily	10mg daily	2.5, 5, 10
Carvedilol (Coreg®, generic)	3.125mg bid	25mg bid	6.25, 12.5, 25
Metoprolol tartrate³ (Lopressor®, generic)	6.25-12.5mg bid	100mg bid	25, 50, 100

¹Target doses based on clinical trials, but are limited to patient tolerance

²Agents are considered first line supported with clinical trials

³Clinical trials used CR/XL (metoprolol succinate) formulation, but not available in Canada. Metoprolol tartrate long acting available in 100mg and 200mg strengths only.

* Beta-selective: preferred in airway disease

Patient counseling tips:

- BB may worsen HF symptoms initially (particularly fatigue), but in long run will improve symptoms
- BB are started at low dose, titrated slowly to minimize adverse effects
- Self-monitoring for symptoms is key
- Daily weights are important; call your health care provider if your weight increases by:
 - 2-3 lbs in 1-2 days or 5 lbs in 1 week
- Stopping high dose BB abruptly may result in a rapid HR, exacerbation of HF symptoms—titrate dose down when possible

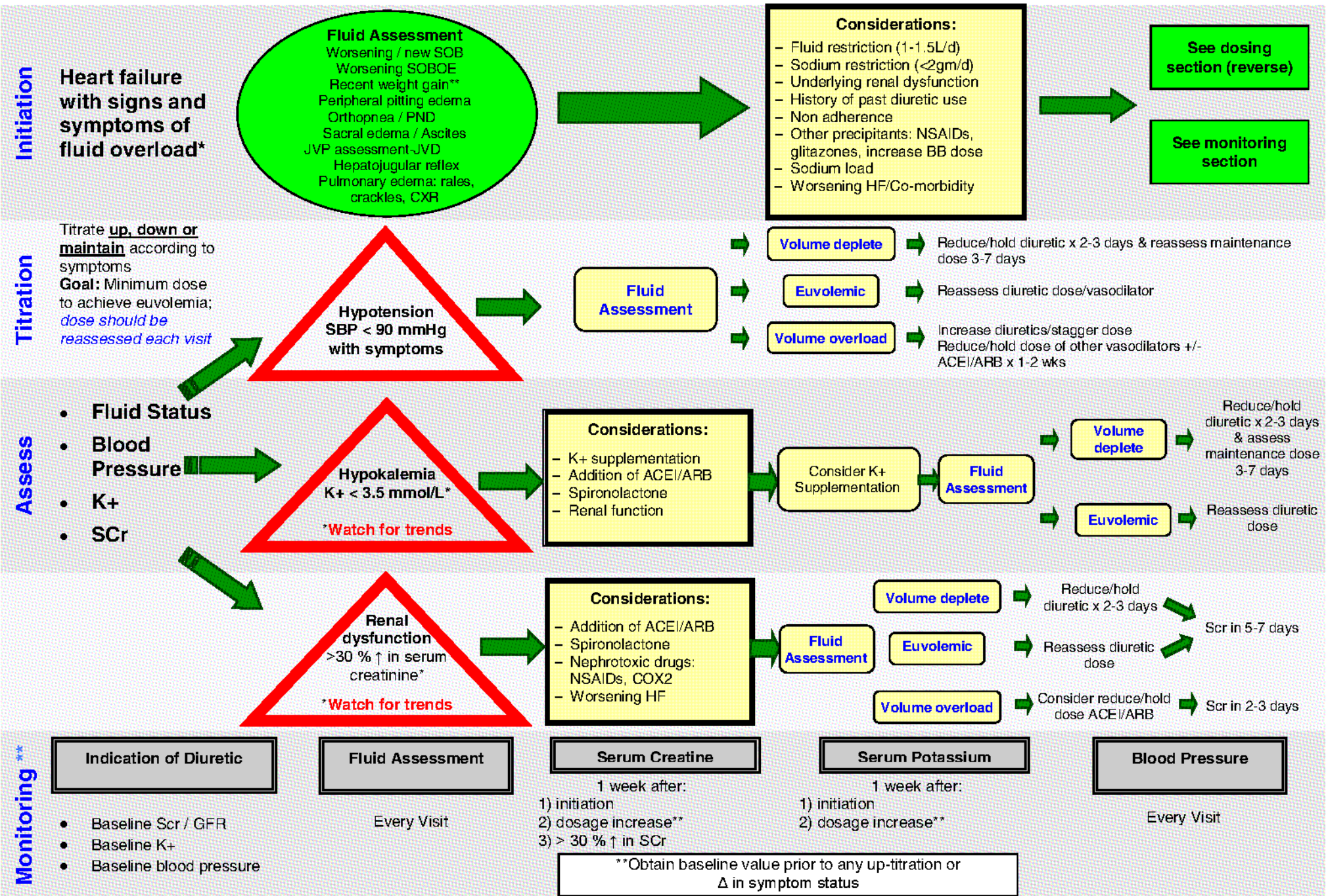
- Goal is to keep patient at target or maximally tolerated dose of evidence based medication*
- Clinical course of HF is variable—frequent reassessment of medication regime required*
- Complete and thorough history and physical assessment essential with each dose adjustment*
- Titrate one medication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

Key points:

- BBs are first line treatment for NYHA II-IV HF**
- Gradual titration of dosing is important to prevent HF exacerbations and improve tolerability*
 - fluid assessment is very important
 - titrate doses by 50-100% as tolerated every 2-4 weeks—individualize to patient
 - avoid reducing diuretic doses (unless adverse effects i.e. dehydration) while up-titrating
 - BB may be considered in patients with recent HF exacerbations as long as they are stable and euvolemic
- Compliance is increased with once daily dosing
- Consider beta-selective agents in airway disease*
- Given that the main side effects of BBs are **hypotension**, and **bradycardia**, assessment for reduction / sacrifice of other non mortality / morbidity reducing medications that precipitate these effects is warranted:
 - 1) Hypotension: nitrates, antihypertensive agents, hydralazine, diuretics
 - 2) Bradycardia: digoxin, verapamil, diltiazem, amiodarone, dronedarone

Diuretics

Heart Failure Medication Initiation and Titration



*Common signs and symptoms include new and worsening shortness of breath, weight gain, HF cough, orthopnea, paroxysmal nocturnal dyspnea, peripheral edema, ascites

**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

Drug	Initial Dose*	Maximum Daily Dose	Dosage forms (mg)
Loop Diuretics			
Furosemide (generic, Lasix®)	20-40mg OD-BID	200mg (caution > 120mg)	20mg, 40mg
Bumetanide (Burinex®)	0.5-1.0mg OD-BID	10mg	1mg, 5mg
Ethacrynic Acid (Edecrin®)	50-100mg	400mg (200mg BID)	25mg
Thiazide Diuretics			
Metolazone (Zaroxolyn®)	2.5mg daily	20mg	2.5mg
Hydrochlorothiazide (generic)	—	—	—
Indapamide (generic, Lozide®)	—	—	—
Chorthalidone (generic)	—	—	—
Potassium-sparing Diuretics			
Spironolactone (generic, Aldactone ®)	12.5-25mg	25mg	25mg, 100mg
Amiloride (generic)	—	—	—
Triamterene (generic)	—	—	—

*Doses of commonly used agents in heart failure listed only. All agents listed to indicate which agents have diuretic effects. Note that mild diuretic can be used in those with minimal fluid retention.

Key points:

- Diuretics are for **symptomatic relief—*should never be used alone***
- Goal of treatment—fluid balance control at the *minimum effective dose***
- Regular fluid assessment is key
- Encourage **daily weights** to monitor shifts in fluid balance
- If titration of dose is limited by **hypotension**:
 - reassess diuretic use*
 - consider staggering dosing with other antihypertensives or dosing at bedtime*

Other adverse effects:

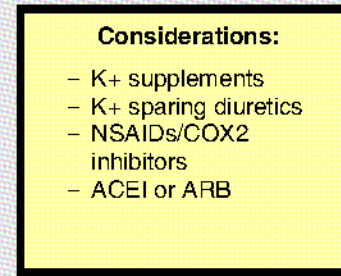
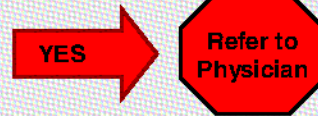
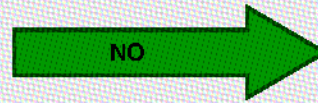
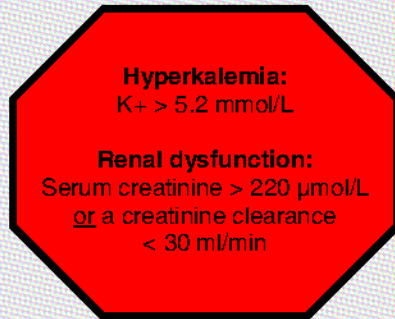
- Electrolyte disturbances:** ↓ K⁺ (except K⁺ sparing), Mg⁺, Na⁺, Ca⁺⁺ (except thiazides)
- ↑ **uric acid** may predispose patients to gout attacks
- Combination antihypertensive products which include diuretics—avoid combinations of multiple diuretic agents.
- If non-responsive consider:**
 - *adherence*
 - *increase sodium intake*
 - *NSAID / COX2 use*
 - *renal dysfunction (may requiring higher doses)*

- **Clinical course of HF is variable—frequent reassessment of medication regime required**
- **Complete and thorough history and physical assessment essential with each dose adjustment**
- **Small dose changes may result in significant clinical ones (i.e. symptoms, BW)**

Spironolactone/Eplerenone Heart Failure Medication Initiation and Titration

Initiation

Symptomatic heart failure (NYHA III-IV or high risk NYHA II*) on ACEI/BB and LVEF < 35%

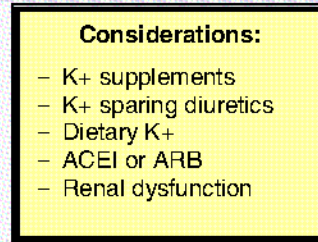


See key points

See monitoring section

Titration

Titrate monthly depending on tolerance
Goal: Target dose (see dosing below) or maximum tolerated dose



K+ 5.2-5.5

Stop K+ supplements, Reduce/hold spironolactone

Serum K+ in 3-5 days

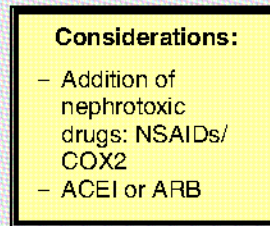
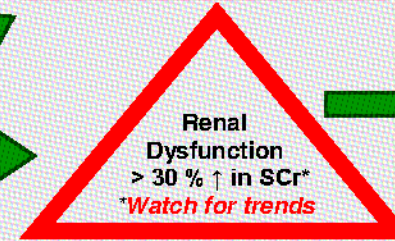
K+ > 5.5

Stop K+ supplements, Hold spironolactone Reduce/hold ACEI/ARB Refer to physician

Serum K+ in 2-3 days

Assess

- K+
- Scr



Fluid assessment

Volume deplete

Reduce/hold diuretic x 2-3 days Scr in 5-7 days

Euvolemic

Reduce/hold spironolactone Scr in 5-7 days

Consider re-challenge at lower dose

Volume overload

Reduce/hold spironolactone Scr in 2-3 days

Monitoring**



- Baseline Scr / GFR
- Baseline K+
- After initiation: 3 days, 1 week, 4 weeks, then monthly x 3
- Prior to any up-titration of Spironolactone, ACEI, or ARB
- 1 week post up-titration of Spironolactone, ACEI, or ARB
- With dehydration, illness, or change in symptom status

Key Points

- Spironolactone therapy is indicated in patients with LVEF < 35 % and NYHA III-IV HF
- *Eplerenone therapy is indicated in high risk NYHA II [aged >55 years and LVEF ≤30%, or LVEF ≤35% and QRS duration >130 ms] and recent hospitalization for HF or elevated BNP/NT-proBNP levels
- DOSING: The usual dose is 50 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. NOTE: Average doses achieved in clinical trials for spironolactone and eplerenone were 26mg and 40mg respectively.

- 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 (i.e. symptoms, BW)

- Triple therapy with ACEI + ARB + spironolactone should be avoided
- Recent evidence has documented significant issues with hyperkalemia and renal dysfunction and warrants close clinical monitoring
- Stop K+ supplementation and other K+ sparing diuretics at initiation of spironolactone
- Should be on max. medical therapy including ACEI/ARB prior to initiation

Other considerations: Gynecomastia (4-5% of males) with spironolactone