Chronic HFrEF · GDMT

Four pillars · Start all four early, titrate to target, then reassess the EF

ALL FOUR, LOW DOSE
beats two at target

THE FOUR PILLARS *every patient with HFrEF, unless contraindicated*

Pillar	Start	Target	Why
1 · ARNI sacubitril/valsartan or ACEi / ARB	24/26 or 49/51 mg BID	**97/103 mg BID**	Preferred over ACEi/ARB. **36-hour washout from an ACEi** before starting — angio-edema risk. Monitor K^+ and creatinine.
2 · Beta-blocker carvedilol, metoprolol succinate, bisoprolol	Carvedilol 3.125 mg BID	**Carvedilol 25 mg BID** Metoprolol succ. 200 mg Bisoprolol 10 mg	Only these three have mortality evidence in HFrEF — they are **not interchangeable** with other beta-blockers. Start when euvolemic, not during decompensation.
3 · MRA spironolactone or eplerenone	12.5–25 mg daily	**25–50 mg daily**	Avoid if **K^+ > 5.0** or eGFR < 30. Check K^+ and creatinine at 1 week, 4 weeks, then periodically.
4 · SGLT2 inhibitor dapagliflozin or empagliflozin	**10 mg daily — no titration needed**		Reduces hospitalization and cardiovascular death **regardless of diabetes**. Easiest pillar to start and the one most often forgotten.

HOW TO SEQUENCE *the modern approach is breadth before depth*

1. **Get all four classes on board at low dose within weeks**, rather than maximizing one drug before adding the next. Benefit appears early and is largely independent between classes.
2. **Start with the two that need no titration and are best tolerated** — the SGLT2 inhibitor and a low-dose beta-blocker or ARNI, guided by blood pressure and volume status.
3. **Titrate every 2 weeks** as blood pressure, heart rate, potassium, and renal function allow. Aim for target doses, or the maximally tolerated dose.
4. **Accept an asymptomatic creatinine rise of up to about 30%** and mild asymptomatic hypotension. These are not reasons to abandon therapy that reduces mortality.
5. **Do not stop GDMT during a hospitalization** unless there is shock, symptomatic hypotension, or worsening renal failure. Continuing therapy through admission improves outcomes; drugs stopped in hospital are often never restarted.

ADD-ONS & DEVICES *after the four pillars are optimized*

ADDITIONAL DRUGS

Loop diuretic for congestion — symptom control, not mortality. **Hydralazine plus isosorbide dinitrate** in self-identified Black patients with persistent NYHA III–IV symptoms on optimal therapy. **Ivabradine** if sinus rhythm and heart rate ≥ 70 despite a maximally tolerated beta-blocker. **Vericiguat** after a recent worsening event. **Digoxin** for symptoms and admission reduction only. **IV iron** for symptomatic iron deficiency.

DEVICES — REASSESS AFTER 3 MONTHS OF GDMT

ICD for primary prevention if **EF ≤ 35%**, NYHA II–III, on optimal therapy for **≥ 3 months**, with expected survival > 1 year. **CRT** if **EF ≤ 35%, sinus rhythm, LBBB with QRS ≥ 150 ms**. **Do not implant early** — a meaningful proportion recover EF above 35% on GDMT and avoid a device altogether.

MONITORING & FOLLOW-UP *the why behind each check*

Check	Interval and reason
Potassium & creatinine	**1–2 weeks after every uptitration** of ARNI/ACEi or MRA, then periodically. Catching hyperkalemia is what keeps the MRA on board long term.
Blood pressure & heart rate	Every visit — they define the room you have to titrate. Resting HR ≥ 70 in sinus rhythm on a maximal beta-blocker raises the ivabradine question.
Weight & volume status	Daily weights at home with a diuretic action plan. A 2–3 kg rise over days is congestion, not diet.
Repeat echo	After **3 months of optimized therapy** — this is the decision point for ICD or CRT, and many EFs improve.
NT-proBNP	Prognostic and useful for trajectory. **On sacubitril/valsartan trend NT-proBNP, not BNP** — neprilysin inhibition raises BNP by design.

TROUBLESHOOTING *the four reasons GDMT gets abandoned, and what to do instead*

Problem	Do this before stopping anything
Hyperkalemia K^+ 5.0–5.5	Stop potassium supplements, NSAIDs, and trimethoprim, and **consider a potassium binder** to keep the MRA on. Halve the dose before abandoning it. **Hold at K^+ > 5.5.**
Hypotension asymptomatic low BP	**Asymptomatic systolic in the 90s is acceptable.** Separate dosing times, cut the loop diuretic if euvolemic, and stop non-GDMT antihypertensives **before** touching a pillar.
Rising creatinine	Accept up to about a **30% rise** that plateaus. Check volume status — over-diuresis is commoner than the ACEi/ARNI. Recheck in 1–2 weeks rather than stopping.
Fatigue on the beta-blocker	Usually **transient over 2–4 weeks**. Warn in advance, slow the titration, and do not withdraw early — benefit builds over months.

HFmrEF & HFpEF *brief, because the questions come up together*

HFmrEF (EF 41–49%)

SGLT2 inhibitor is recommended. ARNI/ACEi/ARB, beta-blocker, and MRA **may be considered**, particularly toward the lower end of the range. Treat as HFrEF-like when the EF is trending down.

HFpEF (EF ≥ 50%)

SGLT2 inhibitor is the cornerstone; add an **MRA**, consider ARB/ARNI in selected patients. **Diuretics for congestion**, and treat the drivers: **hypertension, AF, obesity, sleep apnea**. Screen for **amyloidosis** if the phenotype fits.

PEARLS & PITFALLS

- **All four pillars at low dose beats two at target dose.** Breadth first, then titrate.
- **Only carvedilol, metoprolol succinate, and bisoprolol** have mortality benefit. Atenolol and metoprolol tartrate are not substitutes.
- **A 36-hour washout is mandatory** switching from an ACEi to sacubitril/valsartan, or you risk angio-edema.
- **On an ARNI, trend NT-proBNP rather than BNP.** Neprilysin inhibition raises BNP by design.
- **Wait 3 months before implanting a device.** Recovery of EF on GDMT is common and spares the patient a device.

References: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure (Circulation / JACC, 2022) · 2024 ACC Expert Consensus Decision Pathway for HFrEF · PARADIGM-HF, DAPA-HF, EMPEROR-Reduced.

Educational aid; verify doses against local protocol, renal function, and patient factors.