Heart Failure Treatment in 2026: A Clinical Overview

Written by The Life Science Feed Editorial Team · Published 25 July 2026 · Edited by William Lopes

> Heart failure affects 64 million people worldwide and carries a five-year mortality exceeding 50%. Four-pillar guideline-directed medical therapy -- ACEi/ARNi, beta-blockers, mineralocorticoid receptor antagonists, and SGLT2 inhibitors -- is now the standard of care in HFrEF, and SGLT2 inhibitors are guideline-recommended across all three ejection fraction phenotypes. This article covers the ESC classification framework, GDMT evidence, device therapy, emerging agents, and the implementation gap in real-world care.

KEY TAKEAWAYS

- Heart failure affects 64 million people globally; five-year mortality exceeds 50%, comparable to many cancers
- Four-pillar GDMT (ACEi/ARNi, beta-blockers, MRA, SGLT2 inhibitors) should be initiated and uptitrated in parallel in HFrEF, not sequentially
- STRONG-HF demonstrated rapid uptitration within two weeks of hospitalisation reduces 180-day mortality or rehospitalisation by 34%
- SGLT2 inhibitors (EMPEROR-Preserved, DELIVER) are now guideline-recommended across HFrEF, HFmrEF, and HFpEF
- Real-world implementation of all four GDMT pillars simultaneously remains below 25% in most health systems

Epidemiology and Burden

Heart failure affects an estimated 64 million people worldwide and remains the leading cause of hospitalisation in adults over 65 in high-income countries.1 Five-year mortality exceeds 50% across phenotypes, comparable to many cancers, yet the therapeutic landscape has shifted dramatically since 2019 with the introduction of SGLT2 inhibitors and the widespread adoption of four-pillar guideline-directed medical therapy (GDMT).

Classification: HFrEF, HFmrEF, and HFpEF

The 2021 ESC guidelines stratified heart failure by left ventricular ejection fraction (LVEF) into three phenotypes: heart failure with reduced ejection fraction (HFrEF, LVEF below 40%), heart failure with mildly reduced ejection fraction (HFmrEF, LVEF 40 to 49%), and heart failure with preserved ejection fraction (HFpEF, LVEF 50% or above).2 This distinction matters clinically because evidence for disease-modifying therapy has historically been strongest in HFrEF, though the evidence base for HFpEF has expanded considerably with SGLT2 inhibitor data.

The Four Pillars of GDMT in HFrEF

Current ESC and ACC/AHA guidelines recommend four drug classes as the foundation of HFrEF management, all with mortality benefit demonstrated in large randomised controlled trials:3

Drug Class	Key Agents	Key Trial	Relative Risk Reduction
ACEi / ARB / ARNi	Sacubitril/valsartan, ramipril	PARADIGM-HF	20% CV death/HF hospitalisation
Beta-blockers	Carvedilol, bisoprolol, metoprolol succinate	COPERNICUS, MERIT-HF	34% all-cause mortality
MRA	Spironolactone, eplerenone	RALES, EMPHASIS-HF	30% CV death/HF hospitalisation
SGLT2 inhibitors	Dapagliflozin, empagliflozin	DAPA-HF, EMPEROR-Reduced	25% CV death/worsening HF

All four classes should be initiated and uptitrated in parallel where tolerated, rather than sequentially. The STRONG-HF trial demonstrated that rapid uptitration to target doses within the first two weeks of hospitalisation reduced 180-day HF rehospitalisation or death by 34% compared with standard care.4

HFpEF: An Evolving Evidence Base

Until recently, no therapy had demonstrated mortality benefit in HFpEF. The EMPEROR-Preserved and DELIVER trials changed this: empagliflozin and dapagliflozin both reduced the composite of CV death and worsening heart failure in patients with LVEF above 40%, with consistent benefit across the ejection fraction spectrum.5 SGLT2 inhibitors are now guideline-recommended across all three HF phenotypes. Finerenone, a non-steroidal MRA approved for CKD and diabetes, is under evaluation in HFpEF through the FINEARTS-HF trial, with results expected to influence the 2025/2026 guideline update.

Device Therapy

Cardiac resynchronisation therapy (CRT) is indicated in patients with LVEF below 35%, NYHA class II to IV symptoms, and QRS duration above 150ms with LBBB morphology, where it reduces mortality and improves functional status. Implantable cardioverter-defibrillators (ICDs) reduce sudden cardiac death in HFrEF with LVEF at or below 35% after at least three months of optimal GDMT. The DANISH trial raised questions about ICD benefit in non-ischaemic cardiomyopathy, but current guidelines retain the indication pending further subgroup analysis.

Emerging Therapies in 2026

Several agents are entering or approaching clinical practice. Mavacamten, a cardiac myosin inhibitor approved for obstructive hypertrophic cardiomyopathy (HCM), is under investigation for broader HFpEF populations. Vericiguat, a soluble guanylate cyclase stimulator, received approval following the VICTORIA trial for patients hospitalised for worsening HF, representing a fifth potential pillar in high-risk HFrEF. Omecamtiv mecarbil, a cardiac myosin activator, showed modest benefit in GALACTIC-HF and remains under regulatory review in some jurisdictions.

Remote Monitoring and Integrated Care

Pulmonary artery pressure monitoring via the CardioMEMS HF system is approved by the FDA and EMA for NYHA class III patients and has demonstrated significant reductions in HF hospitalisation in the CHAMPION trial. Integration of remote haemodynamic data with structured multidisciplinary HF clinics represents the current best-practice model for ambulatory management, particularly in patients with recurrent hospitalisation.

Clinical Takeaway

The goal of heart failure management in 2026 is complete implementation of four-pillar GDMT as early as possible after diagnosis, with rapid uptitration and device therapy where indicated. SGLT2 inhibitors have transformed HFpEF

management. Emerging agents and remote monitoring technologies are expanding the toolkit, but the greatest unmet need remains closing the gap between evidence and real-world GDMT implementation rates, which remain below 25% for all four pillars simultaneously in most health systems.

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