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Dear provider of pharmaceutical services,

The American College of Cardiology (ACC) has a long history of developing documents to provide members with guidance on both clinical and non-clinical topics relevant to cardiovascular (CV) care. Since the publication of the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment (ECDP), numerous clinical trials have been reported, providing updated knowledge to inform the clinical management of patients with heart failure with reduced ejection fraction (HFrEF). In addition, more knowledge is now available regarding biomarkers and imaging, management of comorbidities, and the mitigation of difficulties encountered in care coordination. Lastly, the considerable impact of the coronavirus disease 2019 (COVID-19) pandemic on outpatient management of chronic disease states such as HFrEF justifies its consideration in the updated document.

This update can serve as interim guidance while we wait for the comprehensive and definitive heart failure (HF) guideline update under development by the ACC. The following ten (10) issues in HFrEF are addressed in the 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment:

1. How to initiate, add, or switch therapies to new evidence-based guideline-directed treatments for HFrEF.	• Established guideline-directed medical therapy (GDMT) includes: angiotensin receptor-neprilysin inhibitors (ARNIs), angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), beta-blockers, loop diuretics, aldosterone antagonists, hydralazine/isosorbide dinitrate (HYD/ISDN), and ivabradine. • In patients with newly diagnosed Stage C HFrEF, an ARNI/ACEI/ARB or beta-blocker should be started in any order. Initiation of an ARNI/ACEI/ARB is often better tolerated when the patient is still congested ("wet"), whereas beta-blockers are better tolerated when the patient is less congested ("dry"). • Only guideline-recommended beta-blockers (carvedilol, metoprolol succinate, or bisoprolol) should be used in patients with HFrEF. • Among angiotensin antagonists, ARNIs are preferred agents. If making the transition from an ACEI to an ARNI, a 36-hour washout period should be strictly observed to avoid angioedema. A delay is not required when switching from an ARB to an ARNI. • Renal function and potassium should be checked within 1-2 weeks of initiation or dose up-titration of ACEI/ARB/ARNI. • Before initiating ivabradine, the dose of an evidence-based beta-blocker should be increased to the target dose as long as excessive bradycardia is not an issue (sinus rhythm with a resting heart rate ≥70 beats/min). • Sodium-glucose cotransporter-2 (SGLT-2) inhibitors should be considered for HFrEF ≤40% with or without diabetes and in patients with New York Heart

	Association (NYHA) class II-IV. SGLT-2 should be administered in conjunction with a background GDMT.
2. How to achieve optimal therapy given multiple drugs for HF, including the augmented clinical assessment that may trigger additional changes in guideline-directed therapy.	• To achieve the maximal benefits of GDMT in patients with chronic HFrEF, therapies must be initiated and titrated to maximally tolerated doses. Doses higher than those studied in randomized controlled trials are generally not recommended. • Adjustment of therapies should occur every 2 weeks, with monitoring of renal function, potassium, and blood pressure. More rapid titration is reasonable in clinically stable patients. • Diuretics should be added as needed and dose should be titrated to achieve decongestion. • It is not necessary to achieve the target or maximally tolerated doses of other drugs before adding aldosterone antagonists or SGLT2 inhibitors. • African-American patients should receive hydralazine/ isosorbide dinitrate (HYD/ISDN) once target or maximally tolerated doses of beta-blocker, ARNI/ACEI/ARB, and aldosterone antagonists are achieved. • Abnormal renal function and/or hyperkalemia are common barriers to initiation and titration of GDMT. Patients with hyperkalemia should be educated about a low potassium diet. Potassium binders may be considered. • Socioeconomic barriers pose a major barrier to the use of ARNI, SGLT-2 inhibitors, and ivabradine. In these cases, financially feasible options should be considered. • An echocardiogram should be repeated 3-6 months after achieving target doses of therapy for consideration of an implantable cardioverter-defibrillator (ICD)/cardiac resynchronization therapy (CRT). • For patients with the recovery of LVEF to >40%, GDMT should be continued in the absence of a defined, reversible cause for HFrEF.
3. When to refer to an HF specialist.	• Clinical triggers for referral include persistent or worsening symptoms, adverse clinical events, or other features suggesting that the patient is at high risk for disease progression or death.
4. How to address challenges of care coordination.	• Delivering care for HF requires a team-based approach.
5. How to improve medication adherence.	• Medication adherence should be assessed regularly. Interventions helping with adherence include patient education, medication management, pharmacist co-management, cognitive behavioral therapies, medication taking reminders, and incentives to improve adherence.
6. What is needed in specific patient cohorts: African Americans, older adults, and the frail.	• Newer treatments (ARNI/SGLT-2/Ivrabadine) are recommended in African Americans as part of their HF GDMT. • Data is limited for drugs or devices in patients older than 80 years of age. Target doses for GDMT should be attempted in older patients, with close surveillance for any adverse drug reactions. • Potential interventions in frailty include multidomain rehabilitation along with cognitive and nutritional support programs to accompany standard GDMT for HFrEF.
7. How to manage your patients'	• Whenever possible, generic equivalents for GDMT should be considered. • Pharmacists can help navigate insurance coverage and patient assistance programs to make sure that patients have access to the appropriate medications.

costs and access to HF medications.	
8. How to manage the increasing complexity of HF.	• The 2021 ECDP for Optimization of Heart Failure Treatment, establishes several guiding principles that can improve decision-making and adherence to GDMT, which, in turn, are likely to improve patient outcomes.
9. How to manage common comorbidities.	• To optimally manage patients with comorbidities and improve clinical outcomes, clinicians must increasingly consider the diagnosis and treatment of relevant comorbidities alongside the use of evidence-based HF therapies.
10. How to integrate palliative care and the transition into hospice care.	• Goals of care should be addressed during the course of illness with HF and expectations should be calibrated to guide timely decisions. End-of-life care in HF involves meticulous management of HF therapies, and palliative care consultation may help with other noncardiac symptoms such as pain.

Please refer to the 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment for additional important details.

Remember that medical literature is dynamic and is continuously changing as new scientific knowledge is developed. We exhort the frequent revision of treatment guidelines to assure that your recommendations are consistent with the most updated information.

PharmPix is committed to the health and wellness of our members. It is our priority to offer high-quality services and support practices for health promotion and diseases prevention. If you have any questions or wish to have more information regarding this document, you can call us at 787-522-5252, extension 137. In addition, know that you can access our recent communications at our providers' portal: https://www.pharmpix.com/providers/.

Regards,

PharmPix Clinical Department

References:

- Maddox, T., Januzzi, J., Allen, L., Breathett, K., Butler, J., & Davis, L. et al. (2021). 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction. Journal Of The American College Of Cardiology, 77(6), 772-810. doi: 10.1016/j.jacc.2020.11.022.