

Heart Failure – Diagnosis and Management

Effective Date: July 26, 2023

Scope

This guideline provides recommendations for the diagnosis and management of people aged \geq 19 years with suspected or confirmed heart failure in the ambulatory primary care setting. Given that heart failure is associated with reduced life expectancy, advanced care planning and palliative care are also addressed.

For specific guidance on heart failure in *acute care settings* refer to the Canadian Cardiovascular Society Heart Failure guidelines.

Key Recommendations

- Echocardiogram (ECHO) is the gold standard for assessing structural and/or functional cardiac abnormalities and determining ejection fraction to guide treatment planning.
- BNP and NT-proBNP tests have a high sensitivity for the detection of heart failure (HF) and can help with diagnosis while waiting for echocardiogram.
- There are cornerstone therapies that improve clinical outcomes (e.g., reduced hospitalizations, and mortality, improved quality of life) in patients with HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF) necessitating their rapid implementation in eligible patients.
- NEW: It is recommended that in the absence of contraindications, patients with HFrEF be treated with combination therapy including one medication from each of the following categories: Angiotensin receptor-neprilysin inhibitors (ARNI) [or Angiotensin-converting enzyme inhibitors (ACEI)/Angiotensin receptor blockers (ARB)]; beta-blockers (β-blockers); Mineralocorticoid receptor antagonists (MRA); and Sodium-glucose cotransporter-2 inhibitors (SGLT2i). These four medications should be initiated and titrated in parallel as quickly as possible.
- Patient and caregiver education about the importance of self-monitoring and early identification of disease decompensation is crucial to avoid hospitalization and to inform acute treatment.
- Consider referral to a heart function clinic or a multi-disciplinary chronic disease management clinic, where available.
- Initiate advance care planning discussions early in the disease course.
- Incorporate a palliative approach as the disease progresses and/or as per patient preference.

Definition

The new universal definition of heart failure (HF):

- Signs and/or symptoms caused by a structural and/or functional cardiac abnormality based on ECHO findings AND
- Elevated natriuretic peptide levels (BNP or NT-proBNP^{*}) OR objective evidence of cardiogenic, pulmonary or systemic congestion.¹

B -Type natriuretic peptide or N-terminal pro B-type natriuretic peptide prohormone of BNP





Epidemiology

According to 2020/2021 data,[†] 2% of the population in BC is affected by HF (prevalence of 137,082), with 18,512 new cases (incidence) in 2020/21.

Diagnosis

Diagnosis begins with a suspicion of HF based on clinical history (risk factors, symptoms) and physical examination, and is then confirmed with natriuretic peptide testing and ECHO.^{2,3} See Figure 1: Diagnosis of Heart Failure.

Edema, fatigue, and dyspnea are typical but not specific symptoms of HF; atypical presentations may need to be considered, particularly for women, elderly and obese patients.^{4,5}

Initial investigations should be targeted to confirm or exclude HF, and to identify systemic disorders that might affect its development or progression (e.g., thyroid dysfunction).

Table 1: Risk factors, Symptoms and Signs of Heart Failure

Risk Factors	Symptoms	Signs
 Hypertension Atrial fibrillation Coronary artery disease Diabetes Obesity Valvular heart disease Preeclampsia Dyslipidemia Family history of cardiomyopathy Poor health behaviors (e.g., smoking, heavy alcohol or substance use, inactivity) 	 Dyspnea, including shortness of breath Fatigue Leg swelling Confusion (especially in the elderly) Orthopnea Paroxysmal nocturnal dyspnea 	 Weight gain (over 2 kg/week) Low blood pressure (BP) Heart rate > 100 BPM Lung crackles Elevated jugular venous pressure Heart murmur 3rd heart sound, 4th heart sound (S3, S4) Displaced apex Positive abdominal jugular reflux Peripheral edema

British Columbia Ministry of Health [data provider]. BC Observatory for Population and Public Health [publisher]. Chronic Disease Dashboard. Available at: http://www.bccdc.ca/health-info/disease-system-statistics/chronic-disease-dashboard



Abbreviations: **BNP** – B -Type Natriuretic Peptide, **CBC** – Complete Blood Count, **CXR** – Chest X-Ray, **ECG** – Electrocardiogram, **NT-proBNP** – N-terminal pro B-type natriuretic peptide

Common etiologies for heart failure include tachyarrhythmia, valvular disease, coronary artery disease, and left ventricular hypertrophy. There are several less common etiologies.

N-terminal pro B-type natriuretic peptide Testing

- Both BNP and NT-proBNP tests have a high sensitivity and clinical utility for the detection of HF and similar clinical utility. In BC, the laboratory determines which test is performed. In most instances in this guideline, the terms BNP and NT-proBNP are used interchangeably.
- An abnormally high BNP test result does not eliminate the need for cardiac imaging, but in many cases it may allow treatment to begin while waiting for ECHO.
- Interpretation of BNP values differ significantly depending on acute versus ambulatory settings.
- In the ambulatory setting, even a mildly elevated BNP (BNP > 50, NTproBNP > 125 ng/L) indicates need for further investigation and treatment.
- BNP is **NOT** recommended to screen asymptomatic patients without risk factors, or for interval monitoring of disease severity or therapeutic response.

Table 2: Natriuretic Peptide cut points for the diagnosis of HF

(adapted from Table 9. Natriuretic peptide cut points for the diagnosis of HF of the 2017 CCS Heart Failure Guidelines)

	Age (years)	HF is unlikely	HF is possible but other diagnoses need to be considered	HF is very likely
Acute setting				
BNP	All	< 100 ng/L	100-400 ng/L	> 400 ng/L
NT-proBNP	< 50	< 300 ng/L	300-450 ng/L	> 450 ng/L
	50-75	< 300 ng/L	450-900 ng/L	> 900 ng/L
	> 75	< 300 ng/L	900-1800 ng/L	> 1800 ng/L
Ambulatory care setting				
BNP	All	< 50 ng/L		
NT-proBNP	All	< 125 ng/L		

BNP – N-terminal pro B-type natriuretic peptide; **HF** – heart failure; **NT-proBNP** – N-terminal propeptide BNP.

Echocardiography

ECHO should be performed in all patients with suspected HF to assess cardiac structure, quantify systolic and diastolic function, and to facilitate treatment planning and prognostication. There is regional variation in timely access to ECHO in BC. Delays in obtaining ECHO should not delay initiation of treatment in cases where HF is likely.

Though not a replacement for ECHO, an estimate of left ventricular function may be obtained through alternate imaging modalities:

- Thallium and Sestamibi (MIBI) scan especially in those patients where ischemia may be the underlying etiology.
- Multi Gated Acquisition Scan (MUGA) or radionuclide angiography especially for patients with chronic obstructive pulmonary disease or obesity, which may affect ECHO image quality.

Ejection Fraction

Left ventricular ejection fraction (LVEF) is the primary measure of left ventricular systolic function. Normal LVEF is approximately 60%. Management of HF is based upon LVEF.

Figure 2: Classifications of Ejection Fraction*

	HF with improved EF (HFimpEF) HF with a baseline LVEF ≤ 40%, a ≥ 10-point increase from baseline LVEF, and a second measurement of LVEF >		
HFrEF (LVEF ≤ 40%)	HFmrEF (LVEF = 41-49%)	HFpEF (LVEF ≥ 50%)	
50%	14% of patients		

Abbreviations: **EF** – Ejection Fraction; **HF** – Heart Failure; **LVEF** – Left Ventricular Ejection Fraction. **HFrEF** – Heart Failure with reduced Ejection Fraction, **HFmrEF** – Heart Failure with mild reduced Ejection Fraction, **HFpEF** – Heart Failure with preserved Ejection Fraction

^{*}Adapted from Bozkurt B et al. Eur J Heart Fail. 2021;23:352

New York Heart Association (NYHA) Functional Classifications

Determine NYHA functional classification in order to guide therapy and determine prognosis.

ClassDegree of Symptoms with Physical Activity and at RestI - mildAsymptomatic with ordinary physical activity, no limitations on physical activity, comfortable at restII - mildSymptoms with ordinary activity, slight limitations on physical activity, comfortable at restIII - moderateSymptoms with less than ordinary activity, noticeable limitations on physical activity, and comfortable at restIV - severeSymptoms at rest, unable to perform any activity without symptoms

Table 3: New York Heart Association (NYHA) Functional Classifications³

Management

Patients with HF benefit from frequent assessments and continuity of care, ideally with multi-disciplinary support.

Self-Monitoring and Health Behavior Changes⁶

HF care may benefit from the patient and their caregiver's understanding of, and participation in, optimal care in a culturally safe context. Educate the patient and their caregiver(s) on health behavior changes (see Appendix A: Health Behavior Modifications and Self-monitoring Recommendations), HF Zones (see Appendix B: Heart Failure Zones Reference Guide), and medications (see HealthLinkBC: *Heart Failure Medications*, RxFiles: SADMANS medications in heart failure). See Patient, Family and Caregiver Resources section for a list of patient resources.

Pharmacologic Management

For all patients with HF *regardless* of LVEF:

- Initiate appropriate treatment for HF (even while awaiting ECHO).
- Once an ECHO is completed, treatment is guided by LVEF.
- Consider diuretic therapy to relieve volume overload and for symptom management.
- Consider initiation of a sodium-glucose cotransporter-2 inhibitor (SGLT2i) and mineralocorticoid receptor antagonist (MRA) to improve cardiovascular outcomes.
- If recently discharged from hospital or experiencing worsening HF symptoms, rapid initiation and up-titration of guideline directed medical therapy (GDMT) reduces cardiovascular mortality and future HF hospitalization.
- GDMT refers to the combination pharmacotherapy used for the treatment of patients with HFrEF and HFpEF.
- Those who fall under the HFimpEF category have a 56% decrease in mortality risk and reduction in hospitalizations.^{5,7} However, there is evidence of relapse when GDMT is reduced or eliminated, so continuing with GDMT is recommended.⁸
- Treat co-morbidities like atrial fibrillation, hypertension, diabetes mellitus, renal disease, and sleep apnea based on established BCGuidelines.ca.
- Review medications for intended and unintended effects (e.g., polypharmacy, drug-drug interactions, and aggravation of co-morbid conditions).
- Although studies demonstrating the benefits of HF therapy did not include frail elderly patients, age alone should not preclude attempts to optimize GDMT.⁹

Heart Failure with Reduced Ejection Fraction (LVEF \leq 40%)

- Patients with HFrEF should be treated early with a combination of four medications, one from each of the following classes: angiotensin receptor-neprilysin inhibitor (ARNI), beta-blocker (β-blocker), MRA, and SGLT2 inhibitor (SLGTi). This GDMT/quadruple therapy has been shown to have substantial and sustained reductions in mortality, HF hospitalizations, and symptom burden, even at low doses.^{5,10-17}
- It is preferable to titrate medication doses simultaneously and as quickly as possible ("in-parallel" approach), rather than titrating one medication before initiating an additional agent ("strict sequential" approach).¹⁸
- The principles behind treatment are to: treat early, use combination of all four medications, up titrate rapidly, and aim for target dose of each medication.
- Consider IV iron therapy for patients with HFrEF who meet all of the following criteria: ejection fraction \leq 40%, serum ferritin < 100 µg/L or between 100-299 µg/L, and TSAT < 20%.¹⁸
- See Appendix C: Commonly Used Drugs for in Heart Failure Care for dosages, Pharmacare coverage and therapeutic considerations for drug classes used in the management of patients with HF. The appendix also includes titration and renal function considerations. Consider consultation with your local specialist or a RACE line clinician when further guidance is needed.

Figure 3: GDMT for Heart Failure Reduced Ejection Fraction (HFrEF) LVEF \leq 40%



Treat co-morbidities, prescribe diuretics at minimal effective doses to relieve volume overload, consider IV iron therapy, as appropriate. Support self-management, education and advance care and planning.

Abbreviations: ACEI – Angiotensin Converting Enzyme Inhibitors, ARB – Angiotensin Receptor Blocker, ARNI – Angiotensin Receptor-Neprilysin Inhibitor (ARNI), GDMT – Guideline Directed Medical Therapy, MRA – Mineralocorticoid Receptor Antagonist, SGLT2i – Sodium-Glucose Cotransporter-2 Inhibitor

Heart Failure with Mildly Reduced Ejection Fraction (EF 41-49%) and Heart Failure with Preserved Ejection Fraction (EF \ge 50%)

- To improve symptoms:
 - Use *minimal effective* diuretic dose to achieve and maintain euvolemia.
- To improve outcomes:
 - Initiate an SGLT2i (e.g., empagliflozin and dapagliflozin). SGLT2i therapy reduces hospitalizations as well as allcause and cardiovascular mortality across age, sex, race, HF and EF classification.^{5,19,20}
 - Consider MRA (in all eligible patients) to reduce HF hospitalization.²¹
 - In select patients, consider initiating an angiotensin receptor-neprilysin inhibitor (ARNI). In large randomized clinical trials, patients with HFmrEF had fewer hospitalizations when treated with an ARNI compared to an Angiotensin Converting Enzyme Inhibitors (ACEI).

Figure 4: GDMT for Heart Failure with Mildly Reduced Ejection Fraction (LVEF 41-49%) and Heart Failure with Preserved Ejection Fraction (LVEF \geq 50%)



Abbreviations: ACEI – Angiotensin Converting Enzyme Inhibitors, ARB – Angiotensin Receptor Blocker, ARNI – Angiotensin Receptor-Neprilysin Inhibitor (ARNI), GDMT – Guideline Directed Medical Therapy, MRA – Mineralocorticoid Receptor Antagonist, SGLT2i – Sodium-Glucose Cotransporter-2 Inhibitor

Reassessment and Follow-up

- For all patients, regardless of their EF status, periodic assessment of renal function and potassium is recommended. Renal function and electrolytes should be checked with each adjustment of diuretic, MRA, and/or ACEI/ARB/ARNI dose.
- For patients with HFrEF, EF should be reassessed after maximally tolerated GDMT has been achieved, and before deciding on further treatment options.
- Once clinically optimized, *routine surveillance* with ECHO is *not indicated* unless the patient's clinical status changes. A follow-up ECHO may be warranted in 3-5 years.

Clinical follow-up frequency recommendations:

1-4 weeks or as clinically indicated:

 Those classified with NYHA III or IV symptoms, recent HF hospitalization, during titration of HF medications, new onset heart failure, complications of HF therapy (e.g., rising creatinine, hypotension), needing to down-titrate or discontinue ß-blockers or ACEI/ARB, severe concomitant and active illness (e.g., COPD, frailty), frequent implantable cardioverter defibrillator (ICD) firings.

1-6 Months:

• Those with no clear features of high or low risk.

6-12 months:

- NYHA I or II.
- No hospitalizations in past year.
- No recent changes in medications, receiving optimal medical/device HF therapies.

Worsening HF:

- By the time a person reports worsening symptoms of fluid overload or has overt signs of fluid overload on clinical exam, they may have been progressing over days or even weeks. They should be addressed as soon as possible to avoid further decline, hospitalization or even death.
- Identify triggers and treat appropriately. Treat volume overload, optimize therapies and reinforce education.
- If a patient fails to improve, consider referral to a heart failure clinic and/or specialist, including RACE.

Indications for Referral

Refer to a Cardiologist/Internist:

- Persistent symptoms or signs of HF despite attempts TO OPTIMIZE medical therapy.
- To aid in diagnosis and management of HF where valvular disease or coronary disease is a significant contributing factor.
- If a rare underlying etiology is suspected.
- For assistance with diagnosis or management, refer the patient to a heart function clinic or a multi-disciplinary chronic disease management clinic, if available.

Refer to a Heart Function Clinic, if available, for:

- Management after a recent admission or repeated admissions to hospital.
- Assessment of asymptomatic left ventricular dysfunction.
- Assistance with multidisciplinary HF care including education on lifestyle management skills.
- Consideration for procedural interventions including PCI, surgery, and implantable devices.
- See Cardiac Services BC for Heart Function Clinics in BC

Device Management:

- Decisions about device management (e.g., implantable cardioverter defibrillator [ICD], cardiac resynchronization therapy [CRT]) are complex and involve a cardiologist/internist/cardiac electrophysiologist/Heart Function Clinic.
- Appropriate ICD utilization is associated with improved mortality, but does not improve quality of life. By contrast, CRT is associated with improved mortality and quality of life (i.e., improved symptom status and functional capacity) in properly selected individuals.¹⁸

ICD may be considered in patients with one of the following:

- · History of hemodynamically significant sustained ventricular arrhythmia;
- Ischemic cardiomyopathy and LVEF ≤ 35% (measured at least 1 month after acute myocardial infarction, or 3 months post coronary artery revascularization); or
- Non-ischemic cardiomyopathy and LVEF ≤ 35% (measured at least 9 months after optimal medical therapy).

ICD **should not be** considered in patients with active NYHA Class IV symptoms.

CRT may be considered in patients with NYHA class II – IV symptoms despite maximally tolerated HF therapies, with a QRS duration \ge 130 ms, and LVEF \le 35%.

Palliative Care and End of Life Care

Palliative care offers the potential to improve quality of life for cardiac patients with advanced disease. Unfortunately, many patients perceive palliative care in a negative context, equating it with hospice care. As a result, very few cardiac patients receive appropriate palliative care. For those who do, it typically occurs quite late in the disease trajectory, limiting the benefit. Do not delay advance care planning conversations or palliative care for a patient with serious illness who has physical, psychological, social, or spiritual distress because they are pursuing disease-directed treatment.

A palliative care approach addresses management of pain, dyspnea, other symptoms, and prioritizes quality of life. This may include support for the patient's family and caregivers.

Some resources include:

- Supportive Cardiology Tool a clinician tool which focuses on delivery of care from the primary care perspective.
- What Really Matters Now, a comprehensive resource for patients with advanced heart failure.
- BCGuidelines.ca: Palliative Care for the Patient with Incurable Cancer or Advanced Disease.
- HealthLinKBC: Palliative Care and MOST forms

Table 4: Reasons to Consider Palliative Care Consultation in Heart Failure*

Any one of the following:

- Two or more hospital admissions for HF in the prior 6 months
- Two or more emergency department visits for HF in the prior 6 months
- · Progressing disease or substantial worsening of prognosis or quality of life
- NYHA class III or IV symptoms
- · Ventricular arrhythmias refractory/not amenable to medication
- Substantial worsening or difficulty in controlling other physical or psychological symptoms from heart failure
- Patient or family request

At least one of the following:

- Ineligible or not interested in advanced heart failure therapies (outpatient inotropic infusion, left ventricular assist device, cardiac transplantation)
- · Consideration for high-risk procedures (cardiac surgery, thoracic surgery)
- Consideration for ICD
- · Consideration for feeding tube placement, tracheostomy, or initiation of renal replacement therapy
- Comorbidity (chronic renal failure, diabetes, cancer, stroke, cancer, human immunodeficiency virus, pulmonary fibrosis, oxygen-dependent chronic obstructive pulmonary disease)
- · Previous/current intensive care/cardiac intensive care unit admission or CPR within past year
- Negative response to the 'surprise' question: "Would you be surprised if the patient died within 1 year?" (although the 'surprise' question does not have great predictive value in non-cancer populations)
- · Significant worsening of comorbidity (e.g., oxygen requirement)
- · Disagreements, uncertainty, or ethical concerns concerning treatment decisions or resuscitation preferences
- Perceived emotional, spiritual, or relational distress to patient, family, or surrogate
- Functional or cognitive decline, loss of independence, complex care requirements
- Withdrawal or significant reduction of evidence-based medication

AND

^{*}Adapted from Slawnych, New Dimensions in Palliative Care Cardiology, CJC, 2018²²

Resources

References

- Bozkurt B, Coats AJ, Tsutsui H, Abdelhamid M, Adamopoulos S, Albert N. Universal Definition and Classification of Heart Failure: A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. Journal of Cardiac Failure 2021 Apr. 1;27(4):387–413.
- 2. Roger VL. Epidemiology of Heart Failure. Circulation Research. 2021 May 14;128(10):1421-34.
- 3. Chamberlain AM, Boyd CM, Manemann SM, Dunlay SM, Gerber Y, Killian JM, et al. Risk Factors for Heart Failure in the Community: Differences by Age and Ejection Fraction. Am J Med. 2020 Jun;133(6):e237–48.
- 4. Ezekowitz JA, O'Meara E, McDonald MA, Abrams H, Chan M, Ducharme A, et al. 2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure. Canadian Journal of Cardiology. 2017 Nov;33(11):1342–433.
- 5. 2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure: Executive Summary ScienceDirect [Internet]. [cited 2022 Jun 8]. Available from: https://www-sciencedirect-com.ezproxy.hlth.gov.bc.ca/science/article/abs/pii/S1071916422000756
- 6. Yu DSF, Li PWC, Li SX, Smith RD, Yue SCS, Yan BPY. Effectiveness and Cost-effectiveness of an Empowerment-Based Self-care Education Program on Health Outcomes Among Patients With Heart Failure: A Randomized Clinical Trial. JAMA Netw Open. 2022 Apr 1;5(4):e225982.
- He Y, Ling Y, Guo W, Li Q, Yu S, Huang H, et al. Prevalence and Prognosis of HFimpEF Developed From Patients With Heart Failure With Reduced Ejection Fraction: Systematic Review and Meta-Analysis. Frontiers in Cardiovascular Medicine [Internet]. 2021 [cited 2023 Apr 18];8. Available from: https://www.frontiersin.org/articles/10.3389/fcvm.2021.757596
- 8. Halliday BP, Wassall R, Lota AS, Khalique Z, Gregson J, Newsome S, et al. Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial. The Lancet. 2019 Jan 5;393(10166):61–73.
- 9. Stolfo D, Sinagra G, Savarese G. Evidence-based Therapy in Older Patients with Heart Failure with Reduced Ejection Fraction. Card Fail Rev. 2022 Apr 28;8:e16.
- 10. Miller RJH, Howlett JG, Fine NM. A Novel Approach to Medical Management of Heart Failure With Reduced Ejection Fraction. Can J Cardiol. 2021 Apr;37(4):632-43.
- 11. Zannad F, Ferreira JP, Pocock SJ, Anker SD, Butler J, Filippatos G, et al. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. The Lancet. 2020 Sep 19;396(10254):819–29.
- 12. Vaduganathan M, Claggett BL, Jhund PS, Cunningham JW, Pedro Ferreira J, Zannad F, et al. Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomised controlled trials. The Lancet. 2020 Jul 11;396(10244):121–8.
- 13. Sodium–Glucose Cotransporter-2 Inhibitors in Patients With Heart Failure: A Systematic Review and Meta-analysis: Annals of Internal Medicine: Vol 0, No 0 [Internet]. [cited 2022 May 20]. Available from: https://www.acpjournals.org/doi/10.7326/M21-4284?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_ pub%3dpubmed
- 14. Cardoso R, Graffunder FP, Ternes CMP, Fernandes A, Rocha AV, Fernandes G, et al. SGLT2 inhibitors decrease cardiovascular death and heart failure hospitalizations in patients with heart failure: A systematic review and meta-analysis. eClinicalMedicine [Internet]. 2021 Jun 1 [cited 2022 Apr 14];36. Available from: https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00213-3/fulltext
- McMurray JJV, Packer M. How Should We Sequence the Treatments for Heart Failure and a Reduced Ejection Fraction?: A Redefinition of Evidence-Based Medicine. Circulation. 2021 Mar 2;143(9):875–7.
- 16. Sharma A, Verma S, Bhatt DL, Connelly KA, Swiggum E, Vaduganathan M, et al. Optimizing Foundational Therapies in Patients With HFrEF. JACC: Basic to Translational Science. 2022 Mar;S2452302X21003594.
- 17. Bauersachs J. Heart failure drug treatment: the fantastic four. European Heart Journal. 2021 Feb 7;42(6):681-3.
- 18. McDonald M, Virani S, Chan M, Ducharme A, Ezekowitz JA, Giannetti N, et al. CCS/CHFS Heart Failure Guidelines Update: Defining a New Pharmacologic Standard of Care for Heart Failure With Reduced Ejection Fraction. Canadian Journal of Cardiology. 2021 Apr 1;37(4):531–46.
- 19. Ghionzoli N, Gentile F, Del Franco AM, Castiglione V, Aimo A, Giannoni A, et al. Current and emerging drug targets in heart failure treatment. Heart Fail Rev. 2022 Jul 1;27(4):1119–36.
- 20. Karamichalakis N, Xanthopoulos A, Triposkiadis F, Paraskevaidis I, Tsougos E. Reshaping Treatment of Heart Failure with Preserved Ejection Fraction. Journal of Clinical Medicine. 2022 Jan;11(13):3706.
- 21. Kjeldsen SE, von Lueder TG, Smiseth OA, Wachtell K, Mistry N, Westheim AS, et al. Medical Therapies for Heart Failure With Preserved Ejection Fraction. Hypertension. 2020 Jan;75(1):23–32.
- 22. Slawnych M. New Dimensions in Palliative Care Cardiology. Canadian Journal of Cardiology. 2018 Jul 1;34(7):914-24.

Abbreviations:

ACEI	Angiotensin-converting enzyme inhibitors
ARNI	Angiotensin Receptor-neprilysin Inhibitor
BNP	B -Type Natriuretic Peptide
CRT	Cardiac Resynchronization Therapy
CVD	Cardiovascular Disease
ECG	Electrocardiogram
ECHO	Echocardiogram
GDMT	Guideline Directed Medical Therapy
HF	Heart Failure
HFmrEF	HF Mild Reduced Ejection Fraction
HFpEF	HF Preserved Ejection Fraction
HFrEF	HF Reduced Ejection Fraction
ICD	Implantable Cardioverter Defibrillator
LVEF	Left Ventricular Ejection Fraction
MIBI	Thallium and Sestamibi scan
MRA	Mineralocorticoid Receptor Antagonist
MUGA	Multi Gated Acquisition Scan
NT-proBNP	N-terminal pro B-type natriuretic peptide Prohormone of BNP
NYHA	New York Heart Association
SGLT2i	Sodium-Glucose Cotransporter-2 Inhibitor
TSH	Thyroid Stimulating Hormone

Practitioner Resources

- **Cardiac Services BC**, www.cardiacbc.ca generates and shares accurate, current, and relevant HF information for health care professionals and patients in BC.
- **RACE: Rapid Access to Consultative Expertise Program** RACE means timely telephone advice from specialist for Physicians, Medical Residents, Nurse Practitioners, Midwives, all in one phone call.
 - Monday to Friday 0800 1700
 - Online at www.raceapp.ca or though Apple or Android mobile device. For more information on how to download RACE mobile applications, please visit www.raceconnect.ca/race-app/
 - Local Calls: 604-696-2131 | Toll Free: 1-877-696-2131
 - For a complete list of current specialty services visit the Specialty Areas page.
- **BC Ministry of Health Advance Care Planning**, HealthLinkBC Planning for Advance Care. Each health authority also has an Advance Care Planning website.

Patient, Family and Caregiver Resources

- CardiacServicesBC (www.cardiacbc.ca): Multiple patient handouts available.
- HealthLinkBC: Heart Failure Overview
- HealthLinkBC: Heart Failure: Taking Medicines Properly
- HealthLinBC: Monitoring and Medicines for Heart Failure
- Island Health Community Virtual Care: Community Virtual Care provides support to people with a range of medical conditions. Registered nurses help you to manage your condition from the comfort of your home. All the tools needed are loaned to you at no cost.
- Canadian Heart Failure Society: Living Well with Heart Failure
- Canadian Heart Failure Society: How to manage your heart failure medication ON SICK DAYS?
- RxFiles: SADMANS medications in heart failure
- Heartlife Foundation: Patients
- Heart Failure Medications: A Patient and Caregiver Guide
- Heart and Stroke Foundation: Heart Failure

Diagnostic Fee Code

428 Heart Failure

Appendices

- Appendix A: Health Behavior Modifications and Self-monitoring Recommendations
- Appendix B: Heart Failure Zones Reference Guide
- Appendix C: Commonly used Drugs in Heart Failure Care

Associated Documents

The following documents accompany this guideline:

- Heart Function Clinic Referral Form
- What to Do with Heart Failure Medications When I am Sick
- List of Contributors

This guideline is based on scientific evidence current as of the effective date.

This guideline was developed by the Guidelines and Protocols Advisory Committee in collaboration with the Provincial Laboratory Medicine Services and adopted under the *Medical Services Act* and the *Laboratory Services Act*.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- · recommend actions that are sufficient and efficient, neither excessive nor deficient
- · permit exceptions when justified by clinical circumstances

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Disclaimer

The Clinical Practice Guidelines (the guidelines) have been developed by the guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem. **We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.**

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Appendix A: Health Behavior Modifications and Self-monitoring Recommendations



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Appendix B: Heart Failure Zones Reference Guide

Check Weight Daily

- Weigh yourself in the morning before breakfast. Write it down. Compare your weight today to your weight yesterday.
- Keep the total amount of fluids you drink to only 6 to 8 glasses each day. (6-8 glasses equals 1500-2000 mL or 48-64 oz)
- Take your medicine exactly how your doctor said.
- Check for swelling in your feet, ankles, legs, and stomach.
- Eat foods that are low in salt or salt-free.
- Balance activity and rest periods.

Which Heart Failure Zone Are You Today? Green, Yellow, or Red



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Appendix C: Commonly Used Drugs for in Heart Failure Care

Generic Name <i>Trade name</i> Dosage form and strengths	Recommended Adult Dose ^A	Approx. Cost per month ^B	PharmaCare Coverage ^c	Adverse Effects ^D	Therapeutic Considerations
Angiotensin Converting En	zyme Inhibitors (ACE-I)				Contraindication: avoid in pregnancy,
Ramipril <i>Altace, G</i> Caps: 1.25, 2.5, 5, 10, 15 mg	Canadian HF guideline ⁵ : Initial: 1.25 – 2.5 mg BID Target: 5 mg BID Once daily dosing3: Initial: 1.25 mg daily Target: 10 mg daily	\$4	Regular benefit RDP (Reference drug) 15 mg: non- benefit	Common • Dry cough (8- 12%) • Hyperkalemia Less Common • Angioedema • Precipitation of	 bilateral renal artery stenosis Monitor symptoms of postural hypotension, SCr and potassium at initiation of therapy and periodically. Reduce initial dose by 50% if on concomitant diuretics (risk of hypotension with hypovolemia). Cough associated with ACE-I is dry, backing, and non-productive and
Enalapril <i>Vasotec, G</i> Tabs: 2.5, 5, 10, 20 mg	Initial: 1.25 – 2.5 mg BID Target: 10 mg BID (20 mg BID in NYHA IV)	\$15	Partial benefit RDP	renal failure in patients with renovascular disease, volume depletion or	 typically occurs within months of initiation of therapy. Risk factors for hyperkalemia include renal dysfunction, diabetes and concomitant use of potassium
Lisinopril Prinivil, Zestril, G Tabs: 5, 10, 20 mg	Initial: 2.5 – 5 mg daily Target: 20 – 35 mg daily	\$6	Partial benefit RDP	concomitant NSAID use	 supplements, potassium-sparing diuretics, or potassium-containing salts. For patients who experience reduced
Perindopril <i>Coversyl, G</i> Tabs: 2, 4, 8 mg	Initial: 2 – 4 mg daily Target: 4 – 8 mg daily	\$7	Partial benefit RDP		antihypertensive effect hear the end of the 24-hour dosing interval, divide total daily dose into two equal doses given every 12 hours or increase once daily
Trandolapril <i>Mavik, G</i> Caps: 0.5, 1, 2, 4 mg	Initial: 1 – 2 mg daily Target: 4 mg daily	\$8	Partial benefit RDP		 dose. Longer-acting ACEIs such as perindopril or ramipril might be associated with less hypotension in patients
Angiotensin receptor block	er (ARB)				with chronic HF, particularly in older
Candesartan <i>Atacand, G</i> Tabs: 4, 8, 16, 32 mg	Initial: 4 – 8 mg daily Target: 32 mg daily	\$8	Limited Coverage RDP (Reference Drug) 4 mg: non- benefit	Hypotension, renal impairment, hyperkalemia, angioedema (rare)	 patients⁵ An increase in serum creatinine or decrease in estimated glomerular filtration rate (eGFR) of up to 30% in th absence of oliguria is not unexpected when an ACEI or ARB is introduced; if the increase stabilizes at 30%, there is no immediate need to decrease the drug dose, but closer long-term
Valsartan <i>Diovan, G</i> Tabs: 40, 80, 160, 320 mg	Initial: 40 mg BID Target: 160 mg BID	\$7	Limited Coverage RDP (Reference Drug)		monitoring might be required⁵

Generic Name <i>Trade name</i> Dosage form and strengths	Recommended Adult Dose ^A	Approx. Cost per month ^B	PharmaCare Coverage ^c	Adverse Effects ^D	Therapeutic Considerations			
Angiotensin receptor nepri	Angiotensin receptor neprilysin inhibitor (ARNI)							
Sacubitril-valsartan Entresto Tabs: 24/26, 49/51, 97/103 mg	Initial: 24/26 mg - 49/51 mg BID Target: 97/103 mg BID	\$250	Limited Coverage (Currently limited to Internal Medicine and Cardiology special authority, consider RACE consultation to obtain approval)	 Hypotension (18%) Hyperkalemia Increased SCr AKI Dizziness Angioedema Cough (9%) 	 Stop ACEI 36h prior to starting ARNI to minimize potential for life-threatening angioedema Wash out period not necessary when switching from ARB Valsartan in this combination tablet is more bioavailable than valsartan in other marketed formulations; Valsartan 26, 51 and 103 mg is equivalent to 40, 80 and 160 mg in other marketed tablet formations respectively. Monitoring: renal function and electrolytes Contraindications: Pregnancy and lactation Circulating levels of BNP may increase after initiation of sacubitril-valsartan. Interpret BNP with caution^{7,8} 			
Beta-blockers								
Bisoprolol ^E <i>Monocor, G</i> Tabs: 5, 10 mg	Initial: 1.25 mg daily Target: 10 mg daily	\$4	Regular benefit	Orthostatic hypotension, worsening heart	 Beta blockers should be started at low doses and increased slowly. Transient fluid retention might occur with 			
Metoprolol ^E Lopressor, Betaloc, G IR Tabs: 25, 50, 100 mg SR tabs: 100, 200 mg	IR tabs: Initial: 12.5 – 25 mg BID Target: 100 mg BID SR tabs: Initial: use IR tab Target: 200 mg daily	IR: \$8 SR: \$12	Regular benefit	failure, worsening fluid retention, bronchospasm, dyspnea, bradycardia, malaise, fatigue, asthenia, erectile dysfunction, masking of	failure, worsening fluid retention, bronchospasm, dyspnea, bradycardia, malaise, fatigue, asthenia, erectile dysfunction, masking of	 Initiation or up titration of beta blockers and might require assessment of diuretic dosage. If concomitant reactive airways disease is present, consider using more selective B-1 blockade (e.g. bisoprolol) If indicated as per practice guidelines, consider ICD/CRT implantation to mitigate risk of bradycardia 		
Carvedilol <i>Coreg, G</i> Tabs: 3.125, 6.25, 12.5, 25 mg	Initial: 3.125 mg BID Target: 25-50 mg BID	\$15	Limited Coverage	symptoms of hypoglycemia.				

Generic Name <i>Trade name</i> Dosage form and strengths	Recommended Adult Dose ^A	Approx. Cost per month ^B	PharmaCare Coverage ^c	Adverse Effects ^D	Therapeutic Considerations
Mineralocorticoid receptor	antagonist (MRA)				
Spironolactone <i>Aldactone, G</i> Tabs: 25, 100 mg	Initial: 12.5 mg daily Target: 25 – 50 mg daily	\$3	Regular benefit	Hyperkalemia, dehydration, nausea, gynecomastia (usually reversible upon discontinuation).	 Monitor serum creatinine and potassium 3 and 7 days after initiation or titrating the dose. Repeat every 1-3 months once stable. Concomitant use with ACEI, ARB and potassium supplements can lead to hyperkalemia
Eplerenone <i>Inspra, G</i> Tabs: 25, 50 mg	Initial: 25 mg daily Target: 50 mg daily	\$75	Non-benefit	Hyperkalemia, dehydration, dizziness, diarrhea, nausea.	 diuretic effect, worsening renal function, hyperkalemia Advantage of eplerenone over spironolactone is lack of binding to progesterone and androgen receptors which is associated with drug induced gynecomastia, breast pain and impotence.⁶ Contraindications: Pregnancy Contraindications specific to eplerenone: Use with strong inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole, ritonavir, nelfinavir, clarithromycin, telithromycin, nefazodone) can significantly increase eplerenone levels.
Sodium Glucose Transport	2 (SGLT2) inhibitors				
Dapagliflozin <i>Forxiga, G</i> Tabs: 5, 10 mg	Initial: 10 mg daily Target: 10 mg daily	\$22	Regular benefit	Genital mycotic infections (highest risk for women,	 Contraindications: pregnancy, renal impairment (refer to product monograph for details), dialysis.
Empagliflozin Jardiance Tabs: 10, 25 mg	Initial: 10 mg daily Target: 10 mg daily	\$90	Non-benefit for HF indicationhx of genital mycotic infections, uncircumcised men); typically can be managed with antifungals and do not require discontinuation of therapySGLT2 inhib individuals v have factors ketoacidosis20Non-benefit for HF individuals v have factors ketoacidosis• SGLT2 inhib individuals v have factors ketoacidosis20Non-benefit for HF indication• SGLT2 inhib individuals v have factors ketoacidosisLimited Coverage for treatment of type 2 diabetes mellitis• SGLT2 inhib individuals v have factors therapy	 SGLT2 inhibitors should not be used in individuals with type 1 diabetes or in individuals with type 2 diabetes who have factors predisposing to diabetic ketoacidosis 	
Canagliflozin ^E <i>Invokana</i> Tabs: 100, 300 mg	Initial: 100 mg daily Target: 100 – 300 mg daily	\$95	Non-benefit	reduction of eGFR, which generally resolves within 1-3 months AKI Hypoglycemia (rare in absence of other hypoglycemics) Diabetic ketoacidosis	

Generic Name <i>Trade name</i> Dosage form and strengths	Recommended Adult Dose ^A	Approx. Cost per month ^B	PharmaCare Coverage ^c	Adverse Effects ^D	Therapeutic Considerations
Vasodilators					
Hydralazine [⊧] <i>G</i> Tabs: 10, 25, 50 mg	Initial: 10 – 37.5 mg TID Target: 75 – 100 mg TID to QID	\$20	Regular benefit	Hypotension, GI complaints, SLE- like syndrome, tachyphylaxis, may worsen oxygen demand.	 Should be used in combination with isosorbide dinitrate or nitroglycerin.
Isosorbide Dinitrate [⊧] G Tabs: 10, 30 mg	Initial: 10 – 20 mg TID Target: 40 mg TID	\$10	Regular benefit	Headache, flushing, hypotension.	 Should be used in combination with hydralazine. Different from isosorbide mononitrate (long-acting formulation). Contraindication: use with phosphodiesterase-5 inhibitors (increased risk of hypotension)
Diuretics					
Furosemide <i>Lasix, G</i> Tabs: 20, 40, 80 mg	Initial: 20 – 40 mg daily Max: 200 mg/d	\$2	Regular benefit	Dehydration, hypokalemia, hypocalcemia, nausea, hypotension, azotemia, hypomagnesemia,	 Concomitant lithium can lead to lithium toxicity. Concomitant digoxin can lead to digoxin toxicity if K+ depleted
Metolazone <i>Zaroxolyn</i> Tabs: 2.5 mg	Initial: 2.5 mg daily Max: 20 mg/d	\$7	Regular benefit		 Concomitant use of oral corticosteroids may enhance hypokalemia effect of diuretic. Concomitant NSAIDs can lead to reduced diuretic effect, increased renal toxicity
Digoxin					
Digoxin <i>Toloxin, G</i> Tabs: 0.0625, 0.125 mg	Initial: 0.0625 - 0.125 mg daily Max: Titrate to lowest effective dose due to high toxicity profile. Recommend starting at lowest dose.	\$11	Regular benefit	Digoxin toxicity: Apical slowing < 60bpm, AV conduction block, supraventricular tachycardia, confusion, forgetfulness, hallucinations, dizziness, psychosis, nightmares, color changes, halos, anorexia, nausea, vomiting, diarrhea, abdominal pain	 Routine digoxin levels are not required and titrating to digoxin levels has not been tested in clinical trials. Reasons for digoxin levels: Concern about compliance Suspected toxicity Inadequate therapy despite high doses Drug interactions If levels are required, should be drawn minimum 6 hours post dose (due to long distribution t1/2). Steady state achieved in 5-7 days for normal half-life; 1-3 weeks renal dysfunction. Digoxin has a narrow therapeutic index and there is a large overlap between toxic and therapeutic doses Digoxin levels < 1.2 ng/mL are associated with less treatment related morbidity. Can cause atrial and ventricular arrhythmias particularly in the presence of hypokalemia and/or worsening renal function and levels should be monitored accordingly

Generic Name <i>Trade name</i> Dosage form and strengths	Recommended Adult Dose ^A	Approx. Cost per month ^B	PharmaCare Coverage ^c	Adverse Effects ^D	Therapeutic Considerations
Sinus node inhibitor					
Ivabradine <i>Lancora</i> Tabs: 5, 7.5 mg	Initial: 2.5 – 5 mg BID Max: 7.5 mg BID	\$110	Limited coverage	Bradycardia, hypertension, heart block, sinoatrial arrest, atrial fibrillation	 Has no direct effect on blood pressure, myocardial contractility, or renal function and as such is well tolerated in patients who are unable to initiate or titrate beta blockers for these reasons Typical reductions in resting sinus heart rate after treatment with beta blockers range from 10-15 bpm, with little change (< 5 bpm) between low and high doses. This consideration might assist in the decision to use further medications for sinus heart rate control Ivabradine may be considered for patients with either stable or decompensated chronic HFrEF who are intolerant of β-blockers, symptoms despite guideline-directed medical treatments and with a resting heart rate in sinus rhythm of > 70 bpm Ivabradine selectively inhibits the depolarizing Ifcurrent in the sinus node. It thus requires sinus rhythm to provide its pharmacological effect.

Abbreviations: **BID** twice a day; bpm beats per minute; **CAP** capsules; **CR** controlled release; **CRT** cardiac resynchronization therapy; **G** generics; **IR** immediate release; **ODT** oral dissolving tablet; **ICD** implantable cardioverter-defibrillator CRT **LA** long acting; **SCr** serum creatinine; **SR** sustained release; **Tab** tablets; **XR** extended release

- A For normal renal and hepatic function. Consult product monograph for detailed dosing instructions and dose adjustments for unique patient populations
- B Drugs costs are average retail cost of the generic, when available. Current as of Feb 2022 and does not include retail markups or pharmacy fees.
- C PharmaCare coverage as of Feb 2022 (subject to revision). Regular Benefit: Eligible for full reimbursement*. Limited Coverage: Requires Special Authority to be eligible for reimbursement*. Non-benefit: Not eligible for reimbursement. *Reimbursement is subject to the rules of a patient's PharmaCare plan, including any deductibles. In all cases, coverage is subject to drug price limits set by PharmaCare. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy. html for further information.
- D Not an exhaustive list. Check the product monograph (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp) or an interaction checker (e.g., Lexicomp^(c)) before prescribing
- E Medications are used off-label for heart failure.

References:

- 1. Gray Jean, editor. e-Therapeutics+ [Internet]. Ottawa (ON): Canadian Pharmacists Association; c20194 [Accessed Feb 2022.
- 2. e-CPS [Internet]. Ottawa, ON: Canadian Pharmacists Association; c20194 [Accessed April 3, 2019].
- 3. Jobson MD. UpToDate [Internet]. Waltham, MA: UpToDate Inc.; c2019 [Accessed April 3, 2019]
- 4. Health Canada Drug Product Database Product Monographs. Ottawa, ON: Health Canada; 20194 [Accessed April 3, 2019].
- 5. McDonald M, Virani S, Chan M, et al. CCS/CHFS Heart Failure Guidelines Update: Defining a New Pharmacologic Standard of Care for Heart Failure with Reduced Ejection Fraction. *Canadian Journal of Cardiology*. 2021;37(4):531-546. doi: 10.1016/j.cjca.2021.01.017
- Barnes BJ, Howard PA. Eplerenone: A Selective Aldosterone Receptor Antagonist for Patients with Heart Failure. Annals of Pharmacotherapy. 2005;39(1):68-76. doi:10.1345/aph.1e306
- 7. Caution Needed When Interpreting BNP in Sacubitril/Valsartan Treatment. Mass General Advances in Motion. Published September 3, 2020. Accessed February 2, 2022. https://advances.massgeneral.org/cardiovascular/journal.aspx?id=1656
- Myhre PL, Vaduganathan M, Claggett B, et al. B-Type Natriuretic Peptide During Treatment with Sacubitril/Valsartan. Journal of the American College of Cardiology. 2019;73(11):1264-1272. doi: 10.1016/j.jacc.2019.01.018