# Appendix C: Commonly Used Drugs in Heart Failure Care

| Generic Name<br>*Trade name*<br>Dosage form and strengths | Recommended Adult Dose[A] | Approx. Cost per month[B] | PharmaCare Coverage[C] | Adverse Effects[D] | Therapeutic Considerations |
|---|---|---|---|---|---|
| **Angiotensin Converting Enzyme Inhibitors (ACE-I)** | | | | | • Contraindication: avoid in pregnancy, bilateral renal artery stenosis<br>• Monitor symptoms of postural hypotension, SCr and potassium at initiation of therapy and periodically.<br>• Reduce initial dose by 50% if on concomitant diuretics (risk of hypotension with hypovolemia).<br>• Cough associated with ACE-I is dry, hacking, and non-productive and typically occurs within months of initiation of therapy.<br>• Risk factors for hyperkalemia include renal dysfunction, diabetes and concomitant use of potassium supplements, potassium-sparing diuretics, or potassium-containing salts.<br>• For patients who experience reduced antihypertensive effect near the end of the 24-hour dosing interval, divide total daily dose into two equal doses given every 12 hours or increase once daily dose.<br>• Longer-acting ACEIs such as perindopril or ramipril might be associated with less hypotension in patients with chronic HF, particularly in older patients[5]<br>• An increase in serum creatinine or decrease in estimated glomerular filtration rate (eGFR) of up to 30% in the 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 monitoring might be required[5] |
| **Ramipril**<br>*Altace, G*<br>Caps: 1.25, 2.5, 5, 10, 15 mg | Canadian HF guideline[5]:<br>**Initial:** 1.25 – 2.5 mg BID<br>**Target:** 5 mg BID<br><br>Once daily dosing3:<br>**Initial:** 1.25 mg daily<br>**Target:** 10 mg daily | $4 | Regular benefit<br>RDP<br>(Reference drug)<br><br>15 mg: non-benefit | Common<br>• Dry cough (8-12%)<br>• Hyperkalemia<br><br>Less Common<br>• Angioedema<br>• Precipitation of renal failure in patients with renovascular disease, volume depletion or concomitant NSAID use | |
| **Enalapril**<br>*Vasotec, G*<br>Tabs: 2.5, 5, 10, 20 mg | **Initial:** 1.25 – 2.5 mg BID<br>**Target:** 10 mg BID<br>(20 mg BID in NYHA IV) | $15 | Partial benefit<br>RDP | | |
| **Lisinopril**<br>*Prinivil, Zestril, G*<br>Tabs: 5, 10, 20 mg | **Initial:** 2.5 – 5 mg daily<br>**Target:** 20 – 35 mg daily | $6 | Partial benefit<br>RDP | | |
| **Perindopril**<br>*Coversyl, G*<br>Tabs: 2, 4, 8 mg | **Initial:** 2 – 4 mg daily<br>**Target:** 4 – 8 mg daily | $7 | Partial benefit<br>RDP | | |
| **Trandolapril**<br>*Mavik, G*<br>Caps: 0.5, 1, 2, 4 mg | **Initial:** 1 – 2 mg daily<br>**Target:** 4 mg daily | $8 | Partial benefit<br>RDP | | |
| **Angiotensin receptor blocker (ARB)** | | | | | |
| **Candesartan**<br>*Atacand, G*<br>Tabs: 4, 8, 16, 32 mg | **Initial:** 4 – 8 mg daily<br>**Target:** 32 mg daily | $8 | Limited Coverage<br>RDP<br>(Reference Drug)<br><br>4 mg: non-benefit | Hypotension, renal impairment, hyperkalemia, angioedema (rare) | |
| **Valsartan**<br>*Diovan, G*<br>Tabs: 40, 80, 160, 320 mg | **Initial:** 40 mg BID<br>**Target:** 160 mg BID | $7 | Limited Coverage<br>RDP<br>(Reference Drug) | | |

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|---|---|---|---|---|---|
| **Angiotensin receptor neprilysin inhibitor (ARNI)** | | | | | |
| **Sacubitril-valsartan**<br>*Entresto*<br>Tabs: 24/26, 49/51, 97/103 mg | **Initial:** 24/26 mg - 49/51 mg BID<br>**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%)<br>• Hyperkalemia<br>• Increased SCr<br>• AKI<br>• Dizziness<br>• Angioedema<br>• Cough (9%) | • Stop ACEI 36h prior to starting ARNI to minimize potential for life-threatening angioedema<br>• Wash out period not necessary when switching from ARB<br>• 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.<br>• Monitoring: renal function and electrolytes<br>• Contraindications: Pregnancy and lactation<br>• Circulating levels of BNP may increase after initiation of sacubitril-valsartan. Interpret BNP with caution[7,8] |
| **Beta-blockers** | | | | | |
| **Bisoprolol**[E]<br>*Monocor, G*<br>Tabs: 5, 10 mg | **Initial:** 1.25 mg daily<br>**Target:** 10 mg daily | $4 | Regular benefit | Orthostatic hypotension, worsening heart failure, worsening fluid retention, bronchospasm, dyspnea, bradycardia, malaise, fatigue, asthenia, erectile dysfunction, masking of symptoms of hypoglycemia. | • Beta blockers should be started at low doses and increased slowly. Transient fluid retention might occur with initiation or up titration of beta blockers and might require assessment of diuretic dosage.<br>• If concomitant reactive airways disease is present, consider using more selective B-1 blockade (e.g. bisoprolol)<br>• If indicated as per practice guidelines, consider ICD/CRT implantation to mitigate risk of bradycardia |
| **Metoprolol**[E]<br>*Lopressor, Betaloc, G*<br>IR Tabs: 25, 50, 100 mg<br>SR tabs: 100, 200 mg | IR tabs:<br>**Initial:** 12.5 – 25 mg BID<br>**Target:** 100 mg BID<br><br>SR tabs:<br>**Initial:** use IR tab<br>**Target:** 200 mg daily | IR: $8<br><br>SR: $12 | Regular benefit | | |
| **Carvedilol**<br>*Coreg, G*<br>Tabs: 3.125, 6.25, 12.5, 25 mg | **Initial:** 3.125 mg BID<br>**Target:** 25-50 mg BID | $15 | Limited Coverage | | |

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| **Mineralocorticoid receptor antagonist (MRA)** | | | | | |
| **Spironolactone**<br>*Aldactone, G*<br>Tabs: 25, 100 mg | **Initial:** 12.5 mg daily<br>**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.<br>• Concomitant use with ACEI, ARB and potassium supplements can lead to hyperkalemia<br>• Concomitant use with NSAIDs: reduce diuretic effect, worsening renal function, hyperkalemia<br>• 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]<br>• Contraindications: Pregnancy<br>• Contraindications specific to eplerenone: Use with strong inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole, ritonavir, nelfinavir, clarithromycin, telithromycin, nefazodone) can significantly increase eplerenone levels. |
| **Eplerenone**<br>*Inspra, G*<br>Tabs: 25, 50 mg | **Initial:** 25 mg daily<br>**Target:** 50 mg daily | $75 | Non-benefit | Hyperkalemia, dehydration, dizziness, diarrhea, nausea. | |
| **Sodium Glucose Transport 2 (SGLT2) inhibitors** | | | | | |
| **Dapagliflozin**<br>*Forxiga, G*<br>Tabs: 5, 10 mg | **Initial:** 10 mg daily<br>**Target:** 10 mg daily | $22 | Regular benefit | Genital mycotic infections (highest risk for women, hx of genital mycotic infections, uncircumcised men); typically can be managed with antifungals and do not require discontinuation of therapy<br><br>Temporary reduction of eGFR, which generally resolves within 1-3 months<br><br>AKI<br><br>Hypoglycemia (rare in absence of other hypoglycemics)<br><br>Diabetic ketoacidosis (0.1%) | • Contraindications: pregnancy, renal impairment (refer to product monograph for details), dialysis.<br>• 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 |
| **Empagliflozin**<br>*Jardiance*<br>Tabs: 10, 25 mg | **Initial:** 10 mg daily<br>**Target:** 10 mg daily | $90 | Non-benefit for HF indication<br><br>Limited Coverage for treatment of type 2 diabetes mellitis | | |
| **Canagliflozin**[E]<br>*Invokana*<br>Tabs: 100, 300 mg | **Initial:** 100 mg daily<br>**Target:** 100 – 300 mg daily | $95 | Non-benefit | | |

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| **Vasodilators** | | | | | |
| **Hydralazine**[E]<br>*G*<br>Tabs: 10, 25, 50 mg | **Initial:** 10 – 37.5 mg TID<br>**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**[E]<br>*G*<br>Tabs: 10, 30 mg | **Initial:** 10 – 20 mg TID<br>**Target:** 40 mg TID | $10 | Regular benefit | Headache, flushing, hypotension. | • Should be used in combination with hydralazine.<br>• Different from isosorbide mononitrate (long-acting formulation).<br>• Contraindication: use with phosphodiesterase-5 inhibitors (increased risk of hypotension) |
| **Diuretics** | | | | | |
| **Furosemide**<br>*Lasix, G*<br>Tabs: 20, 40, 80 mg | **Initial:** 20 – 40 mg daily<br>Max: 200 mg/d | $2 | Regular benefit | Dehydration, hypokalemia, hypocalcemia, nausea, hypotension, azotemia, hypomagnesemia, | • Concomitant lithium can lead to lithium toxicity.<br>• Concomitant digoxin can lead to digoxin toxicity if K+ depleted.<br>• Concomitant use of oral corticosteroids may enhance hypokalemia effect of diuretic.<br>• Concomitant NSAIDs can lead to reduced diuretic effect, increased renal toxicity |
| **Metolazone**<br>*Zaroxolyn*<br>Tabs: 2.5 mg | **Initial:** 2.5 mg daily<br>Max: 20 mg/d | $7 | Regular benefit | | |
| **Digoxin** | | | | | |
| **Digoxin**<br>*Toloxin, G*<br>Tabs: 0.0625, 0.125 mg | **Initial:** 0.0625 – 0.125 mg daily<br>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.<br>• Reasons for digoxin levels:<br>o Concern about compliance<br>o Suspected toxicity<br>o Inadequate therapy despite high doses<br>o Drug interactions<br>• 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.<br>• Digoxin has a narrow therapeutic index and there is a large overlap between toxic and therapeutic doses<br>• Digoxin levels < 1.2 ng/mL are associated with less treatment related morbidity.<br>• Can cause atrial and ventricular arrhythmias particularly in the presence of hypokalemia and/or worsening renal function and levels should be monitored accordingly |

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|---|---|---|---|---|---|
| **Sinus node inhibitor** | | | | | |
| **Ivabradine**<br>*Lancora*<br>Tabs: 5, 7.5 mg | **Initial:** 2.5 – 5 mg BID<br>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<br>• 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<br>• 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<br>• 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:


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