



Appendix B: Commonly used Drugs in Heart Failure Care^{1, 2, 3}

Generic Name (trade name) (strengths and dosage form)	Adult Dosages	Cost per 30 days*	PharmaCare Coverage	Common Adverse Effects	Therapeutic Considerations & Contraindications	Drug Interactions
Angiotensin Converting Enzyme Inhibitors (ACE-I)						
ramipril Altace®, G (IR capsule: 1.25, 2.5, 5, 10 mg)	Initial: 1.25–2.5 mg BID Target: 5 mg twice BID Max dose: 10 mg BID	\$8-12	Regular Coverage	Hypotension, hyperkalemia, dry cough, renal insufficiency, angioedema, skin rashes, taste disturbance, proteinuria, neutropenia, headache, dizziness.	Titrate dosage slowly by 50–100% every 2–4 weeks. Monitor serum creatinine and potassium 7–14 days after initiation of therapy or dose changes. Contraindication: Avoid in pregnancy.	Diuretics: hypotension. Potassium-sparing diuretics, potassium supplements, angiotensin receptors blockers: hyperkalemia. NSAIDs: reduced hypotensive effect, fluid retention, renal failure. Lithium: increased lithium levels and toxicity.
enalapril Vasotec®, G (IR tablet: 2.5, 5, 10, 20 mg)	Initial: 1.25–2.5 mg BID Target: 10 mg BID Max dose: 20 mg BID	\$35	Regular Coverage			
captopril G (IR tablet: 6.25, 12.5, 25, 50, 100 mg)	Initial: 6.25–12.5 mg TID Target: 50 mg TID Max dose: 150 mg TID	\$12–78	Regular Coverage			
lisinopril Prinivil®, Zestril®, G (IR tablet: 5, 10, 20 mg)	Initial: 2.5–5 mg once daily Target: 20–40 mg once daily Max dose: 80 mg once daily	\$8–69	Regular Coverage			
perindopril Coversyl® (IR tablet: 2, 4, 8 mg)	Initial: 2 mg once daily Target: 8 mg once daily Max dose: 8 mg once daily	\$17	Regular coverage			
trandolapril Mavik® (IR capsule: 0.5, 1, 2, 4 mg)	Initial: 0.5–1 mg once daily Target: 4 mg once daily Max dose: 4 mg once daily	\$9–31	Regular coverage			

Generic Name (trade name) (strengths and dosage form)	Adult Dosages	Cost per 30 days*	PharmaCare Coverage	Common Adverse Effects	Therapeutic Considerations & Contraindications	Drug Interactions
Angiotensin Receptor Blockers (ARB)						
candesartan Atacand®, G (IR tablet: 4, 8, 16, 32 mg)	Initial: 4 mg once daily Target: 32 mg once daily	\$9–10	Special Authority (IR tablet: 8, 16, 32 mg) No Coverage (IR tablet: 4 mg)	Hypotension, hyperkalemia, renal insufficiency, angioedema (rare, less frequent than with ACE-I), headache, dizziness.	Angioedema less frequent than with ACE-I. Monitor serum creatinine and potassium 7–14 days after initiation of therapy or dose changes. Contraindication: Avoid in pregnancy.	Diuretics: hypotension. Potassium-sparing diuretics and ACE-I: hyperkalemia. Potassium: hyperkalemia. NSAIDs: reduced hypotensive effect, fluid retention, renal failure. Lithium: increased lithium levels and toxicity.
losartan Cozaar®, G (IR tablet: 25, 50, 100 mg)	Initial: 12.5 mg once daily Target: 150 mg once daily	\$5–\$20	Special Authority			
valsartan Diovan®, G (IR tablet: 40, 80, 160, 320 mg)	Initial: 40 mg BID Target: 160 mg BID	\$18–19	Special Authority			
Beta-Blockers						
carvedilol G (IR tablet: 3.125, 6.25, 12.5, 25 mg)	Initial: 3.125 mg BID Target: 25 mg BID if <75 kg 50 mg BID if >75 kg Max dose: 50 mg BID	\$22–44	Special Authority	Orthostatic hypotension, worsening heart failure, worsening fluid retention, bronchospasm, dyspnea, bradycardia, malaise, fatigue, asthenia, erectile dysfunction, masking of symptoms of hypoglycemia.	Increase by 50–100% every 2 to 4 weeks. HF symptoms may get worse before they get better. More likely to cause orthostatic hypotension than bisoprolol.	Digoxin, amiodarone, diltiazem, and verapamil: bradycardia. Nondihydropyridine calcium channel blockers (e.g. verapamil and diltiazem): additive cardiodepressant effect. CYP2D6 inhibitors (e.g., SSRIs, bupropion, ritonavir, sertraline, St. John's Wort, citalopram, amiodarone): may increase carvedilol levels HF symptoms may get worse before they get better.
bisoprolol G (IR tablet: 5, 10 mg)	Initial: 1.25 mg once daily Target: 10 mg once daily Max dose: 20 mg once daily	\$1–9	Regular Coverage			
Mineralocorticoid Receptor Antagonists (MRAs; also known as aldosterone receptor antagonists)						
spironolactone Aldactone®, G (IR tablet: 25, 100 mg)	Initial: 12.5 mg once daily Target: 25–50 mg/day (>25 mg/day rarely indicated)	\$2–5	Regular Coverage	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. Contraindications: Pregnancy.	ACE-I, ARB, and potassium supplements: hyperkalemia. NSAIDs: reduced diuretic effect, worsening renal function, hyperkalemia.

Generic Name (trade name) (strengths and dosage form)	Adult Dosages	Cost per 30 days*	PharmaCare Coverage	Common Adverse Effects	Therapeutic Considerations & Contraindications	Drug Interactions
eplerenone Inspra® (IR tablet: 25, 50 mg)	Initial: 25 mg once daily or once every 2 days Target: 50 mg once daily	\$43–86	No Coverage	Hyperkalemia, dehydration, dizziness, diarrhea, nausea.	Monitor serum creatinine and potassium 3 and 7 days after initiation or titrating the dose. Repeat every 1–3 months once stable. Contraindications: Use with strong inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole, ritonavir, nelfinavir, clarithromycin, telithromycin, nefazodone): significant increases in eplerenone levels. Pregnancy.	ACE-I, ARB, and potassium supplements: hyperkalemia. NSAIDs: reduced diuretic effect, worsening renal function, hyperkalemia. Strong inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole, ritonavir, nelfinavir, clarithromycin, telithromycin, nefazodone): significant increases in eplerenone levels. Strong inducers of CYP3A4 (e.g., carbamazepine, phenytoin, phenobarbital, St. John's Wort, rifampicin): significant decreases in eplerenone efficacy.
Direct-Acting Vasodilators						
hydralazine G (IR tablet: 10, 25, 50 mg)	Initial: 10–25 mg TID Target: 75 mg TID to QID	\$13–79	Regular Coverage	Hypotension, GI complaints, SLE- like syndrome, tachyphylaxis, may worsen oxygen demand.	Should be used in combination with isosorbide dinitrate or nitroglycerin.	
isosorbide dinitrate G (IR tablet: 10, 30 mg)	Initial: 10–20 mg TID Target: 40 mg TID to QID	\$4–19	Regular Coverage	Headache, hypotension.	Should be used in combination with hydralazine.	Sildenafil, vardenafil and tadalafil: severe hypotension.
Diuretics						
furosemide Lasix®, G (IR tablet: 20, 40, 80 mg)	Initial: 20–40 mg/day once daily or BID Max total daily dose: 600 mg May be administered BID or TID for decompensated HF.	\$1–107	Regular Coverage	Dehydration, hypokalemia, hypocalcemia, nausea, hypotension, azotemia, hypomagnesemia, anorexia, hyperglycemia, hyperuricemia, weakness, fatigue, rash, increased total cholesterol.		Lithium: lithium toxicity. Digoxin: digoxin toxicity if K+ depleted. Oral corticosteroids: hypokalemia. NSAIDs: reduced diuretic effect, increased renal toxicity.
metolazone Zaroxolyn® (IR tablet: 2.5 mg)	Initial: 2.5 mg once daily Max total daily dose: 20 mg	\$7–52	Regular Coverage	Ototoxicity with high doses of furosemide.		

Generic Name (trade name) (strengths and dosage form)	Adult Dosages	Cost per 30 days*	PharmaCare Coverage	Common Adverse Effects	Therapeutic Considerations & Contraindications	Drug Interactions
Digoxin						
digoxin Toloxin®, G (IR tablet: 0.0625, 0.125, 0.25)	0.0625–0.25 mg once daily in the evening. Lower doses may be appropriate in patients with low body mass or impaired renal function. Measure trough serum concentrations at least 8 hours after administration and adjust the dose to maintain the serum concentration between 0.6 and 1 nmol/L.	\$8	Regular Coverage	Anorexia, nausea, vomiting, visual disturbances, fatigue, dizziness, confusion, delirium, cardiac arrhythmia.	May improve symptoms, exercise tolerance, and quality of life, but has not been shown to improve survival. Use only in patients with systolic HF. Electrolytes, creatinine, and digoxin serum concentrations should be obtained 5-7 days after dose adjustments.	Amiodarone, clarithromycin, cyclosporine, erythromycin, itraconazole, propafenone, quinidine, ritonavir, tetracycline, and verapamil: increased digoxin serum levels. Antacids, cholestyramine, colestipol, neomycin, rifampin, St. John's Wort, and sulfasalazine: reduced digoxin serum levels. Amiodarone, beta-blockers, diltiazem, and verapamil: increased risk of bradycardia.

Abbreviations: ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blockers; BID = twice daily; G = generic; GI = gastrointestinal; HF = heart failure; IR = immediate-release; kg = kilogram; mg = milligram; NSAID = nonsteroidal anti-inflammatory drugs; QID = four times daily; SLE = systemic lupus erythematosus; SSRI = selective serotonin reuptake inhibitor; TID = three times daily.

Footnotes: Pricing is approximate as of May 1, 2015 and does not include dispensing fee or additional markups.

Note: Please review product monographs at hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html

PharmaCare Coverage Definitions: **G:** generic(s) are available; **Regular Coverage:** also known as regular benefit; does not require Special Authority. Regular benefits may be fully or partially covered.*; **Limited Coverage:** requires Special Authority for coverage. Limited Coverage benefits approved by Special Authority may be fully or partially covered.*; **RDP:** Reference Drug Program. Drugs included in the RDP are comparable agents of the same therapeutic class. Patients receive full coverage of drugs designated as the Reference Drug(s) of the therapeutic class. Other drugs in the same RDP category are covered up to the price of the Reference Drug; **No coverage:** also known as non-benefit; does not fit the above categories.

* Note: Information on which products PharmaCare covers can be obtained using the B.C. PharmaCare Formulary Search (www.health.gov.bc.ca/pharmacare/benefitslookup/). In all cases, coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

References:

1. eTherapeutics+.
2. RxFiles. Heart Failure: Treatment Overview. 2014.
3. Up-To-Date. Overview of the therapy of heart failure due to systolic dysfunction.