Appendix D: HMG-CoA Reductase Inhibitors (Statins)[1-5, a,b]

Generic Name *trade name* dosage form and strengths	Low Intensity Dosage for <30% reduction in LDL[c]	Moderate Intensity Dosage for 30-49% reduction in LDL[c]	High Intensity Dosage for >50% reduction in LDL[c]	Annual Cost[d]	PharmaCare Coverage	Therapeutic Considerations
atorvastatin *Lipitor, G* Tabs: 10, 20, 40, 80 mg	-	10-20 mg PO once daily	40-80 mg PO once daily	$70-95	Regular benefit, RDP Reference Drug	Max 10 mg in patients with renal impairment Metabolized by CYP3A4
rosuvastatin *Crestor, G* Tabs: 5, 10, 20, 40 mg	-	5-10 mg PO once daily	20-40 mg PO once daily	$50-80	Regular benefit, RDP Reference Drug	Start with 5 mg in patients of Asian descent Max 20 mg in patients with severe liver impairment
fluvastatin *G* Caps: 20, 40 mg	20-40 mg PO once daily	40 mg PO BID	-	$275-770	Partial Benefit, RDP	Not recommended CrCl <30 ml/min Metabolized by CYP2C9 *Not indicated for primary prevention
lovastatin *G* Tabs: 20, 40 mg	20 mg PO once daily	40 mg PO once daily	-	$200-355	Partial Benefit, RDP	Caution CrCl <30 ml/min Metabolized by CYP3A4 *Not indicated for primary prevention
pravastatin *G* Tabs: 10, 20, 40 mg	10-20 mg PO once daily	40-80 mg PO once daily	-	$115-275	Partial Benefit, RDP	Start with 10 mg in patients with renal or liver impairment
simvastatin *Zocor, G* Tabs: 5, 10, 20, 40, 80 mg	10 mg PO once daily	20-40 mg PO daily	-	$80-100	Partial Benefit, RDP	Start with 5 mg in patients with severe renal insufficiency 80 mg is no longer recommended Metabolized by CYP3A4

Adverse Effects of Statins

The most common adverse events in patients treated with a statin include headache, GI disturbances, and myalgia.[6]

Meta-analyses of RCTs show no significant difference in the rate of adverse events, or in the rate of discontinuation due to adverse events between those taking a statin vs placebo.[5,6] There continued to be no significant difference when looking at subgroups such as primary vs secondary prevention, the statin used or discontinuation specifically due to myalgia, muscle pain or myopathy.[6,7]

There is increasing awareness and concern about rare but serious adverse effects of statins.

The development of diabetes is associated with an NNH of 255 over 4 years.[4,7]

While the risk of myalgia is common (2-11%), the risk of more serious adverse events such as rhabdomyolysis is low (<0.1%; NNH 22,727 over 1 year)[9] and is seen in patients with additional risk factors such as comorbidities (i.e. hypothyroid, renal/hepatic impairment), age (>80), genetic factors (i.e. SLCO1B1), or concurrent drug therapy (i.e. CYP3A4 inhibitors or inducers, gemfibrozil, protease inhibitors, cyclosporine).[5,9] Advise patients to report muscle pain and/ or weakness. CK elevation is of concern only when it is significantly elevated (i.e., >5X).[4]

Statins are associated with a dose-dependent risk of elevated liver enzymes (NNH of 96).4 Investigations are warranted if ALT >3 times the upper limit of normal.

Statin therapy was not associated with cognitive impairment in a meta-analysis of RCTs involving cognitively normal and cognitively impaired patients.[10]

Management options for the above adverse effects include statin discontinuation, switching to an alternative statin, dose decreases, and alternate day dosing.[4,5] Data on efficacy of these management options is limited or missing.

Abbreviations: BID = twice daily; **CrCl** = creatinine clearance in milliliters per minute; **G** = generics available; **mg** = milligram; **RDP** = reference drug program; **Tabs** = tablets;

Footnotes: [a] Not an exhaustive list; [b] Consult product monograph for detailed dosing instructions, dose adjustments for unique patient populations, and drug interactions. Product monographs available from Government of Canada: Drug Product Database, Health Canada advisories, warnings and recalls available from Government of Canada: Recalls and Safety Alerts, and drug interaction software such a Lexicomp. [c] For normal renal and hepatic function. Consult product monograph for detailed dosing instructions and dose adjustments for unique patient populations. [d] Pricing is approximate as of Dec 2021 and does not include dispensing fees or additional markups.

PharmaCare Coverage Definitions: Regular Benefit: Eligible for full reimbursement*; does not require Special Authority. **Limited Coverage:** Requires Special Authority to be eligible for reimbursement*. **RDP:** Reference Drug Program. Drugs included in the RDP are comparable agents of the same therapeutic class. **RDP Reference Drug:** Eligible for full reimbursement* within the therapeutic class, subject to Benefit status of the therapeutic class. **Partial Benefit RDP:** Eligible for limited reimbursement* under the RDP program up to the price of the Reference Drug. **Non-benefit:** Not eligible for coverage under any circumstances.

Note: Information on which products PharmaCare covers can be obtained using the B.C. PharmaCare Formulary Search
*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: Drug Coverage.

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