

Cardiovascular Drugs and Therapies

HMG CoA^a REDUCTASE INHIBITORS (available in Canada)

Generic Name	Atorvastatin Calcium	Fluvastatin Sodium	Lovastatin	Pravastatin Sodium	Rosuvastatin	Simvastatin
Trade Name	LIPITOR, generics	LESCOL, LESCOL XL	MEVACOR, generics	PRAVACHOL, generics	CRESTOR	ZOCOR, generics
Dosage Forms	10 mg, 20 mg, 40 mg, 80 mg tablets	20 mg, 40 mg immediate release (IR) capsules 80 mg extended release (XL) tablets	20 mg, 40 mg tablets	10 mg, 20 mg, 40 mg tablets	5 mg, 10 mg, 20 mg, 40 mg tablets	5 mg, 10 mg, 20 mg, 40 mg, 80 mg tablets
Dosing Range	10-80 mg once daily ²	20-80 mg daily* in the evening or at bedtime *(80 mg daily as 40 mg bid of IR capsule or 80 mg once daily of XL tablet at any time of day)	20-80 mg once daily with the evening meal	20 - 80 mg once daily at hs ^b	5-40 mg once daily ^{2*} *(5-20 mg in Asian patients)	10-40 mg once daily* in the evening *(80mg associated with more side effects)
Dosing Based on Desired	~25% N/A	40 mg	20 mg	20 mg	N/A	10 mg
	~40% 10-20 mg	N/A	80 mg+	80 mg+	5-10 mg	40-80 mg
LDL Reduction^{1,2,3}	Note: In general, for each doubling of statin dose, one can expect an average 6% further reduction in LDL					
Bioavailability	12%	24% saturable first pass metabolism at doses >20 mg	<5%	17%	20%	<5%
Metabolism	Extensive via CYP 450-3A4	Extensive via CYP enzymes: 2C9: 75%, 3A4: 20%, 2C8: 5%	Extensive via CYP 3A4	Extensive; NOT via CYP 3A4	NOT extensive; ~10% via CYP 2C9	Extensive via CYP 3A4

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a - HMG CoA = 3-hydroxy-3-methyl glutaryl co-enzyme A

b - In general, reduction in cholesterol is best when HMG Co A Reductase Inhibitors are taken in the evening. However, with atorvastatin and rosuvastatin timing does not influence efficacy; these may be taken without regard to time of day.

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Active Metabolite	Yes; accounts for 70% of activity	No	Yes – accounts for its activity	Yes – but minimal activity compared to parent	Yes – 50% activity compared to parent	Yes
Elimination	<2% renal	5% renal	<10% renal	20% renal	10% renal	13% renal
Half-Life (hours)	Atorvastatin: 14 h Active metabolite: 20-30 h	IR: 3 h XL: 9 h	3-4 h	1.5-2 h	19 h	3 h
Dose Adjustment	Renal: suggest to use lowest dose (10 mg) Hepatic: caution as plasma levels are ↑	Renal: not recommended for those with severe renal dysfunction (Cr >260) Hepatic: use with caution	Renal: caution with doses >20 mg in patients with CrCl <30 mL/min	Renal or hepatic: starting dose of 10 mg recommended	Renal: initial dose 5 mg and max. 10 mg when CrCl <30mL/min Hepatic: max. 20 mg daily in severe impairment	Renal: caution with doses >10mg in patients with CrCl <30mL/min
Note: Active liver disease or unexplained persistent elevations of serum transaminases are contraindications						
Drug Interactions^c	↓ pioglitazone ↑ atorvastatin level: amiodarone, azole antifungals, clarithromycin, colchicines, corticosteroids, cyclosporine, diltiazem, dronedarone, erythromycin, fibrates, fusidic acid, grapefruit juice, HIV protease inhibitors,	↑ warfarin ↑ fluvastatin level: amiodarone, colchicines, fibrates, fluconazole, fluvoxamine, H ₂ antagonists, isoniazid, niacin, omeprazole, probenecid, sertraline, voriconazole, zafirlukast	↑ warfarin ↑ lovastatin level: amiodarone, azole antifungals, clarithromycin, colchicine, cyclosporine, diltiazem, dronedarone, erythromycin, fibrates, grapefruit juice, HIV protease inhibitors, nefazodone, niacin, voriconazole, verapamil	↓ propranolol ↑ pravastatin level: cyclosporine, gemfibrozil, nefazodone, darunavir, colchicine ↓ pravastatin level: propranolol, efavirenz	Contraindicated with concomitant cyclosporine ↑ warfarin, oral contraceptives ↑ risk of myopathy if given in combination with: ezetimibe, fibrates, niacin ↑ <u>rosuvastatin level:</u> amiodarone, azole antifungals,	↑ warfarin, digoxin ↓ levothyroxine ↑ <u>simvastatin level:</u> amiodarone, azole antifungals, ciprofloxacin, clarithromycin, corticosteroids, cyclosporine, diltiazem, dronedarone, erythromycin, fibrates, fusidic acid, grapefruit juice,

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Generic Name	Atorvastatin Calcium	Fluvastatin Sodium	Lovastatin	Pravastatin Sodium	Rosuvastatin	Simvastatin
Drug Interactions,^c <i>cont'd</i>	nefazodone, niacin, verapamil <u>↓ atorvastatin level:</u> phenytoin, rifampin, antacids, bosentan, St. John's Wort	<u>↓ fluvastatin level:</u> rifampin, St. John's Wort	<u>↓ lovastatin level:</u> phenytoin, rifampin, exenatide		cyclosporine*, gemfibrozil, HIV protease inhibitors <u>↓ rosuvastatin level:</u> rifampin, antacids, St. John's Wort	HIV protease inhibitors, nefazodone, niacin, risperidone, verapamil, voriconazole <u>↓ simvastatin level:</u> bosentan, carbamazepine, efavirenz, phenytoin, rifampin, antacids, St. John's Wort
Unit Cost[*]	\$0.31/10 mg \$0.39/20 mg \$0.42/40 mg \$0.42/80 mg	\$0.22/20 mg \$0.31/40 mg \$1.54/80 mg XL tab	\$0.49/20 mg \$0.90/40 mg	\$0.40/10 mg \$0.48/20 mg \$0.58/40 mg	\$0.23/5 mg \$0.24/10 mg \$0.30/20 mg \$0.36/40 mg	\$0.18/5 mg \$0.36/10 mg \$0.45/20 mg \$0.45/40 mg \$0.45/80 mg
30 Day[#] Patient Cost	<i>tr</i> For daily dosing \$10 (10 mg) \$12.60 (20 mg) \$13.60 (40 mg) \$13.60 (80 mg)	<i>For daily dosing</i> For daily dosing \$7.10 (20 mg) \$10 (40 mg) \$59.90 (80 mg XL)	<i>osing</i> For daily dosing \$15.90 (20 mg) \$29.20 (40 mg)	For daily dosing \$13 (10 mg) \$15.60 (20 mg) \$18.80 (40 mg)	<i>t</i> For daily dosing \$7.45 (5 mg) \$7.80 (10 mg) \$9.70 (20 mg) \$11.70 (40 mg)	<i>tr</i> For daily dosing \$5.80 (5 mg) \$11.70 (10 mg) \$14.60 (20,40,80 mg)
ODB^d	Yes	Yes	Yes	Yes	Yes	Yes
MSH^e	Yes	No	No	Yes	Yes	Yes
UHN^e	Yes	No	No	Yes	Yes	Yes

* List prices from the Ontario Drug Benefit (ODB) Formulary, Ontario Ministry of Health. Last Updated: 01/04/2011 Version 2.2. All prices represent the generic medication option.

30 day patient costs represented by ODB generic price + 8% markup. These prices do not include a dispensing fee, which can range from 4.99 – 11.99. Pricing is based on a typical dosing regimen.

c - Clinically important pharmacokinetic drug interactions; not meant to be all-inclusive. Refer to additional references or consult pharmacist for more detail.

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d -ODB – indicates an item on the Ontario Drug Benefit (ODB) Formulary

e - MSH - indicates an item on the Mount Sinai Hospital Formulary; UHN - indicates an item on the University Hospital Network Formulary

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REFERENCES

1. Kendrach MG, Kelly-Freeman M. Approximate equivalent rosuvastatin doses for temporary statin exchange programs. *Ann Pharmacother*. 2004;38:1286-1292.
2. Jones P, Kafonek S, Laurora I, Hunninghake D. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin and fluvastatin in patients with hypercholesterolemia (CURVES study). *Am J Cardiol*. 1998;81:582-587.
3. Jones PH, Davidson MH, Stein EA, et al. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin and pravastatin across doses (STELLAR* trial). *Am J Cardiol*. 2003;92:152-160.
4. e-Formulary Ontario Drug Benefit Formulary/Comparative Drug Index; electronic version. Accessed 2011 January. (Cost based on generic formulations wherever possible.)

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The contents of this Handbook are approved and endorsed by the UHN Cardiovascular Subcommittee of the Pharmacy and Therapeutics Committee.

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Notice to Healthcare Providers:

The Pharmacotherapy Handbook is intended to be used as a tool to aid in the appropriate prescribing and administration of cardiovascular formulary agents.

This information in this Handbook is intended for use by and with experienced physicians and pharmacists. The information is not intended to replace sound professional judgment in individual situations, and should be used in conjunction with other reliable sources of information. Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about Cardiovascular illness and the treatments in question.

Due to the rapidly changing nature of cardiovascular treatments and therapies, users are advised to recheck the information contained herein with the original source before applying it to patient care.

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