

Comparison of HMG CoA-reductase Inhibitors (From product package insert information unless noted otherwise)

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Statin		Lovastatin (<i>Mevacor</i> ®) Available in generic	Pravastatin (<i>Pravachol</i> ®) Available in generic	Simvastatin (<i>Zocor</i> ®) Available in generic	Fluvastatin (<i>Lescol</i> ®)	Atorvastatin (<i>Lipitor</i> ®)	Rosuvastatin (<i>Crestor</i> ®)
Average reduction in LDL cholesterol	Up to 20%		10 mg: 22%		20 mg: 22%		
	21-30%	20 mg: 27%	20 mg: 32%	10 mg: 28%	40 mg: 25%		
	31-40%	40 mg: 31%	40 mg: 34% 80 mg: 37%	20 mg: 38% 40 mg: 41%	80 mg: 35%	10 mg: 39%	5 mg: 43%
	41-50%	80 mg: 42%		80 mg: 47%		20 mg: 43%	10 mg: 50%
	>50%					40 mg: 50% 80 mg: 54-60%	20 mg: 53% 40 mg: 62%
Lipophilicity^a		Lipophilic	Hydrophilic	Lipophilic	Hydrophilic	Lipophilic	Hydrophilic
Drug Interactions		<ul style="list-style-type: none"> • A significant CYP3A4 enzyme substrate^b • May ↑ warfarin effect; monitor warfarin closely - <u>Do not exceed 20mg per day when combining with:</u> niacin ≥1gm/day, gemfibrozil, cyclosporine, danazol - <u>Do not exceed 40mg per day when combining with:</u> verapamil, amiodarone 	<ul style="list-style-type: none"> • Very few drug interactions, no apparent metabolism through cytochrome P450 enzymes. • Antacids, BAS: Separate administration times 	<ul style="list-style-type: none"> • A significant CYP3A4 enzyme substrate^b • 20% ↑ digoxin levels • May ↑ warfarin effect - <u>Do not exceed 10mg per day when combining with:</u> niacin ≥1gm/day, gemfibrozil, cyclosporine, danazol - <u>Do not exceed 20mg per day when combining with:</u> verapamil, amiodarone 	<p>A CYP2C9 enzyme system substrate, less DI's vs. CYP3A4:</p> <ul style="list-style-type: none"> • <u>CYP2C9 inducers</u> (↓'s fluvastatin levels) - Rifampin, phenobarbital, phenytoin, carbamazepine • May ↑ cyclosporine or phenytoin levels • <u>CYP2C9 inhibitors</u> (↑ fluvastatin levels)- fluvoxamine, amiodarone, omeprazole, ritonavir, tolbutamide, cimetidine, azole antifungals • 20% ↑ digoxin levels • Antacids, BAS: Separate administration times • May ↑ warfarin effect 	<ul style="list-style-type: none"> • A significant CYP3A4 enzyme substrate^b • 20% ↑ digoxin levels • Antacids, BAS: Separate administration times • <u>May ↓ warfarin effect</u> 	<ul style="list-style-type: none"> • Only 10% of parent drug metabolized by CYP2C9. • Max rosuvastatin dose = 5mg w/ cyclosporine & 10mg w/ gemfibrozil (but not fenofibrate) due to ↑'s rosuvastatin plasma concentrations. • May ↑ warfarin effect. • Take aluminum & magnesium-containing antacids 2 hours after rosuvastatin. • Chinese & Japanese subjects have 2-fold higher maximum plasma concentrations and area under the plasma-concentration time curve vs. other ethnic groups.
Dosing / Food Interactions		<u>MUST TAKE WITH FOOD</u> in the evening; otherwise, bioavailability reduced by up to 50% ^c	Take with or without food Take any time of the day (Long half-life of parent + metabolites)	Take with or without food Take in the evening only	Take with or without food Take in the evening only	Take with or without food. Take any time of the day.	
Liver Function Testing		At initiation or at every dose increase: ACC/AHA/NHLBI recommends liver function testing at baseline, 12 weeks, then annually or more often if indicated.					
Renal Considerations		Reduce initiation dose x 50% (i.e., 10mg) if creatinine clearance < 30 mL/min; titrate to response	Reduce initiation dose x 50% (i.e., 10mg) if creatinine clearance < 60 mL/min; titrate to response	Reduce initiation dose x 50% (i.e., 5mg) if creatinine clearance < 30 mL/min; titrate to response	No dose modification necessary for renal impairment.	No dosage modification necessary for renal impairment.	<ul style="list-style-type: none"> • If creatinine clearance < 30 mL/min: Initial dose = 5mg QD, max. dose = 10mg QD • Routine urinalysis for proteinuria (no frequency recommended by manufacturer), particularly for 40 mg dose.

^a Hydrophilic statins are less likely to cross the blood brain barrier, may be associated w/ less insomnia. May consider in patients who develop insomnia (<3% incidence) while taking lipophilic statins. This is NOT a primary consideration in initial statin selection. In addition, there is no evidence of hydrophilicity being associated with less risk of myopathy.

^b **CYP3A4 Drug Interactions:**

CYP3A4 inducers (↓'s levels of lova-, simva-, and atorvastatin)	phenytoin, phenobarbital, barbiturates, rifampin, danazol, carbamazepine, St. John's Wort
CYP3A4 inhibitors (↑'s levels of lova-, simva-, and atorvastatin)	Antiretroviral protease inhibitors, amiodarone, ketoconazole*, itraconazole*, fluconazole*, viroconazole*, erythromycin*, clarithromycin*, troleandomycin*, telithromycin*, nefazadone, cyclosporine, verapamil, diltiazem, grapefruit juice

* ↓ dose of lova-, simva-, or atorvastatin x 50% when given concomitantly with these medications

^c Altoprev® (extended-release lovastatin) should be taken AT BEDTIME on an EMPTY STOMACH for maximal absorption; maximum dose=60 mg/day (slightly more potent than immediate release lovastatin due to sustained activity)