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## on Drugs and Therapeutics

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### IN BRIEF

## Pitavastatin Magnesium (*Zypitamag*) for Hyperlipidemia

The FDA has approved the HMG-CoA reductase inhibitor (statin) pitavastatin magnesium (*Zypitamag* – Zydus) for use in adults with primary hyperlipidemia or mixed dyslipidemia. The FDA considers pitavastatin magnesium bioequivalent to pitavastatin calcium (*Livalo*), which was approved in 2009.<sup>1</sup>

**Pronunciation Key**  
*Zypitamag*: zai pit' a mag"

Statins remain the treatment of choice for most patients who require lipid-lowering therapy. Taken as an adjunct to diet modification, increased exercise, and smoking cessation, statins can reduce the risk of primary and secondary cardiovascular events and death in patients

with or at high risk for atherosclerotic cardiovascular disease.<sup>2</sup> Even in patients at low risk for cardiovascular disease, treatment with a statin can significantly reduce the incidence of cardiovascular events.<sup>3</sup>

Controlled trials in patients with cardiovascular disease have shown that high-intensity statin therapy (defined as reducing LDL-cholesterol [LDL-C] by  $\geq 50\%$  on average) reduces the incidence of cardiac events, stroke, and coronary death significantly more than less intensive regimens. In one meta-analysis, each additional 1 mmol/L (39 mg/dL) reduction in LDL-C was associated with a 20% reduction in major vascular events and a 10% reduction in all-cause mortality.<sup>4</sup> In a randomized trial in 13,054 Japanese patients with stable coronary artery disease, over a median follow-up of 3.9 years, patients taking pitavastatin calcium 4 mg daily were significantly less likely than those taking 1 mg daily to have a cardiovascular event (4.3% vs 5.4%).<sup>5</sup>

Table 1. Statins

Drug	Some Formulations	Usual Adult Dosage <sup>1</sup>	Average LDL-C Reduction <sup>2</sup>	Cost <sup>3</sup>
Atorvastatin – generic <i>Lipitor</i> (Pfizer)	10, 20, 40, 80 mg tabs	Initial: 10-20 mg once/d Maximum: 80 mg once/d	35-40% 50-60%	\$11.00 299.40
Fluvastatin – generic <i>Lescol</i> (Novartis)	20, 40 mg caps	Initial: 40 mg bid Maximum: 40 mg bid	20-25% 30-35%	239.80 305.50
extended-release – generic <i>Lescol XL</i>	80 mg tabs	Initial: 80 mg once/d Maximum: 80 mg once/d	35-38%	199.50 323.00
Lovastatin – generic	10, 20, 40 mg tabs	Initial: 20 mg once/d Maximum: 80 mg once/d <sup>4</sup>	25-30% 35-40%	6.70
extended-release – <i>Altoprev</i> (Watson/Actavis)	20, 40, 60 mg tabs	Initial: 20 mg once/d Maximum: 60 mg once/d	20-25% 40-45%	877.20
Pitavastatin – <i>Livalo</i> (Kowa) <sup>5</sup> <i>Zypitamag</i> (Zydus) <sup>5</sup>	1, 2, 4 mg tabs	Initial: 2 mg once/d Maximum: 4 mg once/d	35-40% 40-45%	276.30 232.50
Pravastatin – generic <i>Pravachol</i> (BMS)	10, 20, 40, 80 mg tabs	Initial: 40 mg once/d <sup>6</sup> Maximum: 80 mg once/d	30-35% 35-40%	21.60 169.70
Rosuvastatin – generic <i>Crestor</i> (AstraZeneca)	5, 10, 20, 40 mg tabs	Initial: 10-20 mg once/d <sup>7,8</sup> Maximum: 40 mg once/d <sup>9</sup>	45-50% 50-60%	8.30 260.90
Simvastatin – generic <i>Zocor</i> (Merck)	5, 10, 20, 40, 80 mg tabs	Initial: 10-20 mg once/d <sup>10</sup> Maximum: 40 mg once/d <sup>11,12</sup>	35-40% 45-50%	3.80 138.60

1. FDA-approved dosage. Some expert clinicians use lower doses for initial treatment of patients with only modest elevations of LDL-C or a history of poor tolerance to these drugs. For patients who require a large reduction in LDL-C, some would use higher doses initially. Statins are generally most effective when taken in the evening. Dosage adjustment may be needed for patients with renal or hepatic impairment.
2. The listed ranges correspond to the initial and maximum dosages. Statin dosages that lower LDL-C by  $\geq 50\%$  are considered high-intensity therapy. Those that lower LDL-C by 30--50% are considered moderate-intensity therapy. LDL-C reductions may vary significantly among individuals.
3. Approximate WAC for 30 days' treatment at the lowest initial dosage unless otherwise specified. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. June 5, 2018. Reprinted with permission by First Databank, Inc. All rights reserved. ©2018. www.fdbhealth.com/policies/drug-pricing-policy.
4. Or 40 mg bid.
5. *Livalo* is the calcium salt of pitavastatin and *Zypitamag* is the magnesium salt of pitavastatin. Although equivalent strengths of *Livalo* and *Zypitamag* contain the same amount of pitavastatin base, the drugs are not interchangeable.
6. 10 mg initially for patients with significant renal impairment.
7. Higher serum concentrations of rosuvastatin have been reported in Asian patients; an initial dose of 5 mg once/day is recommended.
8. Patients with severe renal impairment not on hemodialysis should start with 5 mg and not exceed 10 mg/day.
9. Maximum dose is 20 mg/day in Asian patients (E Lee et al. Clin Pharmacol 2005; 78:330).
10. Patients with severe renal impairment should start with 5 mg.
11. Patients who have taken 80 mg/day of simvastatin for  $\geq 12$  months without evidence of myopathy can continue at this dose.
12. The maximum dose of simvastatin is 10 mg if taken with diltiazem or verapamil and 20 mg if taken with amiodarone, amlodipine, or ranolazine.

Approval of pitavastatin magnesium was based on the results of trials with pitavastatin calcium; no new efficacy trials were required. *The Medical Letter's* review of pitavastatin calcium concluded that recommended doses of the drug had not been shown to decrease LDL-C more than other statins with longer safety records and there was no good reason to use it. That conclusion applies to pitavastatin magnesium as well. ■

1. Pitavastatin (Livalo) – the seventh statin. *Med Lett Drugs Ther* 2010; 52:57.
2. Lipid-lowering drugs. *Med Lett Drugs Ther* 2016; 58:133.
3. CTT Collaboration et al. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. *Lancet* 2012; 380:581.
4. CTT Collaboration et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet* 2010; 376:1670.
5. I Taguchi et al. High-dose versus low-dose pitavastatin in Japanese patients with stable coronary artery disease (REAL-CAD): a randomized superiority trial. *Circulation* 2018; 137:1997.

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