

PITAVASTATIN

About pitavastatin

- Pitavastatin is a novel, fully synthetic statin that significantly reduces elevated low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and triglycerides (TG).¹
- Pitavastatin also produces consistent increases in high-density lipoprotein cholesterol (HDL-C) levels, over the short- and long-term.^{2,3}
- Pitavastatin 4mg has been shown to deliver equivalent coronary plaque volume reduction to atorvastatin 20mg in patients with Acute Coronary Syndrome (JAPAN-ACS).⁴
- Pitavastatin has a novel cyclopropyl group on its base structure, leading to a low potential for CYP3A4 drug-to-drug interactions.²
- Pitavastatin has been shown not to induce diabetes when administered to Japanese patients with impaired glucose tolerance.⁵

Recently, a study in 13,054 Japanese patients with stable coronary artery disease (the REAL-CAD study) has shown that a dose of pitavastatin 4 mg daily can reduce the rate of cardiovascular events to a greater extent than a 1 mg dose.⁶

Indication

Livazo is indicated for the reduction of elevated total cholesterol (TC) and LDL-C, in adults, adolescents and children aged 6 years or older with primary hypercholesterolaemia, including heterozygous familial hypercholesterolaemia, and combined (mixed) dyslipidaemia, when response to diet and other non-pharmacological measures is inadequate.¹

QUICK FACTS

- Pitavastatin is a fully synthetic, novel statin²
- Pitavastatin's cyclopropyl group on the base structure allows for minimal metabolism and low risk of CYP3A4 mediated drug-to-drug interactions^{2,9}
- Pitavastatin's safety and tolerability are comparable to other commonly prescribed statins^{4,7,8}
- Pitavastatin does not appear to increase the risk of developing diabetes in Japanese subjects⁵
- Pitavastatin has been granted approval in a number of countries, in Europe, Asia, South America and USA.

Dosing

Pitavastatin is available in three strengths; 1 mg, 2 mg and 4 mg¹

The usual starting dose for is 1mg once daily. Adjustment of dose should be made at intervals of 4 weeks or more. Doses should be individualized according to LDL-C levels, the goal of therapy and patient response. The maximum daily dose is 4mg..¹

Children and adolescents aged 6 years and over: Livazo use in children should only be carried out by physicians experienced in the treatment of hyperlipidaemia and progress should be regularly reviewed. In children and adolescents with heterozygous familial hypercholesterolaemia the usual starting dose is 1mg once daily. Adjustment of dose should be made at intervals of 4 weeks or more. Doses should be individualized according to LDL-C levels, the goal of therapy and patient response. In children 6 to 9 years of age the maximum daily dose is 2mg. In children 10 years or older the maximum daily dose is 4mg.¹

Pitavastatin can be taken at any time of the day with or without food, allowing flexibility for patients.¹

Pitavastatin structure

Pitavastatin's novel chemical structure has the following consequences:

- Minimal metabolism – pitavastatin is only minimally metabolised by the liver through the cytochrome P450 pathway, a common pathway for the metabolism of many other medications.⁷ Pitavastatin's lack of metabolism in the gut probably contributes its high bioavailability.²
- Low potential of interactions – due to its lack of metabolism by CYP, pitavastatin has a low potential for CYP3A4-mediated drug-to-drug interactions.³

Pitavastatin's low potential for CYP3A4-mediated drug-to-drug interactions makes it an option for patients who are on multiple medications² and/or who are receiving anti- retroviral therapy (ART) for the treatment of HIV (Human Immuno-Deficiency Virus).¹

ART is known to increase the risk of impaired glucose tolerance and dyslipidaemia; putting patients at increased risk of CVD.⁸⁻¹⁰

Phase III clinical studies

- Pitavastatin effectively reduced LDL-C and achieved European Atherosclerosis Society (EAS) guideline targets in the majority of patients with primary hypercholesterolaemia or combined dyslipidaemia, similar to reductions seen with atorvastatin¹¹ and simvastatin¹² after 12 weeks of treatment.
- Pitavastatin 2 mg was statistically significantly superior compared with simvastatin 20 mg in lowering LDL-C, non-HDL-C and TC after 12 weeks of treatment.¹²
- Pitavastatin effectively reduced LDL-C in the elderly¹² and also improved LDL-C and other parameters of lipid metabolism in patients at high cardiovascular risk.²
- Pitavastatin was statistically significantly superior to pravastatin in improving LDL-C at all dose comparisons in elderly patients (≥ 65 years) after 12 weeks of treatment.^{2,12}
- Pitavastatin 4 mg demonstrated a gradual and sustained increase in HDL-C over the long-term, supported by data from a 52 week extension study.³

Safety and tolerability

The overall safety and tolerability of pitavastatin are consistent with other commonly prescribed statins. In pivotal clinical studies, pitavastatin demonstrated:

- **Low incidence of adverse events (AEs)**
 - ▷ In Phase III studies comparing pitavastatin with atorvastatin,¹⁰ simvastatin¹¹ and pravastatin² over 12 weeks, the comparable tolerability profile of pitavastatin was demonstrated, with a low incidences of AEs.
- **Comparable tolerability**
 - ▷ In patients with primary hypercholesterolaemia or combined dyslipidaemia, pitavastatin demonstrated a similar tolerability profile to atorvastatin and simvastatin respectively, at comparable therapeutic doses.^{11,12}
 - ▷ All three doses of pitavastatin (1, 2 and 4 mg) demonstrated a comparable tolerability profile to 10, 20 and 40 mg of pravastatin over 12 weeks¹³
 - ▷ In patients with primary hypercholesterolaemia or combined dyslipidaemia, pitavastatin demonstrated long-term tolerability (52 weeks) with no serious treatment-emergent adverse event (TEAEs) being attributed to pitavastatin.^{2,3}
- **Long-term safety profile**
 - ▷ Pitavastatin has demonstrated a long-term safety profile (to 52 weeks),³ comparable to that of simvastatin or atorvastatin.^{13,14}
 - ▷ Furthermore, the two year follow-up in a post-marketing surveillance study conducted in nearly 20,000 patients in Japan showed a low incidence of overall AEs, the majority of which were mild. Serious adverse reactions were rare; with only two reports of rhabdomyolysis requiring hospitalisation (0.01% of patients).¹
- **Risk of diabetes**
 - ▷ Some evidence suggests that statins as a class raise blood glucose and in some patients at high risk of future diabetes, may produce a level of hyperglycaemia where formal diabetes care is appropriate. This risk, however, is outweighed by the reduction in vascular risk with statins and therefore should not be a reason for stopping statin treatment. Patients at risk of hyperglycaemia (fasting glucose 5.6 to 6.9 mmol/L, BMI>30 kg/m², raised triglycerides, hypertension), should be monitored both clinically and biochemically according to national guidelines.¹⁵
 - ▷ there has been no confirmed signal of a diabetes risk for pitavastatin either in post-marketing safety surveillance studies or in prospective studies.¹
 - ▷ The only prospective trial to evaluate the effect of a statin on the development diabetes was published in 2013.⁵ Results showed that pitavastatin did not increase the risk of diabetes among Japanese patients with impaired glucose tolerance after a median of 2.8 years.⁵

Approval

Pitavastatin was first launched in Japan in 2003 and launched around the world including China and the USA.

Pitavastatin achieved a positive outcome from the UK Regulatory Authority (MHRA) acting as the Reference Member State for 16 European Union countries in 2010 and subsequently it has been approved and launched in many EU countries.

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