European Medicines Agency

London, 15 March 2010
Doc. Ref.: EMA/CHMP/736379/2009 rev.1
EMEA/H/A-30/1078

Questions and answers on the referral for
Lescol and associated names
Capsules containing 20 mg or 40 mg fluvastatin
Prolonged-release tablets containing 80 mg fluvastatin

The European Medicines Agency has completed a review of Lescol and associated names. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that there is a need to harmonise the prescribing information for Lescol and associated names in the European Union (EU), as well as Norway and Iceland.
The review was carried out under an 'Article 30' referral[1].

What is Lescol?
Lescol contains the active substance fluvastatin. Fluvastatin belongs to a group of medicines called 'statins', which are cholesterol-lowering agents. It works by blocking the activity of an enzyme called HMG-CoA reductase. HMG-CoA reductase is responsible for the production of cholesterol. By blocking this enzyme, the amount of cholesterol in the blood is reduced.
Lescol is used to treat dyslipidaemia (abnormal levels of fat in the blood), particularly 'primary hypercholesterolaemia' and 'mixed dyslipidaemia'. Primary hypercholesterolaemia is when the levels of cholesterol in the blood are high. Primary means that the hypercholesterolaemia does not have any identifiable cause. Patients with mixed dyslipidaemia have high blood levels of 'bad' LDL cholesterol and triglycerides (a type of fat), and low levels of 'good' HDL cholesterol.
Lescol is also used to prevent further serious cardiac events (such as a heart attack) in patients after they went through percutaneous coronary intervention (a surgical procedure that is used to unblock narrowed coronary arteries).

Lescol is also available in the EU under other trade names: Canef, Cardiol, Cardiol XL, Cranoc, Digardil, Digaril Prolib, Fluvastatin Novartis, Fluvastatina, Fractal, Leposit Prolib, Lescol Depot, Lescol Exel, Lescol LP, Lescol MR, Lescol Prolib, Lescol XL, Lipaxan, Lipaxin, Liposit, Locol, Lymetel, Primesin, Vaditon and Vaditon Prolib.
The company that markets these medicines is Novartis.

Why was Lescol reviewed?
Lescol is authorised in the EU via national procedures. This has led to divergences among Member States in the way the medicine can be used, as seen in the differences in the Summaries of Product Characteristics (SPCs), labelling and package leaflets in the countries where the product is marketed. Lescol has been identified as needing harmonisation by the Co-ordination Group on the Mutual and Decentralised Procedures – Human (CMD(h)).
On 9 February 2009, the European Commission referred the matter to the CHMP in order to harmonise the marketing authorisations for Lescol in the EU.

[1] Article 30 of Directive 2001/83/EC as amended, referral on the grounds of divergent decisions adopted by member States

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 84 16
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

What are the conclusions of the CHMP?
The CHMP, in the light of the data submitted and the scientific discussion within the Committee, was of the opinion that the SPCs, labelling and package leaflets should be harmonised across the EU. The areas harmonised include:

4.1 Therapeutic indications

The CHMP agreed on two harmonised indications (the diseases for which the medicine may be used):

"Dyslipidaemia
Treatment of primary hypercholesterolaemia or mixed dyslipidaemia, as an adjunct to diet, when response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate.
Secondary prevention in coronary heart disease
Secondary prevention of major adverse cardiac events in adults with coronary heart disease after percutaneous coronary interventions (see section 5.1)."

The Committee noted that the indication "*to slow the progression of coronary atherosclerosis in patients with primary hypercholesterolemia, including mild forms, and coronary heart disease*", which was not approved in some Member States, should be removed because the results from the clinical study did not supported this indication.

4.2 Posology and method of administration

The CHMP noted that for the treatment of dyslipidaemia, the main differences in dosing recommendations were related to the starting dose. The Committee concluded that initial dosing ranging from 20 to 80 mg/day is appropriate. For patients with coronary heart disease after percutaneous coronary interventions, the CHMP agreed that the recommended daily dose is 80 mg. The dosage in specific populations, such as children and patients with kidney problems, was also harmonised.

4.3 Contra-indications

The CHMP also agreed on a harmonised wording for the contra-indications (situations where the medicine must not be used):

"*- in patients with known hypersensitivity to fluvastatin or any of the excipients;*
- in patients with active liver disease, or unexplained, persistent elevations in serum transaminases (see sections 4.2, 4.4 and 4.8);
- during pregnancy and lactation (see section 4.6)."

The Committee noted that some contra-indications that were included in the SPC in some Member States could be removed. The contra-indications that were removed were: use in children, in patients with myopathic disorders and patient with severe renal impairment, as warnings and cautionary statements are already included in sections 4.2 and 4.4.

Other changes

The CHMP harmonised the SPC section on special warnings and included warnings related to the use of Lescol in children.

The amended information to doctors and patients is available here.

The European Commission issued a decision on 15 March 2010.

Rapporteur:	Alar Irs (Estonia)
Co-rapporteur(s):	Catherine Moraiti (Greece)
Referral start date:	19 February 2009
Company responses provided on:	29 May 2009, 16 October 2009
Opinion date:	19 November 2009