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Questions and answers on Losec and associated names (omeprazole, 10, 20 or 40 mg capsules and tablets, and 40 mg solution for injection and solution for infusion)

Outcome of a procedure under Article 30 of Directive 2001/83/EC

The European Medicines Agency has completed a review of Losec. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that there is a need to harmonise the prescribing information for Losec and associated names in the European Union (EU).

What is Losec?

Losec is used to treat diseases where the stomach produces too much acid. These include:

- reflux disease, to treat symptoms such as heartburns and acid regurgitation (acid flowing up in the mouth),
- reflux oesophagitis (inflammation of the gullet, due to acid),
- stomach or duodenal ulcer, including preventing the ulcer from coming back (relapse),
- Zollinger-Ellison syndrome (a condition caused by oversecretion of acid in the stomach).

Losec can also be used for the prevention and treatment of the stomach ulcers that are caused by medicines used to treat pain and inflammations called non-selective non-steroidal anti-inflammatory drugs (NSAIDs), when the patient needs continuous NSAID treatment. Together with antibiotics, it can be used to help rid the stomach of a bacterium called *Helicobacter pylori (H. pylori)*, which is known to cause stomach ulcers.

The active substance in Losec, omeprazole, is a proton pump inhibitor (PPI). It works by blocking 'proton pumps', proteins found in specialised cells in the stomach lining that pump acid into the stomach. By blocking the pumps, omeprazole reduces acid production.

Losec is also available in the EU under other trade names: Antra, Logastric, Losec Forte, Mopral, Omeprazen, Omeprazole AstraZeneca and Zoltum. The company that markets these medicines is AstraZeneca.

The 10 and 20 mg tablets may be available as non-prescription medicines (over-the-counter, OTC) in some Member States.

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Why was Losec reviewed?

Losec 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 (SmPCs), labelling and package leaflets in the countries where the product is marketed. Losec has been identified as needing harmonisation by the Co-ordination Group on the Mutual and Decentralised Procedures – Human (CMD(h)).

On 27 June 2008, the European Commission referred the matter to the CHMP in order to harmonise the marketing authorisations for Losec in the 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 SmPCs, labelling and package leaflets should be harmonised across the EU. The areas harmonised include:

4.1 Therapeutic indications

The CHMP agreed on harmonised indications (the diseases for which the medicine may be used). The Committee agree that the capsules and tablets can be used for the same indications, namely:

In adults:

- duodenal ulcers (treatment and prevention of relapse),
- stomach ulcers (treatment and prevention of relapse),
- *H. pylori* eradication in stomach and duodenum ulcer disease in combination with antibiotics,
- NSAID associated ulcers (treatment and prevention),
- reflux oesophagitis (treatment, including long-term management after healing),
- symptomatic gastro-oesophageal reflux disease,
- Zollinger-Ellison syndrome.

In children:

- reflux oesophagitis,
- heartburn and acid regurgitation in gastro-oesophageal reflux disease.
- In combination with antibiotics in the treatment of duodenal ulcer caused by *H. pylori*.

The CHMP agreed that the indications for the injectable form of Losec should be the same as for the tablets, but that the injection should only be used when the administration of the tablets or capsules is not possible.

Losec was also indicated for use before surgery to prevent acid aspiration (acid moving from the gullet into the lungs during anaesthesia, causing pneumonia). The CHMP recommended that this indication be removed as the studies presented by the company did not show an improved effectiveness when compared with placebo (a dummy treatment).

When used as an OTC medicine, the CHMP recommended that the indication be the treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults.

4.2 Posology and method of administration

The way the medicine is taken has been harmonised, clarifying the starting doses and maintenance doses for all the recommended indications. The information on how to handle administration in patients who cannot swallow the tablets and capsules has also been harmonised.

The Committee noted that there were differences between Member States regarding the use of Losec in *H. pylori* eradication treatment, especially with regards to the number of antibiotics to combine with Losec (either one or two), and the recommended antibiotics and their doses. The CHMP acknowledged that the differences existed because of differences in the availability of, and pattern of resistance to, various antibiotics between Member States. The final agreed wording describes some possible combinations.

4.3 Contra-indications

The CHMP also agreed on a harmonised wording for the contra-indications (situations where the medicine must not be used). Losec must not be used in people who are allergic to omeprazole or to any other ingredients in the medicine, and in people being treated with nelfinavir.

4.4 Special warnings and precautions for use

Co-administration of atazanavir with a PPI such as Losec is not recommended. However, if the combination of atazanavir with a PPI is judged unavoidable, close clinical monitoring (e.g. virus load) is recommended while high doses of PPI should be avoided. The Committee also recommended that, as a precaution, use of Losec in patients receiving clopidogrel should be discouraged. The CHMP also included a warning that treatment with Losec and other PPIs may lead to an increase in infections of the gut.

4.5 Interactions with other medicinal products

The CHMP noted that, due to interactions, the concomitant use of PPIs may affect the efficacy of atazanavir and other HIV medications whose absorption is pH-dependent. The CHMP also noted that there was some interaction with clopidogrel, but the clinical implications of this is not clear.

Other changes

The CHMP harmonised the SmPC sections on pregnancy and lactation, the ability to drive and use machines, undesirable effects and overdose.

The amended information to doctors and patients is available here.

The European Commission issued a decision on 10 June 2010.

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