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Questions and answers on the review of Zerit (stavudine) Outcome of a renewal procedure

The European Medicines Agency has completed a review of Zerit as part of the procedure for the renewal of the medicine's marketing authorisation. The Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended that the marketing authorisation for Zerit should be renewed but that the use of the medicine should be severely restricted in both adults and children.

What is Zerit?

Zerit is a medicine that contains the active substance stavudine. It is available as capsules and as a powder to be made up into an oral solution.

Zerit is used in combination with other antiviral medicines to treat adults and children who are infected with human immunodeficiency virus (HIV), the virus that causes acquired immune deficiency syndrome (AIDS).

The active substance in Zerit, stavudine, is a nucleoside reverse transcriptase inhibitor (NRTI). It blocks the activity of reverse transcriptase, an enzyme produced by HIV that allows it to infect cells in the body and make more viruses.

Zerit has been authorised in the EU since 8 May 1996 and is marketed in 20 EU Member States and Norway¹.

Why was Zerit reviewed?

The marketing authorisation for Zerit has been renewed twice since it was first granted in 1996. The authorisation was due to expire again on 9 May 2011. Therefore, the company that makes Zerit submitted an application for renewal in September 2010.

Which data has the CHMP reviewed?

As part of this renewal procedure, the CHMP looked at all the relevant information on the medicine's safety and effectiveness that has become available since the last authorisation. The Committee looked

¹ Zerit is marketed in Austria, Belgium, Bulgaria, Cyprus, Germany, Greece, Denmark, Finland, France, Hungary, Ireland, Italy, Lithuania, the Netherlands, Norway, Portugal, Romania, Slovakia, Spain, Sweden and the United Kingdom.



at a number of recent scientific publications on the medicine as well as safety data from post-marketing reports of side effects. During the renewal procedure, the CHMP also convened a meeting of HIV experts to provide advice on the medicine's benefits and risks.

What are the conclusions of the CHMP?

The CHMP noted that post-marketing reports and recent published literature have improved the understanding of the side effects of Zerit. The medicine is known to have a toxic effect on the energy-producing components of cells called the mitochondria, which can result in a number of side effects: lipoatrophy (a loss of fat in some areas of the body which can cause disfigurement), lactic acidosis (a build-up of lactic acid in the body) and peripheral neuropathy (damage to the nerves in the extremities). The Committee noted that these side effects are serious, usually appear with long term use and are more commonly seen with Zerit than with other NRTI medicines.

In view of the side effects seen with the medicine, the CHMP recommended that the marketing authorisation for Zerit should be renewed with restrictions. The Committee recommended that, for both adults and children, it should be used for as short a time as possible and only when there are no appropriate alternatives.

The Committee also agreed that the company should provide a letter to the healthcare professionals who prescribe Zerit, explaining the updated safety information and restricted use.

The full changes made to the information to doctors and patients are detailed [here](#).

What are the recommendations for patients and prescribers?

- Prescribers are reminded of the severe side effects seen with Zerit and should only use the medicine when other appropriate treatments are not available;
- Patients being treated with Zerit should be assessed frequently and switched to appropriate alternatives as soon as possible;
- Prescribers should consult the updated prescribing information and the communication letter that will be sent to them for more information;
- Patients should continue reporting any possible side effects to their doctor and should contact their doctor or pharmacist with any questions they have concerning their treatment.

A European Commission decision on this opinion will be issued in due course.

The current European public assessment report for Zerit can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports.