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EPAR summary for the public

Zerit

stavudine

This is a summary of the European public assessment report (EPAR) for Zerit. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Zerit.

What is Zerit?

Zerit is an antiviral medicine containing the active substance stavudine. It is available as capsules containing 15, 20, 30 and 40 mg stavudine. Zerit is also available as a powder to make up into an oral solution.

What is Zerit used for?

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).

Zerit is used for as short a time as possible and only when other antiviral medicines cannot be used.

The medicine can only be obtained with a prescription.

How is Zerit used?

Treatment with Zerit should be initiated by a doctor who has experience in the treatment of HIV infection. The dose to use is calculated based on the age and weight of the patient. Adults weighing less than 60 kg and children weighing over 30 kg take a dose of 30 mg, and adults over 60 kg take 40 mg. Children over the age of 14 days receive 1 mg per kilogram body weight, unless they weigh more than 30 kg. Babies less than 13 days old should be given 0.5 mg/kg body weight. All doses should be taken every 12 hours.

Zerit should be taken on an empty stomach, at least one hour before a meal. If this is not possible, it may be taken with a light meal. The capsules should be swallowed whole or opened carefully and their

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contents mixed with food. The oral solution should be used in patients below three months of age. The dose may need to be adjusted in patients who have problems with their kidneys or experience certain side effects.

Zerit is to be used for as short a time as possible and the patients switched to appropriate alternatives whenever possible. Patients taking Zerit should be assessed frequently. For more information, see the summary of product characteristics (also part of the EPAR).

How does Zerit work?

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. By blocking this enzyme, Zerit, taken in combination with other antiviral medicines, reduces the amount of HIV in the blood and keeps it at a low level. Zerit does not cure HIV infection or AIDS, but it may delay the damage to the immune system and the development of infections and diseases associated with AIDS.

How has Zerit been studied?

The effectiveness of Zerit was assessed in four main studies. The first study compared the effects of Zerit taken alone with those of zidovudine (another antiviral medicine) in 822 HIV-infected patients who had been taking zidovudine for at least six months. Its main measure of effectiveness was how long it took for the patients to develop a disease associated with AIDS or to die. The second study compared two doses of Zerit in over 13,000 patients who did not respond to, or could not take, other types of antiviral medicine. This study measured survival rates.

Two further studies assessed the effectiveness of Zerit, taken in combination with lamivudine and efavirenz (other antiviral medicines) in 467 treatment-naïve patients (who had not taken treatment for HIV infection before). The main measures of effectiveness were the levels of HIV in the blood (viral load) and the number of CD4 T cells in the blood (CD4 cell count) after 48 weeks of treatment. CD4 T cells are white blood cells that are important in helping to fight infections, but which are killed by HIV.

What benefit has Zerit shown during the studies?

The studies showed that Zerit could reduce the rates of disease progression in HIV-infected patients. Patients taking Zerit alone developed an AIDS-related disease or died at a similar rate to those taking zidovudine. Patients taking either of two doses of Zerit also had similar survival rates over 22 weeks.

When taken in combination with lamivudine and efavirenz, around 70% of the patients taking Zerit had viral loads below 400 copies/ml after 48 weeks. The patients' CD4 cell counts also rose from around 280 cells/mm^3 before treatment by an average of around 185 cells/mm^3.

What is the risk associated with Zerit?

The most common side effects when taking Zerit (seen in between 1 and 10 patients in 100) are peripheral neuropathy (damage to the nerves in the extremities causing tingling, numbness and pain in the hands and feet), diarrhoea, nausea, abdominal (stomach) pain, dyspepsia (heartburn), tiredness, lipoatrophy (a loss of fat in some areas of the body which can cause disfigurement), dizziness, insomnia (difficulty sleeping), abnormal thinking or dreams, somnolence (sleepiness), headache, depression, rash, pruritus (itching) and hyperlactataemia (elevated lactic acid levels in the blood).

Three side effects are possibly related to the medicine's toxic effect on mitochondria (the energy-producing components within cells): lipoatrophy, lactic acidosis (a build-up of lactic acid in the body) and peripheral neuropathy. These side effects are serious, usually appear with long-term use and are more commonly seen with Zerit than with other NRTI medicines.

Zerit must not be used in people who are taking another HIV medicine called didanosine, which can also have toxic effects on mitochondria. For the full list of side effects and restrictions with Zerit, see the package leaflet.

Why has Zerit been approved?

The CHMP decided that Zerit's benefits are greater than its risks and recommended that it be given marketing authorisation. Since its authorisation, post-marketing reports and published literature regarding the side effects of Zerit have led the CHMP to update the prescribing information for Zerit, recommending that it should be used for as short a time as possible and only when other antiviral medicines cannot be used.

Other information about Zerit

The European Commission granted a marketing authorisation valid throughout the European Union for Zerit on 8 May 1996.

The full EPAR for Zerit can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Zerit, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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