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EPAR summary for the public

Sirturo

bedaquiline

This is a summary of the European public assessment report (EPAR) for Sirturo. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Sirturo.

For practical information about using Sirturo, patients should read the package leaflet or contact their doctor or pharmacist.

What is Sirturo and what is it used for?

Sirturo is a tuberculosis medicine that contains the active substance bedaquiline. Tuberculosis is an infection caused by the bacterium *Mycobacterium tuberculosis*. Sirturo is used in combination with other tuberculosis medicines in adults with tuberculosis that is affecting the lung and that is multi-drug resistant (resistant to at least isoniazid and rifampicin, two standard tuberculosis medicines). It is given when combinations without Sirturo cannot be used, either because the disease is resistant to them or because of their side effects.

Because the number of patients with tuberculosis is low in the EU, the disease is considered ‘rare’, and Sirturo was designated an ‘orphan medicine’ (a medicine used in rare diseases) on 26 August 2005.

How is Sirturo used?

Sirturo can only be obtained with a prescription. Treatment should be started and monitored by a doctor who is experienced in the treatment of multi-drug resistant tuberculosis. In addition, it is recommended that patients are directly observed by a healthcare professional as they take the medicine.

The medicine is available as 100 mg tablets. The recommended dose is 4 tablets once a day for the first 2 weeks and then 2 tablets taken 3 times a week for the next 22 weeks. The tablets should be taken with food. For further information, see the package leaflet.

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How does Sirturo work?

The active substance in Sirturo, bedaquiline, works by specifically blocking an enzyme inside the *M. tuberculosis* bacteria called ATP synthase, which the bacteria need to generate energy. Without the ability to generate energy, the bacteria die and the patient's condition can start to improve.

What benefits of Sirturo have been shown in studies?

In a main study in adults with multi-drug resistant tuberculosis affecting the lung, Sirturo was compared with placebo (a dummy treatment) when added to combination treatment with other standard tuberculosis medicines. The study showed that after 24 weeks, 79% of the patients given Sirturo (52 out of 66 patients) tested negative for the bacteria in the sputum (phlegm) compared with 58% of patients given placebo (38 out of 66 patients). The average time it took to clear the bacteria from the sputum was also shorter for patients in the Sirturo group than for those in the placebo group (83 days versus 125 days).

What are the risks associated with Sirturo?

The most common side effects with Sirturo (which may affect more than 1 in 10 people) are headache, dizziness, nausea (feeling sick), vomiting, and arthralgia (joint pain). For the full list of all side effects and restrictions, see the package leaflet.

Why is Sirturo approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Sirturo's benefits are greater than its risks and recommended that it be approved for use in the EU. Sirturo increased the number of patients who tested negative for the tuberculosis bacteria and shortened the average time it took to clear the bacteria from the sputum.

The Committee highlighted the need for new medicines to treat multi-drug resistant tuberculosis and noted that Sirturo was the first of a new class of medicines for which cross-resistance with other medicines had not yet been seen. Cross-resistance is when bacteria develop resistance to a medicine after being exposed to another one, which is often the case with multi-drug resistant tuberculosis.

With regard to safety, the side effects reported in the Sirturo group in the main study were not markedly different from those in the placebo group, though there were higher levels of liver enzymes and some reports of alterations in the heart's electrical activity (known as prolonged QT interval). There was also a higher number of reported deaths in the Sirturo group. Although an analysis of these deaths did not support the conclusion that they were caused by Sirturo, the CHMP has required the company to provide more information from a long-term follow-up study to allay any concerns.

Sirturo has been given 'conditional approval'. This means that there is more evidence to come about the medicine, which the company is required to provide. Every year, the European Medicines Agency will review any new information that becomes available and this summary will be updated as necessary.

What information is still awaited for Sirturo?

Since Sirturo has been granted a conditional approval, the company that markets Sirturo will provide additional data on the medicine's benefits and safety when used with different combinations of medicines. The company will also provide longer term safety data on the medicine.

What measures are being taken to ensure the safe and effective use of Sirturo?

A risk management plan has been developed to ensure that Sirturo is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Sirturo, including the appropriate precautions to be followed by healthcare professionals and patients.

Further information can be found in the summary of the risk management plan.

Other information about Sirturo

The European Commission granted a marketing authorisation valid throughout the European Union for Sirturo on 05/03/2014.

The full EPAR and risk management plan summary for Sirturo 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 Sirturo, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summary of the opinion of the Committee for Orphan Medicinal Products for Sirturo can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

This summary was last updated in 01-2014.