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Sirturo (*bedaquiline*)

An overview of Sirturo and why it is authorised in the EU

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 and children (aged at least 5 years and weighing at least 15 kg) with tuberculosis in the lung that is multi-drug resistant (resistant to at least isoniazid and rifampicin, the two standard tuberculosis medicines). It is given when other combinations cannot be used, either because the disease is resistant to them or because of their side effects.

Tuberculosis is rare in the EU, and Sirturo was designated an 'orphan medicine' (a medicine used in rare diseases) on 26 August 2005. Further information on the orphan designation can be found here: ema.europa.eu/medicines/human/orphan-designations/eu305314.

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 a healthcare professional watches the patients as they take the medicine.

The medicine is available as tablets. The recommended dose in adults is 400 mg once a day for the first 2 weeks and then 200 mg 3 times a week for the next 22 weeks. In children the dose depends on the child's weight. The tablets should be taken with food. For more information about using Sirturo, see the package leaflet or contact your doctor or pharmacist.

How does Sirturo work?

The active substance in Sirturo, bedaquiline, blocks 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 starts to improve.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

What benefits of Sirturo have been shown in studies?

In a main study in patients 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).

The way Sirturo is handled in the body in children has been shown to be the same as in adults; it is therefore also expected to be effective at treating tuberculosis in children.

What are the risks associated with Sirturo?

The most common side effects with Sirturo in adults (which may affect more than 1 in 10 people) are headache, dizziness, nausea (feeling sick), vomiting, and arthralgia (joint pain). Overall, the side effects in adolescents are similar to those in adults. Blood tests showing increased liver enzymes and other effects on the liver occur in about 1 in 3 younger children. For the full list of all side effects and restrictions, see the package leaflet.

Why is Sirturo authorised in the EU?

The main study showed that 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. Furthermore, Sirturo was the first of a new class of medicines for which cross-resistance had not yet occurred. Cross-resistance is when bacteria resistant to one medicine are also resistant to a different medicine not used previously, which is often the case with multi-drug resistant tuberculosis.

The side effects 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). Also, a higher number of deaths was reported in the Sirturo group. Although an analysis did not conclude that Sirturo caused these deaths, the company will provide more information from a long-term follow-up study to address any concerns.

The European Medicines Agency concluded that Sirturo's benefits are greater than its risks and it can be authorised for use in the EU.

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

What information is still awaited for Sirturo?

Since Sirturo has been given conditional authorisation, the company that markets Sirturo will provide longer term safety data on the medicine.

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

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Sirturo have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Sirturo are continuously monitored. Side effects reported with Sirturo are carefully evaluated and any necessary action taken to protect patients.

Other information about Sirturo

Sirturo received a conditional marketing authorisation valid throughout the EU on 5 March 2014.

Further information on Sirturo can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/sirturo

This overview was last updated in 02-2021.