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EPAR summary for the public

Ixiaro

Japanese encephalitis vaccine (inactivated, adsorbed)

This document is a summary of the European Public Assessment Report (EPAR) for Ixiaro. 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 Ixiaro.

What is Ixiaro?

Ixiaro is a vaccine that contains inactivated Japanese encephalitis virus as the active substance.

What is Ixiaro used for?

Ixiaro is used to protect adults and children aged two months and older against Japanese encephalitis, a disease that causes inflammation of the brain. Japanese encephalitis can be fatal or lead to long-term disability. It is transmitted by mosquitoes and is most common in Asia, particularly in rural areas. Vaccination with Ixiaro should be considered for people who are at risk of exposure to the Japanese encephalitis virus through travel or work.

The medicine can only be obtained with a prescription.

How is Ixiaro used?

Ixiaro is given by injection into a muscle, preferably into the shoulder muscle, or into the thigh muscle in young children. In adults, including those aged above 65 years, and children aged three years and older, a full dose of Ixiaro (0.5 ml) should be given, and an additional 0.5 ml dose should be given four weeks later. Adults from 18 to 65 years can also receive a rapid vaccination course, where the second dose is given seven days after the first dose.

In children aged between two months and three years, half the adult dose of Ixiaro (0.25 ml) should be given, and an additional 0.25 ml dose should be given four weeks later.

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It is recommended that individuals who receive the first dose of Ixiaro should receive both doses. The second dose should be given at least one week before potential exposure to the virus. In adults, the second dose can be given up to 11 months after the first.

Adults from 18-65 years who are likely to be exposed to the Japanese encephalitis virus again or who are at continuous risk of the disease should receive a booster dose of Ixiaro one to two years later and a second booster dose 10 years after the first booster. Children and adolescents may also receive a booster dose one to two years after the initial vaccination.

A booster dose should also be considered for adults aged above 65 years before any further exposure to the Japanese encephalitis virus.

Ixiaro can be injected under the skin in people who have a bleeding disorder such as low blood platelet counts or haemophilia.

How does Ixiaro work?

Ixiaro is a vaccine. Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend itself against a disease. Ixiaro contains small amounts of the virus that causes Japanese encephalitis, which has been inactivated (killed) so that it cannot cause the disease. When a person is given the vaccine, the immune system recognises the inactivated virus as 'foreign' and makes antibodies against it. In future, the immune system will be able to produce antibodies quickly and in large numbers when it is exposed to Japanese encephalitis virus. The antibodies will help to protect against the disease.

The vaccine is 'adsorbed'. This means that the virus is fixed onto aluminium compounds, to stimulate a better response. The virus in Ixiaro is grown in mammal cells ('Vero cells') under laboratory conditions.

How has Ixiaro been studied?

Ixiaro given as two doses 4 weeks apart has been studied in one main study involving 867 healthy adults. The study compared Ixiaro with another vaccine for Japanese encephalitis containing viruses grown in mouse brains. It measured the ability of the two vaccines to trigger the production of antibodies against the Japanese encephalitis virus, four weeks after the final injection.

A study in 660 adults compared a rapid vaccination course (two doses given 7 days apart) with the standard vaccination course (two doses given four weeks apart).

Ixiaro has also been studied in children in one main study involving 1,869 children aged between two months and 18 years. The measure of effectiveness was the ability of the vaccine to trigger the production of antibodies against the Japanese encephalitis virus, four weeks after the final injection.

In addition, the company presented the results of studies looking at the level of protection in adults and in children for up to three years after vaccination with Ixiaro, and at the response to booster doses.

What benefit has Ixiaro shown during the studies?

In adults, Ixiaro (given as two doses 4 weeks apart) was as effective as the comparator vaccine at triggering the production of antibodies against the Japanese encephalitis virus. Before vaccination, most of the people in the study had no protective levels of antibodies against the virus. Four weeks after the final injection, 96% of these people who received both doses of Ixiaro had developed protective levels of antibodies (352 out of 365). This was compared with 94% of the people receiving

the comparator vaccine (347 out of 370). On average, the levels of antibodies were over two times higher in the people receiving Ixiaro than in those receiving the comparator vaccine.

The study looking at the rapid vaccination course found that a 7-day accelerated vaccination course did not produce lower protection than the standard 4-week vaccination course. Long-term antibody levels were similar with both schedules.

In children, four weeks after the final injection, 99% to 100 % of children who received both doses of Ixiaro had developed protective levels of antibodies.

The additional studies showed that protection against Japanese encephalitis virus lasted for at least two to three years in most people vaccinated with Ixiaro. They also showed that a booster dose might be needed to maintain high levels of protection, which may be necessary for people at high risk of exposure to the virus.

What is the risk associated with Ixiaro?

The most common side effects with Ixiaro in adults (seen in more than 1 patient in 10) are headache, myalgia (muscle pain), pain and tenderness at the injection site and tiredness. In children aged less than 3 years, fever, diarrhoea, influenza-like illness, irritability and redness at injection site were the most common side effects (seen in more than 1 of 10 children) and in children aged 3 years and older, fever and injection site pain and tenderness were most common. For the full list of all side effects reported with Ixiaro, see the package leaflet.

Ixiaro must not be used in people who are hypersensitive (allergic) to the active substance, any of the other ingredients or any residual substances in the vaccine such as protamine sulphate. Anyone who has an allergic reaction after the first dose of Ixiaro should not receive the second dose. Vaccination should be postponed in people with recent severe fever.

Why has Ixiaro been approved?

The CHMP decided that Ixiaro's benefits are greater than its risks and noted that the production of the only other vaccine for protection against Japanese encephalitis that was in use outside Asia had been discontinued. The Committee recommended that Ixiaro be given marketing authorisation.

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

A risk management plan has been developed to ensure that Ixiaro 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 Ixiaro, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Ixiaro

The European Commission granted a marketing authorisation valid throughout the European Union for Ixiaro on 31 March 2009.

The full EPAR for Ixiaro 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 Ixiaro, read the Package Leaflet (also part of the EPAR).

This summary was last updated in 04-2016.