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Ixiaro (*Japanese encephalitis vaccine (inactivated, adsorbed)*)

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

What is Ixiaro and what is it used for?

Ixiaro is a vaccine that helps protect adults and children aged 2 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.

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 3 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 2 months and 3 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.

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.

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Ixiaro can only be obtained with a prescription. For more information about using Ixiaro, see the package leaflet or contact your doctor or pharmacist.

How does Ixiaro work?

Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend 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 identifies 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 again. 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.

What benefit of Ixiaro have been shown in studies?

Ixiaro has been shown to trigger the production of antibodies against the Japanese encephalitis virus in 3 main studies:

- The first study involved 867 healthy adults and compared Ixiaro with another vaccine for Japanese encephalitis containing viruses grown in mouse brains. Ixiaro (given as 2 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 2 times higher in the people receiving Ixiaro than in those receiving the comparator vaccine.
- The second main study in 660 adults compared a rapid vaccination course (2 doses given 7 days apart) with the standard vaccination course (2 doses given 4 weeks apart). The 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.
- The third main study involved 1,869 children aged between 2 months and 18 years. 99% to 100% of children who received both doses of Ixiaro had developed protective levels of antibodies against the Japanese encephalitis virus 4 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 3 years after vaccination with Ixiaro, and at the response to booster doses. These additional studies showed that protection against Japanese encephalitis virus lasted for at least 2 to 3 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 are the risks associated with Ixiaro?

The most common side effects with Ixiaro in adults (which may affect more than 1 in 10 people) are headache, myalgia (muscle pain), pain and tenderness at the injection site and tiredness. In children, fever, diarrhoea, influenza-like illness, irritability, and reactions at the injection site (such as redness,

pain and tenderness) were the most common side effects (which may affect more than 1 of 10 children). For the full list of side effects of Ixiaro, see the package leaflet.

Ixiaro must not be used in people who are hypersensitive (allergic) to 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 must be postponed in people with recent severe fever. For the full list of restrictions, see the package leaflet.

Why is Ixiaro authorised in the EU?

The European Medicines Agency decided that Ixiaro's benefits are greater than its risks and it can be authorised for use in the EU. The Agency noted that the production of the only other vaccine for protection against Japanese encephalitis that was in use outside Asia had been discontinued.

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

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

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

Other information about Ixiaro

Ixiaro received a marketing authorisation valid throughout the EU on 31 March 2009.

Further information on Ixiaro can be found on the Agency's website:

ema.europa.eu/medicines/human/EPAR/Ixiaro.

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