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 viruses 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 deep injection into a muscle, preferably into the shoulder muscle, or into the thigh muscle in young children. In adults and children aged three years and older, a full dose of Ixiaro (0.5 ml) should be given, repeated four weeks later. In children aged between two months and three years, half the adult dose of Ixiaro (0.25 ml) should be given, repeated four weeks later.

It is recommended that individuals who receive the first dose of Ixiaro should complete both doses. In adults, if the second dose is missed for any reason, it can be given up to 11 months after the first.
Adults 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.

Ixiaro should never be injected into a blood vessel. It 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 viruses that cause Japanese encephalitis, which have been inactivated (killed) so that they cannot cause the disease. When a person is given the vaccine, the immune system recognises the inactivated viruses as ‘foreign’ and makes antibodies against them. In the future, the immune system will be able to produce antibodies more quickly when it is exposed to Japanese encephalitis viruses. The antibodies will help to protect against the disease.

The vaccine is ‘adsorbed’. This means that the viruses are fixed onto aluminium compounds, to stimulate a better response. Unlike other vaccines against Japanese encephalitis, which use viruses grown in mouse brains, the viruses in Ixiaro are grown in mammal cells (‘Vero cells’) under laboratory conditions.

**How has Ixiaro been studied?**

Ixiaro 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.

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

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.

**What benefit has Ixiaro shown during the studies?**

In adults, Ixiaro 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 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.

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.
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), and pain and tenderness at the injection site. In children < 3 years of age, fever, diarrhoea, influenza-like illness and irritability were the most common side effects (seen in more than 1 of 10 children) and in children 3 years and older, injection site pain and fever 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 having an allergic reaction after the first dose of Ixiaro should not receive the second dose. Vaccination should be postponed in people with a sudden, 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.

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 here. For more information about treatment with Ixiaro, read the Package Leaflet (also part of the EPAR).

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