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Questions and answers on the review of Ixiaro (Japanese encephalitis vaccine)

Outcome of a procedure under Article 20 of Regulation (EC) No 726/2004

On 15 March 2012, the European Medicines Agency completed a review of the vaccine Ixiaro at the request of the European Commission. This followed the identification of a batch of Ixiaro that was less potent than expected, which raised concerns that it may not provide adequate protection against the Japanese encephalitis virus. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the lower potency had no impact on the effectiveness of Ixiaro, and that the benefits of the vaccine continue to outweigh its risks. Furthermore, the Committee agreed on measures that the company should carry out to ensure that the vaccine continues to provide adequate protection.

What is Ixiaro?

Ixiaro is a vaccine used to protect adults against Japanese encephalitis, a disease that causes inflammation of the brain and can be fatal.

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.

This vaccine is 'adsorbed'. This means that the inactivated viruses are adsorbed (fixed) onto aluminium compounds to stimulate a better immune response.

Ixiaro has been authorised in the European Union (EU) since 31 March 2009 and is marketed in 17 EU Member States[1] as well as Norway and Iceland. The current European public assessment report for Ixiaro can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

[1] Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, the Netherlands, Poland, Portugal, Slovak Republic, Spain, Sweden and the UK.

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Why was Ixiaro reviewed?

In 2011, the Agency was informed by the company that markets Ixiaro, Intercell AG, that a batch of the vaccine[2] had failed a test that measures its activity against the Japanese encephalitis virus (its potency). This batch had passed all the extensive tests required in the EU before vaccines are released onto the market. However a further test in experimental models after many months of shelf life raised concerns that this batch could fail to provide adequate protection against the virus. The company therefore stopped further distribution and started a recall of the affected batch in the four EU countries where it was marketed (France, Italy, Spain and the United Kingdom). At the time, the CHMP recommended that revaccination with a different batch should be considered for people who had received Ixiaro from this batch and were planning to travel to high risk areas

Consequently, on 1 June 2011, the European Commission asked the CHMP to review the impact of these potency results on the effectiveness and safety of Ixiaro and to issue an opinion on whether the marketing authorisation for this medicine should be maintained, varied, suspended or withdrawn across the EU.[3].

Which data has the CHMP reviewed?

The CHMP reviewed results of an investigation performed by the company on the root cause of the problem, as well as data from clinical studies and post marketing surveillance on the effectiveness of the vaccine.

What are the conclusions of the CHMP?

The CHMP concluded that the root cause of the lower potency was the unusually high content of other metals in one specific lot of aluminium compound used in the manufacture of Ixiaro. This lot of aluminium compound was also used in the manufacture of other batches of Ixiaro which were released to the market and used in clinical trials. These batches are now expired and not currently in use. The Committee noted that no effectiveness problems had been reported with the vaccine, either in the post marketing or in clinical studies. Furthermore, no batches of the vaccine, produced using this specific lot of aluminium and within expiry date, are currently on the market.

Based on the evaluation of all available data and the scientific discussion within the Committee, the CHMP concluded that the lower potency had no impact on the effectiveness of Ixiaro and that the benefit-risk balance for Ixiaro remains positive. To ensure that Ixiaro continues to provide adequate protection against the Japanese encephalitis virus, the CHMP agreed that the company should carry out a study to establish the acceptable content of other metals in the aluminium compound used to manufacture the vaccine. Until then, the company is to release only those batches of Ixiaro that comply with more stringent potency requirements at release, and furthermore, potency tests will now be required for all batches after release.

A European Commission decision on this opinion will be issued in due course.

[2] Batch JEV09L37.
[3] See EMA's press release '[European Medicines Agency recommends revaccination for some travellers in need of protection with Ixiaro]'.