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Questions and answers on the recommendation to lift the suspension of Octagam (human normal immunoglobulin 5% and 10%)

Outcome of a procedure under Article 31 of Directive 2001/83/EC as amended

The European Medicines Agency has completed a review of Octagam and associated names that was triggered by reports of serious thromboembolic events in patients using the medicine. The Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended that the EU-wide suspension of the marketing authorisation for Octagam be lifted subject to certain conditions, including a change to the medicine's manufacturing process.

What is Octagam?

Octagam is a solution for infusion (drip into a vein) that contains human normal immunoglobulin extracted from blood as the active substance. Immunoglobulins are antibodies (types of protein) normally found in the blood that help the body to fight infections and other diseases.

Octagam is used in patients who are at risk of infection because they do not have sufficient antibodies including people with primary immunodeficiency syndrome, or children born with acquired immune deficiency syndrome (AIDS). It is also used in people with certain immune disorders such as idiopathic thrombocytopenic purpura and in patients who have had a bone marrow transplant.

The marketing authorisations for Octagam in the EU were suspended by the European Commission, following a review by the CHMP in the September 2010. [1]

Why was Octagam reviewed?

In September 2010, the CHMP, following the suspension of the marketing authorisations of Octagam in Germany and Sweden, recommended that all authorisations for the medicine be suspended across the EU. The background to the suspension was an unexpectedly high number of reports of serious thromboembolic events (problems due to the formation of blood clots in the blood vessels) in patients

[1] The questions and answers document published in September 2010 can be found here.

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using the medicine. These events were thought to be related to problems with the medicine's manufacture, and included stroke, myocardial infarction (heart attack) and pulmonary embolism (clot in a blood vessel supplying the lungs). The CHMP noted at the time that the exact cause of the problems could not be identified with certainty.

The current review was initiated in October 2010 at the request of Germany. The aim of the review was to assess all available data on the safety and quality issues related to the thromboembolic events seen with Octagam.

What data has the CHMP reviewed?

The CHMP reviewed investigations that were carried out into the root cause of the problem and proposed corrective measures, including changes to the manufacturing process and tests to be performed during the manufacturing process and on the final products. The Committee also looked at results of batch analyses and independent testing of batches by Member States, as well as information from inspections of two of the manufacturing sites.

What are the conclusions of the CHMP?

The CHMP concluded that the unexpected presence of factor XIa (an enzyme involved in blood clotting) in Octagam was the main cause of the thromboembolic events. Another enzyme, kallikrein, is considered to play a minor role. In addition, critical steps were identified in the manufacturing process that could explain the presence of substances that triggered the thromboembolic events.

The Committee noted that appropriate corrective measures are now in place at the manufacturing sites. The CHMP also agreed on a test to detect factor XIa or other substances that can cause thromboembolic events before batches are released onto the market. The marketing authorisation holders will also be required to carry out post-marketing safety studies as soon as the medicine is reintroduced into the market in order to confirm the safety of the improved manufacturing process.

The CHMP concluded the review with a recommendation that the suspension of the marketing authorisation for Octagam be lifted in the EU on the basis of the safeguards and the change to the medicine's manufacturing process.

What are the recommendations for prescribers and patients?

- With the new safeguards and improvements to the manufacturing process, doctors are advised that the benefits of the Octagam outweigh its risks and that they can start using the medicine again when it becomes available.
- Post-marketing safety studies will be performed. As with all medicines, doctors are reminded to continue reporting any suspected adverse effects.
- Patients who have any questions should speak to their doctor or pharmacist.

The European Commission issued a decision on this opinion on 30 May 2011.