16 February 2012
EMA/107736/2012
EMEA/H/A-36/1296

# Questions and answers on the review of Vivaglobin (human normal immunoglobulin, solution for injection under the skin)

Outcome of a procedure under Article 36 of Directive 2001/83/EC as amended

The European Medicines Agency (EMA) has completed a review of Vivaglobin, following the detection of impurities in the medicine which could cause thromboembolic events (problems due to formation of blood clots in blood vessels). The Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended changes to the manufacturing process to prevent the presence of these impurities and thus reduce the risk of thromboembolic events.

## What is Vivaglobin?

Vivaglobin is a solution for injection under the skin that contains human normal immunoglobulin extracted from blood as the active substance. Human normal immunoglobulins are antibodies (types of protein) normally found in the blood that help the body to fight infections and other diseases.

Vivaglobin is used to provide antibodies to adults and children with primary immunodeficiency syndromes (people who are born with abnormally low levels of antibodies). It is also used to provide antibodies to cancer patients who lack them.

Vivaglobin is authorised in the EU under a mutual recognition procedure and is available in the following EU member states: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Hungary, Italy, Luxembourg, the Netherlands, Poland, Portugal, Spain, Sweden, as well as Norway.

## Why was Vivaglobin reviewed?

On 10 March 2011, the German medicines regulatory agency informed the EMA of a few cases of thromboembolic events, including strokes and pulmonary embolism (clot in a blood vessel supplying the lungs), in patients receiving the medicine. Although thromboembolic events are known to occur with immunoglobulins given by injection into a vein, they had not previously been linked with immunoglobulins given by injection under the skin.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
**Telephone** +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
**E-mail** info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

Investigations by the company found that some of the materials used during the extraction of Vivaglobin from human blood produced impurities capable of triggering the formation of blood clots. Therefore, the company took corrective action to remove these impurities by modifying the manufacturing process. This modification of the manufacturing process was in line with the approved marketing authorisation.

On 17 March 2011, the German medicines regulatory agency decided to refer the matter to the CHMP so that the Committee could conduct an EU review of the root cause of the problem and evaluate the measures introduced in order to issue an opinion on whether the marketing authorisation of Vivaglobin should be maintained, varied, suspended or withdrawn.

## What are the conclusions of the CHMP?

Based on evaluation of the root cause of the problems that occurred during the manufacture of Vivaglobin, the CHMP concluded that the changes to the manufacturing process effectively reduce the risk of thromboembolic events. Therefore, the Committee recommended that the changes in the manufacturing process should be formally included in the marketing authorisation of Vivaglobin.

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