25 May 2012
EMA/CHMP/331339/2012
Press Office

Press release

European Medicines Agency confirms positive benefit-risk balance of MabThera

Batches produced at the Vacaville manufacturing site do not pose risk to public health

Following a quality review of the genetically engineered monoclonal antibody MabThera, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the batches of the active substance of MabThera, rituximab, produced at the Vacaville manufacturing site in the United States do not present a risk to public health.

MabThera is indicated in non-Hodgkin's lymphoma (follicular lymphoma and diffuse large B-cell lymphoma), chronic lymphocytic leukaemia (CLL) and rheumatoid arthritis.

The review of MabThera was initiated after the unexpected detection of *Leptospira licerasiae* at an early stage (pre-harvest) of the manufacturing process of rituximab in bioreactors at Vacaville. The contaminant was not detected at later stages of manufacturing of the active substance or the finished product, and all material in which the bacteria had been detected was discarded.

Leptospira licerasiae is a bacterial species that can cause leptospirosis, a water-borne disease transmitted from animals to humans.

The CHMP reviewed all available quality data provided by the company and looked for the root cause of the contamination with the aim of ensuring safe supply of the medicine to patients. At the request of the CHMP, the Danish Health and Medicines Authority inspected the Vacaville site, covering laboratories, warehouses, manufacturing and utility facilities and quality management systems at the site.

The CHMP concluded that *L. licerasiae* had most likely been introduced into the cell culture media used in the bioreactors through personnel acting as external carriers and/or through the media preparation process itself.

The Committee noted that batches of active substance produced from cultures which tested positive at pre-harvest are not being further processed and adequate corrective and preventive measures have

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now been introduced at the Vacaville site, which should minimise any potential contamination and help improve the detection of the bacteria.

The Committee was reassured that the findings were not associated with any clinically relevant risk for patients treated with MabThera, as no bacteria were detected in the active substance or in the finished product, and that the manufacturing process is robust enough to eliminate any bacteria and proteins released by the bacteria.

Therefore, the CHMP concluded that the benefit-risk balance of MabThera made using the active substance produced at the Vacaville site continued to be positive.

The CHMP's recommendation has been forwarded to the European Commission for the adoption of a binding decision.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. A question-and-answer document on this review is available on the Agency's website.
3. MabThera was approved in the European Union on 2 June 1998. The marketing authorisation holder is Roche Registration.
4. More information on MabThera is available in the European public assessment report (EPAR).
5. The review of MabThera was conducted in the context of a formal review, initiated by the European Commission on 15 December 2011 under Article 20 of Regulation (EC) No 726/2004/EC.
6. According to the World Health Organization (WHO) in 2001, there were 0.1 to 1 cases of leptospirosis per 100000 inhabitants per year in temperate climates. The early stages of leptospirosis may include high fever, severe headache, muscle pain, chills, redness in the eyes, abdominal pain, jaundice, haemorrhages in skin and mucous membranes (including pulmonary bleeding), vomiting, diarrhoea and a rash. More information on leptospirosis can be found on the WHO website: http://www.who.int/water_sanitation_health/diseases/leptospirosis/en/
7. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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