16 March 2012
EMA/CHMP/185096/2012
Press Office

Press release

European Medicines Agency recommends transfer of manufacturing sites for Caelyx and Ceplene

Final two opinions on medicines made at Ben Venue Laboratories

The European Medicines Agency has recommended that the manufacturing processes for the anticancer medicines Caelyx (doxorubicin hydrochloride) and Ceplene (histamine dihydrochloride) be transferred from the Ben Venue Laboratories in Ohio, United States, to alternative facilities.

While the transfers are ongoing, the Agency's Committee for Medicinal Products for Human Use (CHMP) is recommending that the marketing authorisations of the two medicines be maintained because both medicines are considered to be essential for patients and no alternative suppliers or alternative formulations are currently available. The Committee also considered the fact that no concerns have been raised from the safety monitoring of these medicines.

During this time, Caelyx and Ceplene continue to be manufactured at the Ben Venue facility, because it is the only site where these medicines are made for the European Union (EU) market.

In the meantime, the Agency is recommending that the interim measures introduced in November and December 2011 be continued.

For **Caelyx**, no new patients should be started on the medicine and Caelyx manufactured at Ben Venue should only be used to complete treatment that has already been initiated. This recommendation remains valid until the sterile filtration and aseptic filling processes have been transferred to a new manufacturing site and supply can be guaranteed from this site. This should be completed by September 2012. Following this, the marketing-authorisation holder, Janssen-Cilag International NV, should transfer the remaining steps in the manufacturing process to a new site by the end of 2014.

Whilst stocks from Ben Venue are still being used in the EU, the marketing authorisation holder of Caelyx is required to promptly inform the CHMP if they become aware of safety concerns, and submit a monthly report detailing reports on effects that could be related to sterilisation problems, such as sepsis. Healthcare professionals should monitor patients closely for such effects and report them immediately to the company.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8427 **Facsimile** +44 (0)20 7418 8409
E-mail press@ema.europa.eu **Website** www.ema.europa.eu

For **Ceplene**, the manufacturing process should be transferred by the end of 2013. The marketing-authorisation holder, EpiCept GmbH, should continue to inspect the vials of the medicine visually for signs of contamination with particles.

The review of medicines manufactured at Ben Venue Laboratories began in November 2011, after a good-manufacturing-practice (GMP) inspection revealed several shortcomings in its quality-assurance processes. These included concerns over the sterility of the filling process and possible contamination with particles.

Despite these concerns, no safety issues have emerged from monitoring of patients receiving Caelyx, Ceplene or any of the 12 other centrally authorised medicines manufactured at the facility.

These are the final two opinions stemming from the shortcomings at the Ben Venue manufacturing facility, where 14 centrally authorised medicines were manufactured. In February 2012, the Committee recommended that Ben Venue be removed as a manufacturing site for the other 12 medicines included in the entire review.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. The European review of Caelyx and Ceplene was conducted in the context of a formal review, initiated at the request of the European Commission under Article 20 of Regulation (EC) No 726/2004, on 17 November 2011.
3. More information on Caelyx and Ceplene is available in their European public assessment reports (EPARs) on the Agency's website.
4. On 13 January 2012, the United Kingdom's medicines regulatory authority, the Medicines and Healthcare Products Regulatory Agency (MHRA), issued a restricted GMP certificate to the Ben Venue facility, allowing it to continue manufacturing essential medicines but stopping it supplying non-essential medicines.
5. The press releases on the previous recommendations on medicines manufactured at the Ben Venue facility, dated 22 November 2011, 9 and 13 December 2011 and 16 February 2012 are available on the Agency's website.
6. The CHMP's recommendations will now be sent to the European Commission for the adoption of EU-wide decisions.
7. All other opinions and documents adopted by the CHMP at its February 2012 plenary meeting will be published on Friday, 16 March 2012 at 12.00 noon United Kingdom time on a dedicated web page.
8. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

Contact our press officers

Monika Benstetter or Sabine Haubenreisser

Tel. +44 (0)20 7418 8427

E-mail: press@ema.europa.eu