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EMA/106872/2012[1] Corr*

Final recommendations on 12 centrally authorised medicines manufactured at Ben Venue Laboratories

The European Medicines Agency has completed a review of 12 out of 14 centrally authorised medicines manufactured at Ben Venue Laboratories, Ohio, USA (Angiox, Busilvex, Vidaza, Vistide, Velcade, Ecalta diluent, Soliris, Cayston, Luminity, Mepact, Torisel and Vibativ)[2], initiated following shortcomings in quality assurance identified at this site. The Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended suspending the marketing authorisations for Vibativ and Luminity until a suitable manufacturing site is approved. For the remaining 10 medicines, the CHMP recommended maintaining the marketing authorisations as alternative suppliers or formulations are available. The review of the two other centrally authorised medicines manufactured at this site, Caelyx and Ceplene, is still ongoing.

Why were these medicines reviewed?

A good manufacturing practice (GMP) inspection of Ben Venue in November 2011[3] highlighted several shortcomings in the quality management system in place at Ben Venue, particularly in relation to the sterile filling process and possible particle contamination during the manufacturing process. During the inspection, Ben Venue decided to cease all manufacture and distribution of medicines from its site.

Consequently, on 18 November 2011 the European Commission asked the CHMP to assess the impact of these shortcomings on the quality and safety of medicines produced at Ben Venue, and to issue an opinion on whether the marketing authorisation for these medicines should be maintained, varied, suspended or withdrawn across the EU.

[1] Procedure numbers: EMEA/H/C/562/A20/0042, EMEA/H/C/996/A20/0024, EMEA/H/C/654/A20/0013, EMEA/H/C/1240/A20/0001, EMEA/H/C/799/A20/0045, EMEA/H/C/791/A20/0036, EMEA/H/C/788/A20/0019, EMEA/H/C/802/A20/0022, EMEA/H/C/539/A20/0056, EMEA/H/C/978/A20/0017, EMEA/H/C/472/A20/0013, EMEA/H/C/121/A20/0035
* Previously it was stated incorrectly that for Vistide and Cayston, Ben Venue Laboratories, Ohio had already been removed as the manufacturing site from the marketing authorisation.
[2] More information on these medicines can be found in the relevant European public assessment reports (EPARs) for each medicine: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.
[3] The November 2011 inspection of the Ben Venue Laboratories manufacturing site conducted by the Medicines and Healthcare Products Regulatory Agency (MHRA) and the Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) jointly with the Food and Drug Administration (FDA) was a follow-up to a previous inspection conducted in March 2011 that had been triggered by the European Medicines Agency as part of a re-inspection program. This inspection had already led to the restriction in the importation of some medicines to the EU from the Ben Venue site.

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What actions have been taken so far?

The CHMP assessed the causes and impact of the possible particle contamination and the sterility assurance problem. Given the potential risks identified, the CHMP issued interim recommendations in November[4] and December 2011[5] recommending that only products that are absolutely essential for patients' needs and for which no alternative supplier or formulation is available should continue to be used.

In addition, on 13 January 2012, the UK's medicines regulatory agency (MHRA) on behalf of the European regulatory network issued a restricted GMP certificate to Ben Venue in order to stop the EU supply of non-essential medicines from Ben Venue, while allowing the continued supply of essential medicines.

What are the final recommendations of the CHMP?

The CHMP has now finalised the assessment for 12 medicines produced at Ben Venue and is recommending the following:

- The suspension of the marketing authorisations for Vibativ and Luminity, which are currently not marketed in the EU and for which no alternative manufacturer or formulation is available. The suspension will remain in place until the company obtains approval for a GMP compliant alternative manufacturing site.
- The maintenance of the marketing authorisations with conditions for Busilvex, Vidaza, Vistide, Velcade, Ecalta diluent, Soliris, Cayston, Mepact, Torisel and Angiox, for which alternative manufacturers are supplying the EU market or alternative formulations[6] are available. All companies involved are required to submit an application to remove Ben Venue as a manufacturing site for these medicines.

The reviews of Caelyx and Ceplene are currently being finalised. The Agency will communicate on their outcome in the near future. The interim recommendations that were issued in November[4] and December 2011[5] for these medicines remain valid.

What are the recommendations to healthcare professionals and patients?

Angiox, Busilvex, Mepact, Vidaza, Vistide, Velcade, Ecalta, Soliris, Torisel and Cayston should continue to be prescribed as normal.

[4] Press release - European Medicines Agency gives interim recommendations to deal with shortcomings in quality assurance at Ben Venue Laboratories

[5] Press release - European Medicines Agency gives further interim recommendations on dealing with shortcomings in quality assurance at Ben Venue Laboratories
Q&A - European Medicines Agency recommends precautionary recall of remaining batch of Vistide manufactured at Ben Venue Laboratories

[6] Alternative formulations for Velcade 1 mg and Ecalta diluent are Velcade 3.5 mg and Ecalta without solvent, respectively.