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Questions and answers on the review of centrally authorised medicines with ingredients manufactured at Roche Carolina Inc., Florence, USA

Outcome of procedures under Article 20 of Regulation (EC) No 726/2004

On 19 July 2012, the European Medicines Agency completed a review of the six centrally authorised medicines Alli (orlistat), Mircera (methoxy polyethylene glycol-epoetin beta), Pegasys (peginterferon alfa-2a), Tamiflu (oseltamivir), Xeloda (capecitabine) and Xenical (orlistat), which contain ingredients manufactured at Roche Carolina Inc., Florence, USA. The review was initiated following shortcomings in quality assurance identified at this site. The Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended that the benefits of these centrally authorised medicines continue to outweigh their risks and recommended that their marketing authorisations be maintained.

Which medicines are affected by the Agency's review?

The Agency's review covers the following six centrally authorised medicines which contain ingredients manufactured at Roche Carolina Inc.:

- Alli and Xenical, containing the active substance orlistat, used for the treatment of obesity;
- Tamiflu, containing the active substance oseltamivir, used for the prevention and treatment of influenza (flu);
- Mircera, containing the active substance methoxy polyethylene glycol-epoetin beta, used for the treatment of anaemia (low red blood cell counts) in chronic kidney disease (long-term, progressive decrease in the ability of the kidneys to work properly);
- Xeloda, containing the active substance capecitabine, used for the treatment of colorectal, gastric and breast cancer;
- Pegasys, containing the active substance peginterferon alfa-2a, used for the treatment of chronic hepatitis B and C (a disease of the liver due to infection with the hepatitis B or C virus).

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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.

Why were these medicines reviewed?

On 9 December 2011, the European Medicines Agency was made aware by Roche of deficiencies in quality assurance at one of its manufacturing sites, Roche Carolina Inc., Florence, USA. The site produces ingredients (active substances, intermediates and other materials) used in the manufacturing process of the above mentioned six centrally authorised medicines. This followed an internal investigation conducted by Roche which revealed deficiencies in good manufacturing practice and included problems with cleaning practices, and data and documentation management. As a result, Roche initiated an investigation, while improvements were made to ensure compliance with good manufacturing practice.

Consequently, on 15 December 2011 the European Commission asked the CHMP to assess the impact of these shortcomings on the quality and safety of the centrally authorised medicines concerned, and to issue an opinion on whether the marketing authorisations for these medicines should be maintained, varied, suspended or withdrawn across the EU.

Which data has the CHMP looked at?

The CHMP carried out an assessment for each of the six centrally authorised medicines to establish whether the identified deficiencies had an impact on the quality and safety of the finished products. The CHMP looked at data from the initial and subsequent internal investigations by the company. In addition, the CHMP requested additional data from the company to clarify remaining concerns and analysed the results of an inspection of the site carried out by the German and UK medicines regulatory agencies in May 2012.

What are the conclusions of the CHMP?

The CHMP has now finalised the assessment for all six medicines. The Committee was satisfied that the recent inspection confirmed that the company is implementing adequate corrective and preventive actions to address the deficiencies identified. Based on these actions and the available data, the CHMP considered that the identified deficiencies would not impact on the quality and safety of the finished products. The CHMP therefore recommended that the marketing authorisations for the six medicines be maintained.

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