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Questions and answers on Isotretinoin Ranbaxy (UK) Limited (isotretinoin 10 and 20 mg capsules)

Outcome of a procedure under Article 29 of Directive 2001/83/EC as amended

The European Medicines Agency has completed an arbitration procedure following a disagreement among Member States of the European Union (EU) regarding the authorisation of the generic isotretinoin-containing medicine from Ranbaxy (UK) Limited. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of this medicine do not outweigh its risks, and the marketing authorisation granted in the United Kingdom cannot be recognised in other Member States of the EU: France and Spain. The marketing authorisation in the United Kingdom should also be suspended.

What is Isotretinoin?

Isotretinoin is a retinoid (a substance derived from vitamin A) that is used to treat severe acne that has not responded to standard treatments.

Acne is a skin disease caused by an excessive production of sebum (the skin's natural oil) from overactive sebaceous glands in the skin. The sebum accumulates under the skin and causes inflammation. Isotretinoin works by decreasing the size and activity of the sebaceous glands in the skin, reducing sebum production and inflammation in the skin.

Isotretinoin capsules from Ranbaxy are a generic medicine based on a 'reference medicine', Roaccutane, which has been marketed in the EU since 1984.

Why was Isotretinoin reviewed?

Ranbaxy (UK) Limited submitted the generic isotretinoin-containing medicine for mutual recognition on the basis of the initial authorisation granted by the United Kingdom (the 'reference Member State') on 20 November 2006. The company wanted the authorisation to be recognised in France and Spain (the 'concerned Member States').

However, the Member States were not able to reach an agreement and the United Kingdom referred the matter to the CHMP for arbitration on 29 July 2010.

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The grounds for the referral were that the bioequivalence study to show that Ranbaxy's isotretinoin capsules produce the same levels of active substance in the body as Roaccutane had been performed under fasting conditions. As the product information states that the capsules should be taken with food, Spain considered that a bioequivalence study under fed conditions would be required for the granting of the marketing authorisation.

What are the conclusions of the CHMP?

The CHMP considered that demonstration of bioequivalence in the fed state was essential and in line with current guidance on investigation of bioequivalence. However, the company was unable to demonstrate bioequivalence under fed conditions.

Based on evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that bioequivalence of the generic isotretinoin capsules to the reference medicinal product has not been shown according to the current requirements. The CHMP therefore concluded that the benefits of the medicine do not outweigh its risks and recommended that the marketing authorisation should not be granted in the concerned Member States. In addition, the Committee recommended that the marketing authorisation for Isotretinoin Ranbaxy (UK) Limited in the United Kingdom be suspended until bioequivalence in the fed state is shown.

The European Commission issued a decision on 18 May 2011.