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Questions and answers on Cardioxane (dexrazoxane, powder for solution for injection, 500 mg)

Outcome of a procedure under Article 13 of Regulation (EC) No 1234/2008

On 18 May 2017, the European Medicines Agency completed an arbitration procedure for Cardioxane (dexrazoxane powder for solution for injection). The Agency had been asked to arbitrate on the removal of the contraindication for children and adolescents treated with high cumulative doses of cancer medicines called anthracyclines. Its Committee for Medicinal Products for Human Use (CHMP) concluded that such a removal is acceptable. The contraindication should however remain in children and adolescents who are given lower cumulative doses of anthracyclines.

What is Cardioxane?

Cardioxane is a medicine used in adults with breast cancer to prevent long-term harmful effects on the heart caused by treatment with the anthracycline cancer medicines doxorubicin and epirubicin. It contains the active substance dexrazoxane.

The way in which dexrazoxane protects the heart is not entirely clear, but may be linked to the way the medicine attaches to charged iron particles that are involved in the processes that make anthracyclines harmful to the heart muscle.

Cardioxane is authorised in the Czech Republic, Germany, France, Italy, the Netherlands, Poland, Spain and the United Kingdom. The company that markets the medicine is Clinigen Healthcare Limited.

Why was Cardioxane reviewed?

Cardioxane is authorised under a 'mutual recognition' procedure[1] based on an initial authorisation granted by France. Because of concerns that it might increase the risk of second cancers developing long after treatment, the CHMP reviewed the medicine[2] in September 2011 and recommended on the basis of the evidence at that time that use of medicines containing dexrazoxane to protect the heart should be explicitly contraindicated in children and adolescents.

[1] A procedure through which an authorisation of a medicine in one European Union Member State is recognised by another Member State.
[2] http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Dexrazoxane/human_referral_000277.jsp&mid=WC0b01ac05805c516f

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In 2015, Clinigen submitted an application to the French medicines regulator ANSM for changes to the terms of the marketing authorisation, including removal of the contraindication in children and adolescents. The company wanted the changes to be recognised in Czech Republic, Germany, France, Italy, the Netherlands, Poland, Spain and the United Kingdom (the 'concerned Member States'). ANSM did not agree to the changes as requested by the company. However ANSM and the concerned Member States were unable to reach agreement on whether the contraindication could be removed just for children and adolescents treated with high cumulative doses of anthracyclines, and, on 31 January 2017, France referred the matter to the CHMP for arbitration.

The grounds for the referral were the concerns of the UK that removing the contraindication in patients less than 18 years old receiving a high cumulative dose of anthracyclines was not justified given the remaining uncertainties regarding the safety and effectiveness of Cardioxane in this population, particularly given the previous decision of the CHMP regarding dexrazoxane medicines.

What are the conclusions of the CHMP?

Based on evaluation of the currently available data, and the scientific discussion within the Committee, the CHMP concluded that the benefits and risks of Cardioxane have not been established in children under the age of 18 years, in whom it is not licensed, particularly given that most young patients do not receive the high total doses of anthracyclines that can cause damage to the heart.

However, as there are a small number of patients under 18 years who require high doses of anthracyclines and who are therefore at greater risk of harmful effects on the heart, the Committee agreed that the contraindication should be lifted for this group.

CHMP therefore concluded that the product information should state that the medicine is contraindicated in patients under 18 years old who are intended to receive a total cumulative dose of less than 300 mg of doxorubicin per m^2 body surface or an equivalent dose of another anthracycline medicine.

The European Commission issued an EU-wide legally binding decision to implement the CHMP recommendations on Cardioxane on 19/07/2017.