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Questions and answers on the review of dexrazoxane-containing medicines, powder for solution for infusion, 500 mg

Outcome of a procedure under Article 31 of Directive 2001/83/EC as amended

The European Medicines Agency has completed a review of the safety and effectiveness of dexrazoxane. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that dexrazoxane should not be used in children and adolescents. The Committee has also made recommendations for changes to the summaries of product characteristics (SmPCs) for dexrazoxane-containing medicines.

What is dexrazoxane?

Dexrazoxane is used in patients with cancer to prevent long-term toxic effects on the heart caused by treatment with the anticancer medicines doxorubicin and epirubicin.

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 toxic to the heart muscle.

Medicines containing dexrazoxane are authorised for the prevention of cardiotoxic effects in Austria, Czech Republic, Germany, Denmark, Finland, France, Greece, Hungary, Ireland, Italy, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia Spain and the United Kingdom under the following invented names: Cardioxane, Cyrdanax, Dexrazoxane Cyathus, Enaxozar and Procard.

Why was dexrazoxane reviewed?

The French medicines regulatory agency raised concerns that dexrazoxane could be linked to an increased risk of two cancers: acute myeloid leukaemia (AML) and myelodysplastic syndrome (MDS). These concerns were based on studies in the United States reporting cases of AML and MDS in children with Hodgkin's disease as well as cases of AML reported in breast cancer patients receiving dexrazoxane. The UK medicines regulatory agency also shared these concerns and asked the CHMP to carry out a full assessment of the benefit-risk balance of dexrazoxane and to issue an opinion on



whether the marketing authorisations for products containing dexrazoxane should be maintained, varied, suspended or withdrawn across the European Union.

Which data has the CHMP reviewed?

The CHMP reviewed reports on AML and MDS in patients receiving dexrazoxane. The Committee also reviewed all available data on the safety and effectiveness of dexrazoxane, including published studies and data submitted by the companies that market the medicines.

What are the conclusions of the CHMP?

The Committee noted that there was evidence of serious harm in children receiving dexrazoxane. Studies showed a three-fold increase in the risk of new cancers such as AML and MDS. There was also an increased risk of severe myelosuppression (a condition in which the bone marrow cannot make enough blood cells) and severe infection. The CHMP concluded that the benefits of dexrazoxane-containing medicines do not outweigh its risk in children and adolescents, and the medicine should not be used in these age-groups. The use of dexrazoxane should be restricted to adult patients with advanced or metastatic breast cancer who have already received a certain amount of doxorubicin and epirubicin. The use of dexrazoxane should be contraindicated in children and adolescents.

The Committee also noted that in one study in breast cancer patients, dexrazoxane was associated with worsened response to cancer therapy while other studies showed an increased risk of dying in the first few months of treatment with dexrazoxane at a dose ratio of 20: 1 (20 parts dexrazoxane for 1 part of doxorubicin).

In addition to the restriction in the medicine's use, the CHMP has recommended a reduced dose ratio of 10:1 with doxorubicin (the dose ratio remains 10:1 for epirubicin) in adults and has included in the SmPCs more information on what is currently known about the risks of dexrazoxane-containing medicine.

The amended information to doctors and patients is available [here](#).

What are the recommendations for patients and prescribers?

- Dexrazoxane should only be used in adult patients with advanced or metastatic breast cancer. The benefits of dexrazoxane do not outweigh its risks in children and adolescents.
- Dexrazoxane should only be used in adult patients who have already received a minimum cumulative anthracycline dose of 300 mg/m² of doxorubicin, or 540 mg/m² of epirubicin.
- When deciding whether to use dexrazoxane prescribers should consider the short- and long-term risks associated with this product (e.g. myelosuppression and the potential for AML), alongside possible benefits in relation to protection of the heart.
- Information on recommended dosing and additional information on the risks associated with dexrazoxane can be found in the updated prescribing information.
- Patients who have any questions should speak to their doctor.

The European Commission issued a decision on 13 September 2011.