REPORT 215
Dexrazoxane for the prevention of anthracycline-induced cardiotoxicity in children

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EXECUTIVE SUMMARY

Technology: Dexrazoxane (Cardioxane®)

Indication: Prevention of anthracycline-induced cardiotoxicity.

Applicant: Brazilian Society of Pediatric Oncology

Background: Cancer treatment with drugs of anthracycline class is frequently associated with the occurrence of cardiotoxicity. This group of drugs is part of approximately 60% of therapeutic protocols in pediatric oncology. In SUS there is no protocol guiding the prevention of cardiotoxicity with the use of anthracyclines. Among the existing strategies, dexrazoxane demonstrated favorable results guided by intermediate outcomes (biochemical biomarkers and echocardiographic measurements). Finalistic clinical outcomes (hospitalizations avoided) were not evaluated.

Question: Is the use of dexrazoxane combined with anthracyclines for cancer treatment in pediatric patients efficient, safe, and cost-effective for the prevention of cardiotoxicity causative of heart failure and other heart diseases in comparison to chemotherapy alone?

Scientific evidence: Among the best evidences retrieved there are 5 studies evaluating efficacy and safety and, among those, clinical studies and cohort studies in the United States and South Korea, respectively. The groups were mostly composed of patients under the age of 18, with acute lymphoblastic leukemia and Hodgkin’s lymphoma and on treatment with anthracyclines, at doses varying from 110 to 410 mg/m2. The outcomes analyzed by the studies are quite heterogeneous. The studies have mostly used biochemical biomarkers and echocardiographic measurements to foresee late cardiotoxicity, mortality and event-free survival. As a result, dexrazoxane has shown to be efficient in the prevention of change in biochemical biomarkers and echocardiographic measurements predictive of late cardiotoxicity. With respect to mortality and the occurrence of secondary neoplasms, there was no statistically significant difference between study analysis arms. In the scope of drug safety, hematologic toxicity measurements have shown to be unfavorable to dexrazoxane use.

Economic evaluation: In a search in the database of Centre for Reviews and Dissemination – CRD of York University, the economic evaluation made by Wong 2014 was found, which served to adapt the economic model on the use of dexrazoxane for the prevention of anthracycline-induced cardiotoxicity in SUS perspective. The use of a preventive strategy was able to produce a QALY gain of 0.77 in a temporal horizon of the entire life of the patient. The incremental cost-effective ratio to incorporate the technology was BRL 7,294.36.
Budget Impact Analysis: In order to build the budget impact evaluation model, the following information was considered: estimative of annual procedures of chemotherapy with anthracyclines conducted in pediatric patients (40,200); average number of eight vials used per procedure; price of the drug per vial obtained in CMED table (PMVG 0%); and technology diffusion rates during 5 years (10%, 30%, 60%, 80%, 100%). During 5 years, the annual budget impact varied from BRL 2,699,309.40 to R$ 30,380,965.11.

Discussion: The interpretation of studies results should be made with caution, since none of them with the follow-up times proposed was able to evaluate important and conclusive clinical outcomes, such as heart failure or hospitalization. Nonetheless, some evidences indicate intermediate outcomes (biochemical biomarkers) can be good predictors of symptomatic cardiac problems in the future. [1]

CONITEC’s Recommendation: CONITEC members present at the 43rd meeting of the plenary session held on March 02 and 03, 2016 have appreciated the proposal and concluded there is a lack of evidence of important and conclusive outcomes proving the efficacy of the drug in the population of interest. Therefore, the plenary session has unanimously decided on the preliminary recommendation unfavorable to incorporation. The subject matter will be made available in Public Consultation.

Public Consultation: 13 technical-scientific contributions and 14 experience or opinion contributions were received. All technical-scientific contributions having technical-scientific argumentation were contrary to initial Conitec recommendation. These had an argument about clinical evidence, economical evaluation, and budget impact analysis. There was no argument enough to change the initial CONITEC recommendation.

Final Resolution: The non-incorporation of dexrazoxane for the prevention of anthracycline-induced cardiotoxicity in children as a specific procedure in SUS Table was recommended. The recommendation will be submitted to Secretary’s decision.

Decision: Do not incorporate dexrazoxane for the prevention of anthracycline-induced cardiotoxicity in children as a specific procedure, in the scope of the Unified Health System – SUS, provided by the Ordinance SCTIE-MS no. 25, published in Official Gazette of the Federal Executive (DOU) no. 110 of June 10, 2016, page 79.