25 July 2019
EMA/553936/2019
Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): doxorubicin

Procedure No. EMEA/H/C/PSUSA/00001172/201811

Period covered by the PSUR: 11 November 2015 To: 11 November 2018

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for doxorubicin, the scientific conclusions of the CHMP are as follows:

Based on the review of the safety data of pegylated liposomal doxorubicin hydrochloride (Caelyx), a signal of lichenoid keratosis was detected with a total of 10 cases reported. Three cases were poorly documented and were excluded from the assessment. Among the seven cases reviewed, the causality was stated as probable in 4 cases and possible in 1 case. Although the biological mechanism of lichenoid keratosis after doxorubicin is not known, the PRAC considers that "lichenoid keratosis" should be included as a new adverse drug reaction in section 4.8 of the SmPC based on the review of the cases. The frequency of lichenoid keratosis was determined as "rare" based on clinical trials. Section 4 of the package leaflet should be updated accordingly with the term "patches of skin thickening".

Furthermore, based on the pooled analysis of 4,231 patients across indications, the SmPC should be updated to in order to better detail the risk of cardiotoxicity associated with Caelyx. In this pooled analysis of 4,231 patients receiving Caelyx, ventricular arrythmia, palpitations, cardiac failure, cardiac arrest, bundle branch block right, and ejection fraction decreased were reported uncommonly, and atrioventricular block, cyanosis, and conduction disorder were reported rarely.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for doxorubicin the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing doxorubicin is unchanged subject to the proposed changes to the product information.

The CHMP recommends that the terms of the Marketing Authorisation(s) should be varied.