5.8.2021

רופא/ה, רוקח/ת נכבד/ה,
ברצוננו להודיעך על עדכון בעלון לרופא של:

CARDIOXANE

קרדיוקסאן

POWDER FOR SOLUTION FOR INFUSION

הרכב:

DEXRAZOXANE 500 mg/vial

התוויה מאושרת :

Prevention of cardiotoxicity in adult women with advanced and/or metastatic breast cancer at High risk of heart failure who have received a prior cumulative dose of 300 mg/m^2 of doxorubicin Or a prior cumulative dose of 540 mg/m2 of epirubicin when further anthracycline treatment is required.

<u>מקרא:</u> טקסט שהוסר מהעלון לרופא – מסומן ~~בקו~~, טקסט שהוסף לעלון לרופא- גופן אדום

<u>להלן העדכונים העיקריים:</u>

4.2 Posology and method of administration

[…]

~~Cardioxane is contraindicated in children and adolescents up to 18 years of age (see section 4.3).~~

Cardioxane is not indicated for children and adolescents under 18 years old.

The safety and efficacy of Cardioxane in children aged 0 to 18 years have not been established .

[…]

4.3 Contraindications

- ~~Children and adolescents up to 18 years of age (see sections 4.4 and 4.8)~~

[…]

4.4 Special warnings and precautions for use

[…]

<u>Second primary malignancies</u>
[…]

Oncology patients have an increased risk of second primary malignancies, regardless of treatment. Patients who have received cancer therapy also have an increased risk of second primary malignancy.

~~In clinical trials, second primary malignancies, in particular acute myeloid leukaemia (AML) and myelodysplastic syndrome (MDS), have been reported in paediatric patients with Hodgkin's disease and acute lymphoblastic leukaemia receiving chemotherapy regimens including several cytotoxics (e.g. etoposide, doxorubicin, cyclophosphamide) (see section 4.8).~~

[…]

~~Early death~~

~~In some studies, a higher incidence of death has been observed in the groups treated with dexrazoxane plus chemotherapy compared to those treated with chemotherapy alone. The possibility that dexrazoxane was a contributing factor to the imbalance cannot be ruled out (see section 5.1).~~

Interference with chemotherapy

Since both dexrazoxane and anthracyclines are topoisomerase inhibitors, it has been suggested that dexrazoxane may interfere with the anti-tumour efficacy of anthracyclines based on mechanism of action. However, in most adult studies no significant difference has been identified in response rate and overall survival between dexrazoxane and control groups. A significant decrease in tumour response rate was reported in one study of advanced breast cancer patients treated with doxorubicin and dexrazoxane compared to patients treated with doxorubicin and placebo. In this study placebo response rate was considered to be high (60.5%), which may be a contributing factor to the observed difference in response rate. Despite the difference in response rates, there was no significant difference in time to progression or overall survival between patients that had received either dexrazoxane or placebo in this study. ~~Since both dexrazoxane and doxorubicin are topoisomerase inhibitors, it is possible that dexrazoxane may interfere with the anti-tumour efficacy of doxorubicin. Use of dexrazoxane in combination with adjuvant breast cancer therapy or chemotherapy intended as curative is therefore not recommended.~~

[…]

Women of child-bearing potential / Contraception in males and females

Since dexrazoxane is a cytotoxic agent, sexually active men and women should use effective contraception during treatment. Women and men should continue using effective methods of contraception for at least ~~3~~ 6 months after cessation of treatment with dexrazoxane (see section 4.6).

[…]

4.8 Undesirable effects

Summary of the safety profile

[…] ~~An increased risk of the development of second primary malignancies, particularly AML, has been reported.~~

[…]

Table 1- adverse reactions

[…]

Blood and lymphatic system disorders
[…]

Common: Neutropenia, thrombocytopenia, febrile neutropenia, granulocytopenia, febrile bone marrow aplasia, white blood cell count decreased

[…]

Description of selected adverse drug reactions

Second primary malignancies

~~Secondary acute myeloid leukaemia (AML) / myelodysplastic syndrome (MDS) has been observed in paediatric patients with Hodgkin's disease or acute lymphoblastic leukaemia receiving dexrazoxane in combination with chemotherapy (see section 4.4).~~ AML has been reported uncommonly in adult breast cancer patients post-marketing.

[…]

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

[…]

The majority of controlled clinical studies were performed in patients with advanced breast cancer and employed a dosing ratio of dexrazoxane:doxorubicin of 20:1 or 10:1. In two clinical studies that used the higher dose ratio (one in breast cancer and one in small cell lung cancer) a higher rate of death was reported in the groups treated with dexrazoxane plus chemotherapy compared to those treated with chemotherapy alone or with placebo. The dose ratio was subsequently reduced to 10:1 in both studies, and no significant differences in survival were reported in patients treated at the lower dose ratio. However, a number of studies that used the higher dose ratio throughout have not reported any difference in survival. ~~Data from adults treated in 8 controlled randomised clinical studies have been reviewed, 780 patients received dexrazoxane plus chemotherapy and 789 received chemotherapy alone. The rate of death on study was higher with the combination dexrazoxane plus chemotherapy (5.0%) compared to chemotherapy alone (3.4%). The difference was not statistically significant and no consistent cause was apparent, however a contribution of dexrazoxane to the difference cannot be ruled out.~~

5.2 Pharmacokinetic properties

After intravenous administration to cancer patients, serum kinetics of dexrazoxane generally follow an open two-compartment model with first-order elimination. The maximum plasma concentration observed after a 12 15 minute infusion of 1000 mg/m2 is around 80 µg/ml with area under the plasma concentration-time curve (AUC) of 130 ± ~~15~~ 27 mg.h/l. The plasma concentrations declined thereafter with an average half-life value of 2.2 ± ~~1.2~~ 0.42 hours. The total body clearance of dexrazoxane in adults is estimated at 14.4 ± ~~1.6~~ 2.8 l/h.

[…]

6.5 Nature and contents of container

Vials (Type I brown glass), containing 500 mg of powder, closed with a stopper (chlorobutyl rubber) and ~~either~~ a cap (aluminium) with a flip-off component (polypropylene) ~~.or a tear-off cap (aluminium) with a pre-cut strip~~. The product is further enclosed in an outer carton.

[…]

העלון לרופא/לצרכן מפורסם במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום.

בברכה,
דויד וגנר
רוקח ממונה