דצמבר 2023

רופא/ה, רוקח/ת נכבד/ה

חברת טבע מודיעה על העדכונים הבאים בעלון לצרכן במתכונת עלון לרופא של התכשיר:

Doxorubicin Teva

Concentrate for solution for infusion

דוקסורוביצין טבע

תמיסה מרוכזת להכנת תמיסה לעירוי

Contains: doxorubicin hydrochloride 2mg/ml

עדכונים בעלון לצרכן במתכונת עלון לרופא

<u>התוויה כפי שאושרה בתעודת הרישום:</u>

Doxorubicin Teva is indicated for producing regression in disseminated neoplastic conditions such as: acute lymphoblastic leukaemia, acute myeloblastic leukaemia, Wilms` tumour, neuroblastoma, soft tissue and bone sarcomas, breast carcinoma, lymphomas of both Hodgkin's and non-Hodgkin's types, bronchogenic carcinoma in which the small cell histologic type is the most responsive compared to other cell types, and gastric carcinoma.

<u>ברצוננו להודיע שהעלון לצרכן עודכן, בפירוט שלהלן כלולים העדכונים העיקריים בלבד (תוספות מסומנות באדום והסרות מידע כטקסט מחוק):</u>

4.4 Special warnings and precautions for use

Cardiac function

[…]

The probability of developing CHF, estimated around 1% to 2% at a cumulative dose of 300 mg/m^2 slowly increases up to the total cumulative dose of 450-550 mg/m^2. Thereafter, the risk of developing CHF increases steeply and it is recommended not to exceed a maximum cumulative dose of 550 mg/m^2.

[…]

Children and adolescents are at an increased risk for developing delayed cardiotoxicity following doxorubicin administration. Females may be at greater risk than males. Follow-up cardiac evaluations are recommended periodically to monitor for this effect.

[…]

Tumour-lysis syndrome

Doxorubicin may induce hyperuricaemia as a consequence of the extensive purine catabolism that accompanies drug-induced rapid lysis of neoplastic cells (tumour-lysis syndrome) in case of high tumour burden. In these circumstances blood uric acid levels, potassium, calcium phosphate and creatinine should be evaluated after initial treatment. Hydration, urine alkalinization, and prophylaxis

with allopurinol to prevent hyperuricaemia may minimize potential complications of tumour lysis syndrome.

Combination with other anticancer chemotherapies
Doxorubicin hydrochloride may potentiate the toxicity of other anticancer chemotherapies (see section 4.5). Exacerbation of cyclophosphamide-induced haemorrhagic cystitis and enhanced hepatotoxicity of 6-mercaptopurine have been reported. Radiation-induced toxicities (myocardium, mucosa, skin and liver) have also been reported.
As with other cytotoxic agents, thrombophlebitis and thromboembolic phenomena including pulmonary embolism (in some cases fatal) have been coincidentally reported with the use of doxorubicin (see section 4.8).

Vaccines
Vaccines are not recommended (see section 4.5).
Administration of live or live-attenuated vaccines in patients immunocompromised by chemotherapeutic agents including doxorubicin, may result in serious or fatal infections. Vaccination with a live vaccine should be avoided in patients receiving doxorubicin. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished. During treatment with doxorubicin hydrochloride patients should avoid contact with recently polio vaccinated persons.

4.5 Interaction with other medicinal products and other forms of interaction

Doxorubicin hydrochloride used in combination with cyclosporin might require dose-adjustment. At concomitant administration of cyclosporin, the clearance of doxorubicin is reduced by approximate 50%. The doxorubicin AUC is increased by 55% and AUC of doxorubicinol by 350%. With this combination a 40% dose reduction of doxorubicin is suggested. Cyclosporin inhibits, similar to verapamil, both CYP3A4 and P-glycoprotein, which might explain the interaction and resulting increase in adverse effects. Literature reports suggest that adding cyclosporine to doxorubicin results in more profound and prolonged haematologic toxicity than that observed with doxorubicin alone. Coma and seizures have also been described with concomitant administration of cyclosporine and doxorubicin.
[…]

In a clinical study increase in doxorubicin AUC (21-47%) and no increase was observed when given with sorafenib 400 mg twice daily. The clinical significance of these findings is unknown.

4.8 Undesirable effects

Infections and infestations

Very common:	Infection.
Common:	Sepsis/septicaemia.

Eye disorders

Common:	Conjunctivitis.
Not known:	~~Conjunctivitis~~, keratitis, increased lachrymation.

Cardiac disorders
[…]
Doxorubicin is cardiotoxic. The risk that the cardiotoxic side-effects become manifest is elevated during and after radiation therapy of the mediastinal region, after pre-treatment with potentially cardiotoxic

agents (e.g., anthracyclines, cyclophosphamide), and in elderly patients (over ~~60~~70 years) and patients with manifest arterial hypertension. (see section 4.4).

Vascular disorders

Common:	Haemorrhage.
Uncommon:	Thromboembolism.
Not known:	Shock.
	Thrombophlebitis.
	Phlebitis.

Gastrointestinal disorders

Very common:	Gastrointestinal disturbance.
	Diarrhoea.
	Nausea and vomiting.
	Mucositis, stomatitis, oesophagitis, colitis.

[…]

Skin and subcutaneous tissue disorders

Very common:	Alopecia (dose-dependent and in most cases reversible).
	Reddening.
	Photosensitization.
	Palmar-plantar erythrodysaesthesia syndrome.
Common:	Local hypersensitivity reactions in the field of radiation (“radiation recall reaction”).
	Pruritus.
	Urticaria.
	Rash (exanthema).
	Hyperpigmentation of skin and nails.

[…]

General disorders and administration site conditions

Very common:	Pyrexia.
	Asthenia.
	Chills.
Uncommon:	Dehydration.
Rare:	Dizziness.
	Injection site reactions (local erythematous reactions along the vein, pain, phlebitis, phlebosclerosis).
Not known:	Malaise.

Investigations

Very common:	Ejection fraction decreased, ECG abnormal, transaminases abnormal, weight increased (reported in patients with early breast cancer receiving doxorubicin- containing adjuvant therapy (NSABP B-15 trial)).