Ontologies Classes Object Properties Data Properties Annotation Properties Individuals Datatypes Clouds

Class: Warnings_and_Precautions_DOXOR

Annotations (1)

- rdfs:comment "5.1 Cardiomyopathy and Arrhythmias Cardiomyopathy Doxorubicin hydrochloride can result in myocardial damage, including acute left ventricular failure. The risk of cardiomyopathy is generally proportional to the cumulative exposure. Include prior doses of other anthracyclines or anthracenediones in calculations of total cumulative dosage for doxorubicin hydrochloride. Cardiomyopathy may develop during treatment or up to several years after completion of treatment and can include decrease in LVEF and signs and symptoms of congestive heart failure (CHF). The probability of developing cardiomyopathy is estimated to be 1 to 2% at a total cumulative dose of 300 mg/m2 of doxorubicin hydrochloride, 3 to 5% at a dose of 400 mg/m2, 5 to 8% at a dose of 450 mg/m2, and 6 to 20% at a dose of 500 mg/m2, when doxorubicin hydrochloride is administered every 3 weeks. There is an additive or potentially synergistic increase in the risk of cardiomyopathy in patients who have received radiotherapy to the mediastinum or concomitant therapy with other known cardiotoxic agents, such as cyclophosphamide and trastuzumab. Pericarditis and myocarditis have also been reported during or following doxorubicin hydrochloride treatment. Assess left ventricular cardiac function (e.g., MUGA or echocardiogram) prior to initiation of Doxorubicin Hydrochloride Injection/for Injection, during treatment to detect acute changes, and after treatment to detect delayed cardiotoxicity. Increase the frequency of assessments as the cumulative dose exceeds 300 mg/m2. Use the same method of assessment of LVEF at all time points [see Use in Specific Populations (8.4)]. Discontinue Doxorubicin Hydrochloride Injection/for Injection in patients who develop signs or symptoms of cardiomyopathy [see Dosage and Administration (2.3)]. Consider the use of dexrazoxane to reduce the incidence and severity of cardiomyopathy due to doxorubicin hydrochloride administration in patients who have received a cumulative doxorubicin hydrochloride dose of 300 mg/m2 and who will continue to receive doxorubicin hydrochloride. Arrhythmias Doxorubicin hydrochloride can result in arrhythmias, including life-threatening arrhythmias, during or within a few hours after doxorubicin hydrochloride administration and at any time point during treatment. Tachyarrhythmias, including sinus tachycardia, premature ventricular contractions, and ventricular tachycardia, as well as bradycardia, can occur. Electrocardiographic changes, including non-specific ST-T wave changes, atrioventricular and bundle-branch block can also occur. These electrocardiographic changes may be transient and self-limited and may not require a dosage modification of doxorubicin hydrochloride. 5.2 Secondary Malignancies The risk of developing secondary acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) is increased following treatment with doxorubicin hydrochloride. Cumulative incidences ranged from 0.2% at five years to 1.5% at 10 years in two separate trials involving the adjuvant treatment of women with breast cancer. These leukemias generally occur within 1 to 3 years of treatment. 5.3 Extravasation and Tissue Necrosis Extravasation of doxorubicin hydrochloride can cause severe local tissue injury manifesting as blistering, ulceration, and necrosis requiring wide excision of the affected area and skin grafting. Extravasation should be considered if a patient experiences a burning or stinging sensation or shows other evidence indicating peri-venous infiltration or extravasation; however, extravasation may be present in patients who do not experience a stinging or burning sensation or when blood return is present on aspiration of the infusion needle. When given via a peripheral venous line, infuse Doxorubicin Hydrochloride Injection/for Injection over 10 minutes or less to minimize the risk of thrombosis or perivenous extravasation. If extravasation is suspected, immediately discontinue the intravenous injection or continuous intravenous infusion [see Dosage and Administration (2.5)]. Apply ice to the site intermittently for 15 minutes, 4 times a day for 3 days. In adults, if appropriate, administer dexrazoxane at the site of extravasation as soon as possible and within the first 6 hours after extravasation. 5.4 Severe Myelosuppression Doxorubicin hydrochloride can cause myelosuppression. In Study 1, the incidence of severe myelosuppression was: grade 4 leukopenia (0.3%), grade 3 leukopenia (3%), and grade 4 thrombocytopenia (0.1%). A dose-dependent, reversible neutropenia is the predominant manifestation of myelosuppression from doxorubicin hydrochloride. When doxorubicin hydrochloride is administered every 21 days, the neutrophil count reaches its nadir 10 to 14 days after administration with recovery usually occurring by day 21. Obtain complete blood counts prior to each treatment and carefully monitor patients during treatment for possible clinical complications due to myelosuppression. Delay next dose of Doxorubicin Hydrochloride Injection/for Injection if severe myelosuppression has not improved. Consider dose reduction for patients with prolonged myelosuppression based on severity of reaction. 5.5 Use in Patients with Hepatic Impairment The clearance of doxorubicin is decreased in patients with elevated serum bilirubin with an increased risk of toxicity [see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)]. Doxorubicin Hydrochloride Injection/for Injection is contraindicated in patients with severe hepatic impairment (defined as Child Pugh Class C or serum bilirubin level greater than 5 mg/dL) [see Contraindications (4)]. Reduce the dose of Doxorubicin Hydrochloride Injection/for Injection in patients with serum bilirubin levels of 1.2 to 5 mg/dL [see Dosage and Administration (2.4)]. Obtain liver tests including ALT, AST, alkaline phosphatase, and bilirubin prior to and during therapy. 5.6 Tumor Lysis Syndrome Doxorubicin hydrochloride can induce tumor lysis syndrome in patients with rapidly growing tumors. Evaluate blood uric acid levels, potassium, calcium,

phosphate, and creatinine after initial treatment. Hydration, urine alkalinization, and prophylaxis with allopurinol to prevent hyperuricemia may minimize potential complications of tumor lysis syndrome. 5.7 Potentiation of Radiation Toxicity and Radiation Recall Doxorubicin hydrochloride can increase radiation-induced toxicity to the myocardium, mucosa, skin, and liver. Radiation recall, including but not limited to cutaneous and pulmonary toxicity, can occur in patients who receive doxorubicin hydrochloride after prior radiation therapy. 5.8 Embryo-Fetal Toxicity Based on findings in animals and its mechanism of action, Doxorubicin Hydrochloride Injection/for Injection can cause fetal harm when administered to a pregnant woman; avoid the use of Doxorubicin Hydrochloride Injection/for Injection during the 1st trimester. Available human data do not establish the presence or absence of major birth defects and miscarriage related to the use of doxorubicin hydrochloride during the 2nd and 3rd trimesters. Doxorubicin hydrochloride was teratogenic and embryotoxic in rats and rabbits at doses lower than the recommended human dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Doxorubicin Hydrochloride Injection/for Injection and for 6 months after treatment. Advise males with female partners of reproductive potential to use effective contraception during treatment with Doxorubicin Hydrochloride Injection/for Injection and for 3 months after treatment. Advise males with pregnant partners to use condoms during treatment with Doxorubicin Hydrochloride Injection/for Injection and for at least 10 days after the final dose [see Use in Specific Populations (8.1, 8.3), Nonclinical Toxicology (13.1)]."(xsd:string)

Superclasses (1)

- Doxorubicin_Hydrochloride_

Disjoints (8)

Adverse_Reactions_DOXOR, Contraindications_DOXOR, Dosage_and_Administration_DOXOR, Dosage_Forms_and_Strengths_DOXOR, Drug_Interactions_DOXOR, Indications_and_Usage_DOXOR, Use_in_Specific_Populations_DOXOR, **Warnings_and_Precautions_DOXOR**

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