For the use of only a Registered Medical Practitioner or a Hospital or a Laboratory

Doxorubicin Hydrochloride Injection USP

ADRIM®

SAFETY WARNINGS

CARDIOMYOPATHY, SECONDARY MALIGNANCIES, EXTRAVASATION AND TISSUE NECROSIS, and SEVERE MYELOSUPPRESSION

Cardiomyopathy: Myocardial damage, including acute left ventricular failure can occur with doxorubicin hydrochloride. The risk of cardiomyopathy is proportional to the cumulative exposure with incidence rates from 1% - 20% for cumulative doses ranging from 300 mg/m^2 to 500 mg/m^2 when doxorubicin hydrochloride is administered every 3 weeks. The risk of cardiomyopathy is further increased with concomitant cardiotoxic therapy. Assess LVEF before and regularly during and after treatment with doxorubicin hydrochloride.

Secondary Malignancies: Secondary acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) occur at a higher incidence in patients treated with anthracyclines, including doxorubicin hydrochloride.

Extravasation and Tissue Necrosis: Extravasation of doxorubicin hydrochloride can result in severe local tissue injury and necrosis requiring wide excision of the affected area and skin grafting. Immediately terminate the drug and apply ice to the affected area.

Severe myelosuppression resulting in serious infection, septic shock, requirement for transfusions, hospitalization, and death may occur.

DESCRIPTION:

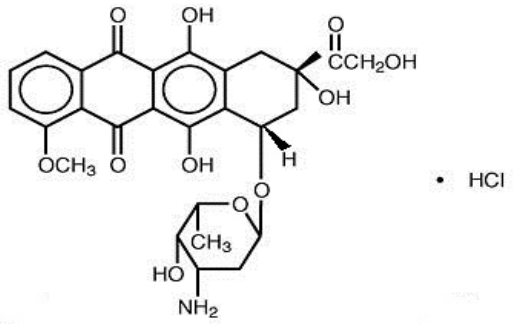
ADRIM® is a cytotoxic anthracycline antibiotic isolated from the cultures of *streptomyces peucetius* var. *caesius*. Doxorubicin consists of a naphthacenequinone nucleus linked through a glycosidic bond at ring atom 7 to an amino sugar, daunosamine.

ADRIM® is a clear, red solution.

COMPOSITION:

Each ml contains:	
Doxorubicin Hydrochloride USP	2 mg
Sodium Chloride USP	9 mg
Hydrochloric Acid USNF	q.s. to adjust pH
Water for Injection USP	q.s.

CHEMICAL STRUCTURE:



Chemically, Doxorubicin Hydrochloride is 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-α-L-*lyx*o hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxylacetyl)-1-methoxy -hydrochloride (8S-*cis*).

Doxorubicin binds to nucleic acids, presumably by specific intercalation of the planar anthracycline nucleus with the DNA double helix. The anthracycline ring is lipophilic, but the saturated end of the ring system contains abundant hydroxyl groups adjacent to the amino sugar, producing a hydrophilic center. The molecule is amphoteric, containing acidic functions in the ring phenolic groups and a basic function in the sugar amino group. It binds to cell membranes as well as plasma proteins.

PHARMACOLOGY

Pharmacodynamic properties

Pharmacotherapeutic group: Anthracyclines and related substances, ATC code: L01DB01

Doxorubicin is an antitumour agent. Tumour cells are probably killed through drug-induced alterations of nucleic acid synthesis although the exact mechanism of action has not yet been clearly elucidated.

Proposed mechanism of action includes:
DNA intercalation (leading to an inhibition of synthesis of DNA, RNA and proteins), formation of highly reactive free-radicals and superoxides, chelation of divalent cations, the inhibition of Na-K ATPase and the binding of doxorubicin to certain constituents of cell membranes (particularly to the membrane lipids, spectrin and cardiolipin). Highest drug concentrations are attained in the lung, liver, spleen, kidney, heart, small intestine and bone-marrow. Doxorubicin does not cross the blood-brain barrier.

Pharmacokinetic properties

After IV administration, the plasma disappearance curve of doxorubicin is triphasic with half-lives of 12 minutes, 3.3 hours and 30 hours. The relatively long terminal elimination half-life reflects doxorubicin's distribution into a deep tissue compartment. Only about 33 to 50% of fluorescent or tritiated drug (or degradation products), respectively, can be accounted for in urine, bile and faeces for up to 5 days after IV administration. The remainder of the doxorubicin and degradation products appear to be retained for long periods of time in body tissues.

In cancer patients, doxorubicin is reduced to adriamycinol, which is an active cytotoxic agent. This reduction appears to be catalysed by cytoplasmic and pH-dependent aldo-keto reductases that are found in all tissues and play an important role in determining the overall pharmacokinetics of doxorubicin.

Microsomal glycosidases present in most tissues split doxorubicin and adriamycinol into inactive aglycones. The aglycones may then undergo 0-demethylation, followed by conjugation to sulphate or glucuronide esters, and excretion in the bile.

Route of Administration:
Intravenous, intravesical, intra-arterial

INDICATIONS:

ADRIM® has been used successfully to produce regression in neoplastic conditions such as: acute leukaemia, Wilms' tumour, neuroblastoma, soft tissue and bone sarcomas, breast carcinoma, lymphomas of both Hodgkin's and non-Hodgkin's type, bronchogenic (lung) carcinoma, thyroid carcinoma, hepatomas, ovarian carcinoma, etc. The main antitumour activities are listed below. ADRIM® is also indicated by intravesical administration in the primary management of non-metastatic carcinoma of the bladder. (Tis, T1, T2).

Doxorubicin Antitumour Activity

	Tumour Type	**Response Rate (%)**	**Median Duration**	**First Line Chemotherapy**
Established Activity	Breast	35	3-6	√
	Ovary	38	3-6	?
	Lung	30	3	?
	Sarcoma	30	4	√
	Wilms'	66	4	√
	Bladder	28	4-6	?
	Neuroblastoma	41	4	√
	Hodgkin's	36	4-6	?
	Non-Hodgkin's	40	4-6	√
	Lymphoma Acute	35	3	?
	Leukaemia	32	4-6	√
	Hepatoma Thyroid	30	6-10	√
Some Response	Stomach	30	2-4	√?
	Cervix	32	2-6	?
	Head & Neck	19	2-4	
	Testicle	20	3-6	
	Myeloma	33	3	
	Endometrial	36	4-6	√?

Unresponsive	Colorectal Pancreas Renal Melanoma Brain			

CONTRAINDICATIONS:

Hypersensitivity to doxorubicin or to any of the excipients listed in composition, other anthracyclines or anthracenediones.

Intravenous (IV) use:

• persistent myelosuppression

• severe hepatic impairment

• severe myocardial insufficiency

• recent myocardial infarction

• severe arrhythmias

• previous treatment with maximum cumulative doses of doxorubicin, daunorubicin, epirubicin, idarubicin, and/or other anthracyclines and anthracenediones

ADVERSE EFFECTS:

Adverse reactions reported in association with doxorubicin therapy are listed below by MedDRA System Organ Class and by frequency. Frequencies are defined as: Very common (≥10%), Common (≥1%, <10%), Uncommon (≥0.1%, <1%), Rare (≥0.01%, <0.1%), Very rare (<0.01%), and Not known (cannot be estimated from available data).

Adverse Reactions Table	
Infections and Infestations	
Very common	Infection
Common	Sepsis
Neoplasms Benign, Malignant and Unspecified (including cysts and polyps)	
Not known	Acute lymphocytic leukaemia, Acute myeloid leukaemia
Blood and Lymphatic System Disorders	
Very common	Leukopenia, Neutropenia, Anaemia, Thrombocytopenia
Immune System Disorders	
Not known	Anaphylactic reaction
Metabolism and Nutrition Disorders	
Very common	Decreased appetite
Not known	Dehydration, Hyperuricaemia
Eye Disorders	

Common	Conjunctivitis
Not known	Keratitis, Lacrimation increased
Cardiac Disorders	
Common	Cardiac failure congestive, Sinus tachycardia
Not known	Atrioventricular block, Tachyarrhythmia, Bundle branch block
Vascular Disorders	
Uncommon	Embolism
Not known	Shock, Haemorrhage, Thrombophlebitis, Phlebitis, Hot flush
Gastrointestinal Disorders	
Very common	Mucosal inflammation/Stomatitis, Diarrhoea, Vomiting, Nausea
Common	Oesophagitis, Abdominal pain
Not known	Gastrointestinal haemorrhage, Gastritis erosive, Colitis, Mucosal discolouration
Skin and Subcutaneous Tissue Disorders	
Very common	Palmar-plantar erythrodysaesthesia syndrome, Alopecia
Common	Urticaria, Rash, Skin hyperpigmentation, Nail hyperpigmentation
Not known	Photosensitivity reaction, Recall phenomenon, Pruritus, Skin disorder
Renal and Urinary Disorders	
Not known	Chromaturia[a]
Reproductive System and Breast Disorders	
Not known	Amenorrhoea, Azoospermia, Oligospermia
General Disorders and Administration Site Conditions	
Very common	Pyrexia, Asthenia, Chills
Common	Infusion site reaction
Not known	Malaise
Investigations	
Very common	Ejection fraction decreased, Electrocardiogram abnormal, Transaminases abnormal, Weight increased[b]
[a]For one to two days after administration [b]Reported in patients with early breast cancer receiving doxorubicin-containing adjuvant therapy (NSABP B-15 trial)	

Effects on Ability to Drive and Use Machine

The effect of doxorubicin on the ability to drive or use machinery has not been systematically evaluated.

DRUG INTERACTIONS:
Doxorubicin is a major substrate of cytochrome P450 CYP3A4 and CYP2D6, and P-glycoprotein (P-gp). Clinically significant interactions have been reported with inhibitors of CYP3A4, CYP2D6, and/or P-gp (e.g, verapamil), resulting in increased concentration and clinical effect of doxorubicin. Inducers of CYP3A4 (e.g, phenobarbital, phenytoin, St. John's Wort) and P-gp inducers may decrease the concentration of doxorubicin.

The addition of cyclosporine to doxorubicin may result in increases in area under the concentration-time curve (AUC) for both doxorubicin and doxorubicinol, possibly due to a decrease in clearance of the parent drug and a decrease in metabolism of doxorubicinol. 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.

High dose cyclosporine increases the serum levels and myelotoxicity of doxorubicin.

Doxorubicin is mainly used in combination with other cytotoxic drugs. Additive toxicity may occur especially with regard to bone marrow/haematologic and gastrointestinal effects. The use of doxorubicin in combination chemotherapy with other potentially cardiotoxic drugs, as well as the concomitant use of other cardioactive compounds (e.g. calcium channel blockers), require monitoring of cardiac function throughout treatment. Changes in hepatic function induced by concomitant therapies may affect doxorubicin metabolism, pharmacokinetics, therapeutic efficacy and/or toxicity.

Paclitaxel can cause increased plasma-concentrations of doxorubicin and/or its metabolites when given prior to doxorubicin. Certain data indicate that a smaller increase is observed when doxorubicin is administered prior to paclitaxel.

The use of trastuzumab in combination with anthracyclines (such as doxorubicin hydrochloride) is associated with an increased cardiotoxic risk. Trastuzumab and anthracyclines should currently not be used in combination, except for well controlled clinical studies with monitoring of cardiac function.

PRECAUTIONS AND WARNINGS:

Doxorubicin should be administered only under the supervision of physicians experienced in the use of cytotoxic therapy.

Patients should recover from the acute toxicities of prior cytotoxic treatment (such as stomatitis, neutropenia, thrombocytopenia, and generalized infections) before beginning treatment with doxorubicin.

The systemic clearance of doxorubicin is reduced in obese patients (i.e. >130% ideal body weight).
Cardiac Function

Cardiotoxicity is a risk of anthracycline treatment that may be manifested by early (i.e. acute) or late (i.e. delayed) events.

Early (i.e. Acute) Events: Early cardiotoxicity of doxorubicin consists mainly of sinus tachycardia and/or ECG abnormalities such as non-specific ST-T wave changes. Tachyarrhythmias, including premature ventricular contractions and ventricular tachycardia, bradycardia, as well as atrioventricular and bundle-branch block have also been reported. These effects do not usually predict subsequent development of delayed cardiotoxicity and are generally not a consideration for discontinuation of doxorubicin treatment.

Late (i.e. Delayed) Events: Delayed cardiotoxicity usually develops late in the course of therapy with doxorubicin or within 2 to 3 months after treatment termination, but later events, several months to years after completion of treatment, have also been reported. Delayed cardiomyopathy is manifested by reduced left ventricular ejection fraction (LVEF) and/or signs and symptoms of congestive heart failure (CHF) such as dyspnoea, pulmonary oedema, dependent oedema, cardiomegaly and hepatomegaly, oliguria, ascites, pleural effusion and gallop rhythm. Subacute effects such as pericarditis/myocarditis have also been reported. Life-threatening CHF is the most severe form of anthracycline-induced cardiomyopathy and represents the cumulative dose-limiting toxicity of the drug.

Cardiac function should be assessed before patients undergo treatment with doxorubicin and must be monitored throughout therapy to minimize the risk of incurring severe cardiac impairment. The risk may be decreased through regular monitoring of LVEF during the course of treatment with prompt discontinuation of doxorubicin at the first sign of impaired function. The appropriate quantitative method for repeated assessment of cardiac function (evaluation of LVEF) includes multi-gated radionuclide angiography (MUGA) or echocardiography (ECHO). A baseline cardiac evaluation with an ECG and either a MUGA scan or an ECHO is recommended, especially in patients with risk factors for increased cardiotoxicity. Repeated MUGA or ECHO determinations of LVEF should be performed, particularly with higher, cumulative anthracycline doses. The technique used for assessment should be consistent throughout follow-up.

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.

Risk factors for cardiac toxicity include active or dormant cardiovascular disease, prior or concomitant radiotherapy to the mediastinal/pericardial area, previous therapy with other anthracyclines or anthracenediones and concomitant use of drugs with the ability to suppress cardiac contractility or of cardiotoxic substances (e.g. trastuzumab) and age over 70 years. Patients receiving anthracyclines after stopping treatment with other cardiotoxic agents, especially those with long half-lives such as trastuzumab, may also be at an increased risk of developing cardiotoxicity. The reported half-life of trastuzumab is variable. Trastuzumab may persist in the circulation for up to 7 months. Therefore, physicians should avoid anthracycline-based therapy for up to 7 months after stopping trastuzumab when possible. If this is not possible, the patient's cardiac function should be monitored carefully.

Cardiac function must be carefully monitored in patients receiving high cumulative doses and in those with risk factors. However, cardiotoxicity with doxorubicin may occur at lower cumulative doses whether or not cardiac risk factors are present.

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.

It is probable that the toxicity of doxorubicin and other anthracyclines or anthracenediones is additive.

Haematologic Toxicity

Doxorubicin may produce myelosuppression. Haematologic profiles should be assessed before and during each cycle of therapy with doxorubicin, including differential white blood cell (WBC) counts. A dose-dependent, reversible leucopenia and/or granulocytopenia (neutropenia) is the predominant manifestation of doxorubicin haematologic toxicity and is the most common acute dose-limiting toxicity of this drug. Leucopenia and neutropenia generally reach the nadir between days 10 and 14 after drug administration; the WBC/neutrophil counts return to normal values in most cases by day 21. Thrombocytopenia and anaemia may also occur. Clinical consequences of severe myelosuppression include fever, infections, sepsis/septicaemia, septic shock, haemorrhage, tissue hypoxia or death.

Secondary Leukaemia

Secondary leukaemia, with or without a preleukaemic phase, has been reported in patients treated with anthracyclines. Secondary leukaemia is more common when such drugs are given in combination with DNA-damaging antineoplastic agents, when patients have been heavily pretreated with cytotoxic drugs or when doses of the anthracyclines have been escalated. These leukaemias can have a 1 to 3 year latency period.

Carcinogenesis, Mutagenesis and Impairment of Fertility

Doxorubicin was genotoxic and mutagenic *in vitro* and *in vivo* tests.

In women, doxorubicin may cause infertility during the time of drug administration. Doxorubicin may cause amenorrhoea. Ovulation and menstruation appear to return after termination of therapy, although premature menopause can occur.

Doxorubicin is mutagenic and can induce chromosomal damage in human spermatozoa. Oligospermia or azoospermia may be permanent; however, sperm counts have been reported to return to normospermic levels in some instances. This may occur several years after the end of therapy. Men undergoing doxorubicin treatment should use effective contraceptive methods.

Liver function

The major route of elimination of doxorubicin is the hepatobiliary system. Serum total bilirubin should be evaluated before and during treatment with doxorubicin. Patients with elevated bilirubin may experience slower clearance of the drug with an increase in overall toxicity. Lower doses are recommended in these patients. Patients with severe hepatic impairment should not receive doxorubicin.

Other

Doxorubicin may potentiate the toxicity of other anticancer therapies. Exacerbation of cyclophosphamide-induced haemorrhagic cystitis and enhanced hepatotoxicity of 6-mercaptopurine have been reported. Radiation-induced toxicities (myocardium, mucosae, 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.

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). 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.

Vaccinations

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.

Excipient Information

Doxorubicin 10 mg/5ml and 50 mg/25 ml contain 17.7 mg and 88.5 mg sodium per each vial, equivalent to 0.9% and 4.43% of the WHO maximum recommended daily intake (RDI) of 2 g sodium for an adult, respectively.

Pregnancy

Doxorubicin has harmful pharmacological effects on pregnancy and/or the foetus/newborn child.

Due to the embryotoxic potential of doxorubicin, this drug should not be used during pregnancy unless clearly necessary. If a woman receives doxorubicin during pregnancy or becomes pregnant

whilst taking the drug, she should be warned of the potential hazard to the foetus. Women of childbearing potential have to use effective contraception during treatment.

Breast-feeding
Doxorubicin is secreted into breast milk. Women should not breastfeed while undergoing treatment with doxorubicin.

DOSAGE AND ADMINISTRATION:

Care in the administration of ADRIM will reduce the chance of perivenous infiltration. It may also decrease the chance of local reactions such as urticaria and erythematous streaking. The recommended dosage schedule is 60-75 mg/m^2 as a single intravenous injection administered at 21-day intervals. The lower dose should be given to patients with inadequate marrow reserves due to old age, or prior therapy, or neoplastic marrow infiltration. An alternative dose schedule is 30 mg/m^2 on each of three successive days repeated every 4 weeks. The adult dosage regimens may be suitable for paediatric cases. The recommended lifetime cumulative dose limit is 550 mg doxorubicin/m^2 body surface area. ADRIM has been administered as an intra-arterial infusion for 1-3 days at doses of 45-100 mg/m^2. It is recommended that the total cumulative dose of doxorubicin for adults aged 70 or older be restricted to 450 mg/m^2 body surface area.

Use in hepatic impairment

Doxorubicin dosage must be reduced if hepatic function is impaired according to the following table:

Serum Bilirubin Levels	BSP Retention	Recommended Dose
20 - 50 µmol/L	9 - 15%	1/2 normal
>50 µmol/L	>15%	dose 1/4

Method of Administration

ADRIM Injection is supplied as 50 mg doxorubicin hydrochloride in 25 mL vials, respectively (doxorubicin concentration 2 mg/mL).

ADRIM Injection must be handled with care. If contact with the skin occurs, wash thoroughly with soap and water. The product contains no antimicrobial preservative. The single dose vials should be used in one patient on one occasion only. Discard any residue. The solution is to be stored under refrigeration (2°C to 8°C) and should be protected from sunlight and retained in the carton until time of use.

Storage of ADRIM Injection at refrigerated conditions can result in the formation of a gelled product. This gelled product will return to a slightly viscous to mobile solution after two to a maximum of four hours equilibration at room temperature (15°C to 25°C).

It is recommended that ADRIM be slowly administered into the tubing of a freely running intravenous infusion of 0.45% and 0.9% w/v Sodium Chloride Injection U.S.P. or 5% Glucose

Injection U.S.P. The tubing should be attached to a butterfly needle inserted preferably into a large vein. The rate of administration is dependent on the size of the vein and the dosage. However, the dose should be administered in not less than 3-5 minutes. A direct push injection is not recommended due to the risk of extravasation, which may occur even in the presence of adequate blood return upon needle aspiration.

Local erythematous streaking along the vein as well as facial flushing may be indicative of too rapid administration. A burning or stinging sensation may be indicative of perivenous infiltration and the infusion should be immediately terminated and restarted in another vein.

ADRIM has been used in combination with other approved chemotherapeutic agents.

Though evidence is available that at least in some types of neoplastic disease combination chemotherapy is superior to single agents the benefits and risks of such therapy have not yet been fully elucidated.

Method of Administration

Intravesical administration

The following procedure is recommended:

1. The bladder should be catheterised and emptied.
2. Dilute ADRIM to a final concentration of 80 mg in 100 mL of normal saline and instil via the catheter into the bladder.
3. The catheter should be removed, and the patient instructed to be on one side. At 15-minute intervals, the patient should alternate to the opposite side over a 1-hour period.
4. The patient should be requested not to urinate for 1 hour, after which the bladder should be emptied of solution.
5. The procedure should be repeated at monthly intervals.

OVERDOSE:
Single doses of 250mg and 500mg of doxorubicin have proved fatal. Such doses may cause acute myocardial degeneration within 24 hours and severe myelosuppression (mainly leucopenia and thromobocytopenia), the effects of which are greatest between 10 and 15 days after administration. Treatment should aim to support the patient during this period and should utilise such measures as blood transfusions and reverse barrier nursing.

Acute overdose with doxorubicin will result in gastrointestinal toxic effects (mainly mucositis). This generally appears early after drug administration, but most patients recover from this within three weeks.

Delayed cardiac failure may occur up to six months after the overdosage. Patients should be observed carefully and should signs of cardiac failure arise, be treated along conventional lines.

STORAGE:
Store under refrigeration 2°C – 8°C. Protect from light.

Storage After Dilution:
Protect from light following preparation until completion of infusion. Use within 07 days in Storage Conditions of infusion Bags: 25 °C +/- 2 °C/60% RH +/- 5% RH and 28 days in Storage Conditions of infusion Bags: 5 °C +/-3 °C.

INCOMPATIBILITIES:
Do not admix ADRIM® with other drugs. If doxorubicin hydrochloride is mixed with heparin or fluorouracil a precipitate may form. Avoid contact with alkaline solutions which can lead to hydrolysis of doxorubicin hydrochloride.

SHELF LIFE:
24 months

HANDLING AND DISPOSAL:
Procedures for proper handling and disposal of anti-cancer drugs should be considered. Several guidelines on this subject have been published. There is no general agreement that all the procedures recommended in the guidelines are necessary or appropriate. However, given the toxic nature of this substance, the following protective recommendations are provided:

- Personnel should be trained in good technique for reconstitution and handling.
- Pregnant staff should be excluded from working with this drug.
- Personnel handling doxorubicin should wear protective clothing: goggles, gowns and disposable gloves and masks.
- A designated area should be defined for reconstitution (preferably under a laminar flow system). The work surface should be protected by disposable, plastic-backed, absorbent paper.
- All items used for reconstitution, administration or cleaning, including gloves, should be placed in high-risk waste-disposal bags for high-temperature incineration.
- Spillage or leakage should be treated with dilute sodium hypochlorite (1% available chlorine) solution, preferably by soaking, and then water.
- All cleaning materials should be disposed of as indicated previously.
- In case of skin contact thoroughly wash the affected area with soap and water or sodium bicarbonate solution. However, do not abrade the skin by using a scrub brush.
- In case of contact with the eye(s), hold back the eyelid(s) and flush the affected eye(s) with copious amounts of water for at least 15 minutes. Then seek medical evaluation by a physician.
- Always wash hands after removing gloves.

Caregivers of pediatric patients receiving doxorubicin should be counselled to take precautions (such as wearing latex gloves) to prevent contact with the patient's urine and other body fluids for at least 5 days after each treatment.

PRESENTATION:
ADRIM® is available as 5 ml and 25 ml vial containing 10 mg and 50 mg of Doxorubicin hydrochloride, respectively, as a ready to use solution.

REFERENCES:

1. Product Information, ADRIAMYCIN® CS (doxorubicin hydrochloride), Pfizer (Perth) Pty Limited, Bentley WA 6102, Australia, February 2020.
2. US Prescribing Information, Doxorubicin Hydrochloride Injection, Pfizer Labs, Division of Pfizer Inc., New York, NY 10017, 03/2020.
3. Summary of Product Characteristics, Doxorubicin 2 mg/ml Solution for Injection. Pfizer Limited, United Kingdom, 04/2021.

Manufactured in India by:
Fresenius Kabi Oncology Limited
Village-Kishanpura,
Tehsil-Nalagarh,
Distt. Solan [H.P.]-174101

VERSION NUMBER: MYS/01/2023

DATE OF RELEASE: DD MMM YYYY