DOXORUBICINA Tedec-Meiji Farma, S.A. **solution for injection 2 mg/ml, 5 ml (10 mg)**

COMPOSITION
One vial contains:
Doxorubicin (INN) hydrochloride 10 mg, sodium chloride 45 mg, hydrochloric acid q.s.f. pH=3 and water for injection q.s.f. 5 ml.

PHARMACEUTICAL FORM AND CONTENTS
One vial with solution for injection. Each pack contains one vial.

ACTIVITY
Doxorubicin belongs to the family of anthracycline antibiotics and exerts its effect by killing the cell. The mechanism of action probably reflects a complex system of multiple mechanisms related to the formation of free radicals, its action on DNA, or on the cell membrane.

PRODUCT LICENCE HOLDER IN SPAIN
TEDEC-MEIJI FARMA, S.A. Carretera M-300, Km 30.500, 28802 Alcalá de Henares, Madrid (Spain)

MANUFACTURER
GP PHARM, S.A. Polígono Industrial Els Vinyets-Els Fogars, 2. Carretera C-244, Km 22, 08777-Sant Quintí de Mediona-Barcelona (Spain)

CONTRAINDICATIONS
Therapy with DOXORUBICINA Tedec-Meiji Farma, S.A. is contraindicated in patients with bone marrow depression (myelosuppression) as a result of previous chemotherapy or radiotherapy; in patients with a history of heart disease, in patients already treated with cumulative doses of DOXORUBICINA Tedec-Meiji Farma, S.A. or other anthracyclines.
DOXORUBICINA Tedec-Meiji Farma, S.A. must not be administered intravesically in patients with urethral stenosis that cannot be catheterised.

PRECAUTIONS
Nausea, vomiting and mucositis have been commonly reported and must be treated adequately. Special attention must be paid to the cardiotoxicity of DOXORUBICINA Tedec-Meiji Farma, S.A. Left ventricular heart failure has

occurred rarely, especially when the recommended limit dose of 550 mg/m^2 is exceeded. Previous or concomitant therapies with anthracycline drugs such as daunorubicin must also be considered. Congestive heart failure and/or cardiomyopathy can occur several weeks after the last administration of DOXORUBICINA Tedec-Meiji Farma, S.A. It is recommended to perform an ECG before and after each treatment cycle. In the event of alterations in the ECG tracing, the suitability of continuing treatment should be carefully evaluated against the risk of irreversible heart damage. Severe arrhythmia can occur during or some hours after the administration of DOXORUBICINA Tedec-Meiji Farma, S.A. Leukopenia is usually transient and returns to normal within 21 days. It is recommended to monitor liver function with routine laboratory tests (SGOT, SGPT, alkaline phosphatase, bilirubin), since worsening of liver levels can increase the toxicity of DOXORUBICINA Tedec-Meiji Farma, S.A. at the recommended doses (see Posology). If DOXORUBICINA Tedec-Meiji Farma, S.A. is extravasated during intravenous administration, itching or burning can occur, even after adequate blood return after removing the injection needle. Like other cytotoxic drugs, DOXORUBICINA Tedec-Meiji Farma, S.A. may induce secondary hyperuricemia. DOXORUBICINA Tedec-Meiji Farma, S.A. may cause a red colour in urine up to 1-2 days after administration.

INTERACTIONS
DOXORUBICINA Tedec-Meiji Farma, S.A. may potentiate other similar therapies.

INCOMPATIBILITIES
Doxorubicin should not be mixed with 5-fluorouracil or heparin. To prevent any incompatibility, it is recommended that DOXORUBICINA Tedec-Meiji Farma, S.A. is not mixed with other medicinal products in the same syringe.

WARNINGS
Pregnancy and breast-feeding. DOXORUBICINA Tedec-Meiji Farma, S.A. is a potential teratogenic agent that can cause toxicity in the embryo; therefore, the advantages of the treatment should be assessed carefully. The use of this medicinal product during pregnancy must be avoided as far as possible. Effective contraceptive measures must be used during treatment and at least three months after treatment completion. DOXORUBICINA Tedec-Meiji Farma, S.A. is excreted in breast milk in small amounts. Therefore, its use during breast-feeding is not recommended.
Effects on ability to drive. The ability to drive and use machines may be affected due to the frequent occurrence of nausea and vomiting.

POSOLOGY

The recommended dose is 60-75 mg/m^2 of body surface area as a single intravenous dose, at 21-day intervals. The lower dose (60 mg/m^2) is recommended for patients with reduced bone marrow reserves due to old age, previous therapies, or neoplastic bone marrow infiltration.

An alternative dosage regimen, 20 mg/m^2 administered for three consecutive days and repeated every 3 weeks, causes a lower incidence of congestive heart failure. The cumulative dose of doxorubicin, regardless of the dosage schedule, must not exceed 550 mg/m^2 of body surface area. The dosage of doxorubicin must be reduced in patients with impaired liver function to prevent an increase in overall toxicity. Moderate renal impairment does not appear to be a reason for modifying the recommended dose, given the low renal excretion of doxorubicin. For intravesical administration, the recommended dose is 10 mg in a volume of 10 ml of saline (see instructions for use). Initially, this dose is administered weekly and then monthly. The duration of treatment ranges from 6 to 12 months. As there is virtually no doxorubicin absorption by this administration route, no restriction of the maximum accumulated dose seems likely.

INSTRUCTIONS FOR CORRECT ADMINISTRATION OF THE PREPARATION

The solution should be made isotonic by adding sterile saline solution to two or three times its volume. The administration is performed by intravenous injection and, in the case of localised treatment, by slow intra-arterial infusion. It is advisable to perform intravenous administration through the phleboclysis tube with saline solution, after ensuring that the needle is fully inserted into the vein. This technique reduces the risk of drug extravasation and assures vein flushing at the end of administration. It must not be administered by the intramuscular or intrathecal route.

If the DOXORUBICINA Tedec-Meiji Farma, S.A. solution comes in contact with the skin or mucous membranes, careful washing is recommended.

OVERDOSE

The strict guidelines followed when administering this medicinal product mean that overdose is unlikely. However, in the event an excessive dose is administered, the patient should be monitored continuously and appropriate treatment applied to prevent symptoms resulting from myelosuppression. Special attention should be paid to any heart disturbances.

Overdose in the event of intravesical administration may lead to severe cystitis.

In case of overdose or accidental ingestion, contact your doctor inmediately or go to the nearest hospital and take the pack with you.

ADVERSE REACTIONS

The dose-limiting toxicities of DOXORUBICINA Tedec-Meiji Farma, S.A. are myelosuppression and cardiotoxicity.

Other side effects seen are: Skin: In most cases, reversible alopecia occurs. In some cases, hyperpigmentation of the nail beds and skin folds, mainly in children, and onychoclasis. Skin reactions caused by previous treatments with radiotherapy can recur. Gastrointestinal: vomiting and nausea are common and may be acute; administer antiemetic therapy if this occurs. Mucositis (stomatitis and oesophagitis) may occur 5-10 days after the start of treatment. Ulceration and necrosis of the colon, especially the cecum, with haemorrhage and acute infections which can be fatal. Occasionally: anorexia and diarrhoea. Phlebosclerosis, especially when using small vessels or the same vein for repeated administration; facial flushing, especially when doxorubicin is given by rapid injection. If DOXORUBICINA Tedec-Meiji Farma, S.A. is extravasated during administration, severe cellulitis, vesication and tissue necrosis can occur. Rash has been reported at the site of injection. Hypersensitivity: Occasionally: fever, chills and urticaria. Anaphylaxis can occur. Cases of cross sensitivity with lincomycin can occur. Other side effects: conjunctivitis and lacrimation.

If you notice any other side effects not described above, ask your doctor or pharmacist.

STORAGE

DOXORUBICINA Tedec-Meiji Farma, S.A. solution for injection 2 mg/ml, 5 ml (10 mg) should be stored protected from light and refrigerated between 2-8^{o}C.

EXPIRY DATE

This medicine should not be used after the expiry date printed on the carton.

MEDICINAL PRODUCTS MUST BE KEPT OUT OF THE SIGHT AND REACH OF CHILDREN

REVISED TEXT mayo2019

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