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TEVA HOSPITALS

PACKAGE LEAFLET: INFORMATION FOR THE USER

Doxorubicin Teva 2 mg/ml Concentrate for Solution for Infusion

doxorubicin hydrochloride

Read all of this leaflet carefully before you start using this medicine, because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1 What Doxorubicin Teva is and what it is used for

The active ingredient in your medicine is Doxorubicin hydrochloride. Doxorubicin belongs to a group of anti-tumour (anti-cancer) medicines called anthracyclines. Doxorubicin damages the tumour (cancer) cells and ensures that they can no longer grow.

Doxorubicin is used in the treatment of:
- breast cancer
- bone cancer (osteosarcoma) given before surgery and given following surgery
- cancer found in the soft tissue (advanced soft-tissue sarcoma in adults)
- lung cancer (small cell lung cancer)
- cancer of the lymphatic tissue (Hodgkin's and non-Hodgkin's lymphoma)
- certain cancers of the blood (acute lymphatic or myeloblastic leukaemias)
- cancer of the bone marrow (multiple myeloma)
- cancer of the lining of the uterus (advanced or recurrent endometrial cancer)
- cancers of the thyroid (advanced papillary/follicular thyroid cancer, anaplastic thyroid cancer)
- certain bladder cancers (locally advanced or spreading stage). It is also used intravesically (in the bladder) in early (superficial) bladder cancer to prevent recurrence of bladder cancer after surgery
- recurrent cancer of the ovaries
- a certain childhood kidney cancer (Wilms' tumour)
- childhood cancer of the nervous tissue (advanced neuroblastoma).

Doxorubicin is also used in combination with other anti-cancer drugs.

As Doxorubicin Teva is an anti-cancer medicine it will be administered to you in a special unit and under the supervision of a doctor qualified in the use of anti-cancer medicines. The unit's personnel will explain to you what you need to take special care of during and after the treatment. This leaflet may help you to remember that.

2 What you need to know before you use Doxorubicin Teva

Do not use Doxorubicin Teva:
- If you are allergic to doxorubicin hydrochloride or any of the other ingredients of this medicine (listed in section 6) or to any other medicines belonging to the same family (so called anthracyclines or anthracenediones).
- If you are breast-feeding.

Depending on the route of administration Doxorubicin Teva will NOT be given to you in the following situations:

Intravenously (in a vein):
- If you have decreased blood cell production, decreased functioning of the bone marrow (myelosuppression) or inflammation of the mouth (stomatitis) due to previous treatment with cancer drugs and/or radiation
- If you have any infectious disease
- If you have a severe impaired liver function
- If you have problems with your heart (severe heart rhythm disorders, reduced heart function, (previous) heart attack, inflammation of the heart). These can be problems that appear quickly but that have a short but severe action
- If you have previously been treated with similar anti-cancer products (other anthracyclines) and have received the maximum dose of these.

Intravesically (in the bladder):
- If the cancer has spread to the wall of your bladder
- If you have a urinary tract infection
- If you have a bladder inflammation
- If there are problems with using a catheter (a tube inserted in the bladder to drain urine)
- If you have blood in your urine (haematuria).

Warnings and precautions

Talk to your doctor before using Doxorubicin Teva. Take special care with Doxorubicin Teva and tell your doctor before treatment:
- If you are elderly
- If you have a history of heart disease
- If you have a history of damage to your bone-marrow
- If you have been treated with radiation in the chest cavity (mediastinum)
- If you have been treated with similar anti-cancer products (other anthracyclines).

Important information about Doxorubicin Teva
- Doxorubicin may cause infertility in both men and women, which can be permanent (see also "Pregnancy, breast-feeding and fertility").
- If you have a stinging or burning sensation at the place where you have been injected with doxorubicin, it may be due to leaking of doxorubicin out of the vein. If this happens please tell your doctor as they will start treatment from a different vein and will monitor the affected area carefully.
- If you have previously been treated with doxorubicin (even up to 20 years ago) and become pregnant your doctor will monitor your heart, even if you have not experienced any heart problems in the past.
- Your urine may be reddish in colour during treatment with Doxorubicin Teva.
- During treatment with Doxorubicin Teva you may experience severe symptoms of nausea, being sick and inflammation in the lining of the mouth or nose. If you have any of these symptoms immediately tell your doctor who will give you any treatment necessary.
- Vaccination during treatment with Doxorubicin Teva is not recommended. You should also avoid contact with persons who have been recently vaccinated with the polio vaccine.

Before and during treatment with Doxorubicin Teva your doctor will:
- check your blood count before each treatment cycle as treatment with doxorubicin is likely to damage your bone marrow which causes a decrease in the amount of white blood cells and may make you more susceptible to infections and bleeding. If there is serious damage to your bone marrow your doctor may reduce, stop or delay treatment.
- check your lungs and chest to ensure your lungs are functioning properly during treatment.
- have an electrocardiogram (ECG) test done, that records your heart's activity, before start of treatment with doxorubicin and during the whole treatment as doxorubicin is likely to cause inflammation of the heart muscles (cardiomyopathy). This particularly can occur if you have a history of heart disease, are over 70 or below 15 years of age, have been previously treated with doxorubicin (or other related anthracycline medicines) or radiation in the chest cavity. A cumulative dose of 450-550 mg/m^2 should not be exceeded, because at higher doses the risk of development of heart failure considerably increases, particularly in children and in patients with a history of heart disease. In children the maximal cumulative dose is usually considered 300 mg/m^2 (under 12 years of age) to 450 mg/m^2 (over 12 years of age). For infants the maximal cumulative dosages may be even lower. Your doctor may also perform other tests to monitor your heart function.
- monitor the uric acid levels in your blood and ensure that you have sufficient fluid intake since doxorubicin may increase the levels of uric acid in the blood (hyperuricemia).
- monitor your mouth and throat regularly during treatment as doxorubicin can cause changes to the lining of your mouth and throat.
- monitor your kidney function. A reduction of the dose may be necessary.
- monitor your liver function (by blood tests). A reduction of the dose may be necessary in case your liver function is decreased.
- check your general health as doxorubicin should not be used if you have any inflammation, ulcers or diarrhoea. Any infections will be treated by your doctor before you receive Doxorubicin Teva.

Other medicines and Doxorubicin Teva

Tell your doctor if you are using or have recently used or might use any other medicines.
Tell your doctor if you:
- have been treated with any other anthracycline drugs or other drugs that may harm your heart such as 5-fluorouracil, cyclophosphamide or paclitaxel (anti-cancer medicines) or any drugs that affect the heart function (like calcium antagonists).
- have been treated or are due to be treated with trastuzumab (anti-cancer medicine) as your doctor will need to monitor your heart function.
- have been treated with 6-mercaptopurine (anti-cancer medicine), the risk of adverse events of the liver is increased.
- have been treated with drugs affecting the functions of the bone marrow such as cytostatic agents (e.g. cytarabine, cisplatin or cyclophosphamide), sulfonamides (for infections), chloramphenicol (for infections), phenytoin (for epilepsy), amidopyrine derivatives (for pain and inflammation), anti-retroviral drugs (for AIDS). This may lead to bone marrow damage causing a decrease in the number of blood cells.
- are taking ciclosporin (to suppress the natural immunity) or cimetidine (for gastric ulcers), the amount of doxorubicin in the blood may increase. Your doctor may consider dose reduction.
- are taking phenobarbital (for epilepsy) or rifampicin (antibiotic), the amount of doxorubicin in the blood may decrease and may result in a reduced effect of Doxorubicin Teva.
- are taking or have taken any radiation therapy, adverse effects may increase.
- have taken cyclophosphamide (anti-cancer medicine), the risk of adverse events of the bladder (hemorrhagic cystitis, an infection of the bladder that causes sometimes blood in the urine) increases.
- are treated or have been treated with paclitaxel (anti-cancer medicine), the effects or side effects of doxorubicin may increase.
- are taking uric acid lowering medicines. Dose adjustments of these medicines may be necessary as doxorubicin may cause increased levels of uric acid in your blood.
- are taking digoxin (for the heart), the effect of digoxin may decrease.
- are taking medicines used to control epilepsy such as phenytoin, carbamazepine, valproate, the effect of these drugs may decrease.
- are also being treated with heparin (used to prevent blood clotting) or 5-fluorouracil (anti-cancer medicine). If administered via the same infusion, doxorubicin may bind to these drugs, and loss of effect of the medicines is possible.

Pregnancy, breast-feeding and fertility

If you are a woman, you should not get pregnant during treatment with doxorubicin or up to 6 months after treatment.
Doxorubicin is not recommended if you are pregnant.

If you are a man, you should take adequate precautions to ensure that your partner does not become pregnant during your treatment with doxorubicin or up to 6 months after treatment. If you are considering becoming parents after the treatment please discuss with your doctor.

Because doxorubicin may cause permanent infertility, it is advised to discuss with your doctor the possibility of freezing sperm before treatment start (cryo-preservation or cryo-conservation).

Breast-feeding must be discontinued for the duration of Doxorubicin Teva therapy.

Driving and using machines

Do not drive or use any tools or machinery if you feel unwell with nausea, vomiting or dizziness.

Doxorubicin Teva contains sodium

This medicine contains 18 mg sodium (main component of cooking/table salt) in each 5 ml vial. This is equivalent to 0.9 % of the recommended maximum daily dietary intake of sodium for an adult.
This medicine contains 35 mg sodium (main component of cooking/table salt) in each 10 ml vial. This is equivalent to 1.8 % of the recommended maximum daily dietary intake of sodium for an adult.
This medicine contains 89 mg sodium (main component of cooking/table salt) in each 25 ml vial. This is equivalent to 4.4 % of the recommended maximum daily dietary intake of sodium for an adult.
This medicine contains 354 mg sodium (main component of cooking/table salt) in each 100 ml vial. This is equivalent to 17.7 % of the recommended maximum daily dietary intake of sodium for an adult.

3 How to use Doxorubicin Teva

You will be given Doxorubicin Teva by a doctor. Your doctor may carry out some tests such as blood tests, ECG, etc. on you before starting the treatment or during the treatment in order to decide the dose of Doxorubicin Teva to be given.

Doxorubicin will be administered to you either in your vein, through an i.v. infusion or into your bladder.

The preparation and administration of your medicine must only be carried out by a trained healthcare professional in hospital.

The dose will depend on your age (the dose may be lowered in children and elderly patients), size and general medical condition. It will also depend on any other treatment you may have received for your cancer. Your doctor will calculate your body surface area in square metres (m^2). The medicine will be administered to you every 3 weeks for a duration of 6 to 12 months. For administration into the bladder, the dose may be repeated with intervals of 1 week to 1 month. The exact duration of your treatment will depend on your condition.

Patients with Kidney or Liver Problems

If you have severe problems with your kidney function or liver function, a reduction of the dose may be necessary.

If you are given more Doxorubicin Teva than you should

As a doctor will be giving you your medicine, it is unlikely that you will receive an overdose. However if you have concerns you should let your doctor or nurse know *immediately*.
The effects of receiving too much Doxorubicin Teva include: Inflammation of your stomach and intestine (particularly the lining), heart problems and severe damage to your bone marrow (myelosuppression). This may be accompanied by an increased risk of bleeding and bruising, and an increased risk of infections (leukopenia).
Treatment will take place in hospital, and consists of administration of antibiotics, blood transfusions (especially white blood cells and platelets) and treatment of any side effects. It is possible that you

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The following information is intended for medical or healthcare professionals only:

Incompatibilities

Doxorubicin is incompatible with heparin, aminophyllin, cephalotin, dexamethasone, fluorouracil and hydrocortisone. Doxorubicin should only be mixed with 9 mg/ml (0.9%) sodium chloride solution for infusion or 50 mg/ml (5%) glucose solution for infusion.

Handling and precautions for disposal

Caution must be exercised in handling Doxorubicin Teva solution. Any contact with solution should be avoided. During preparation a strictly aseptic working technique should be used; protective measures should include the use of gloves, mask, safety goggles and protective clothing. Use of a vertical laminar airflow (LAF) hood is recommended.

Personnel should be trained in good technique for handling cytotoxic drugs. Pregnant staff should be excluded from working with this drug.

If Doxorubicin Teva comes in contact with skin or mucous membranes, the exposed area should be thoroughly washed with soap and water. If the substance gets into the eyes, rinse with water or sterile physiological saline, whereupon an eye specialist should be consulted.

After use, bottles and injection materials, including gloves, should be destroyed according to the rules for cytostatics. Any unused medical product or waste material should be disposed of in accordance with local requirements.

Inactivation of spilled or leaked drug can be obtained with 1% sodium hypochlorite solution or most simply with phosphate buffer (pH>8) until solution is destained. All cleaning materials should be disposed of as indicated previously.

Dosage and administration

The treatment with doxorubicin should be started by, or after consultation with, a doctor with extensive experience of cytostatic treatment. Patients must be carefully and frequently monitored during the treatment.

Doxorubicin may NOT be administered by the intramuscular, subcutaneous, oral or intrathecal route.

Intravenous (i.v.) administration of doxorubicin must be given with great care and it is advisable to give the drug via the tubing of a freely running i.v. saline or 5% glucose within 3-5 minutes. This method minimises the risk of thrombosis development and perivenous extravasation that result in severe cellulitis, vesication and tissue necrosis. Doxorubicin can be administered intravenously as a bolus within minutes, as a short infusion for up to an hour, or as continuous infusion for up to 96 hours. A direct intravenous injection is not recommended due to the risk of extravasation, which may occur even in the presence of adequate blood return upon needle aspiration.
Doxorubicin can be diluted in the concentration range of 0.05 mg/ml to 0.5 mg/ml in 9 mg/ml (0.9%) sodium chloride solution for infusion or in 50 mg/ml (5%) glucose solution for infusion using non-PVC infusion bags.

Intravenous administration:

The dose is usually calculated based on body surface area (mg/m^2). The dosage schedule of doxorubicin administration may vary according to indication (solid tumours or acute leukaemia) and according to its use in the specific treatment regimen (as a single agent or in combination with other cytotoxic agents or as a part of multidisciplinary procedures that include combination of chemotherapy, surgical procedure, and radiotherapy and hormonal treatment).

Monotherapy:

The recommended dose is 60-75 mg/m^2 body surface i.v. as a single dose or in divided doses on 2-3 consecutive days administered intravenously at 21 day intervals. Dosage schedule and dosages may be adjusted according to the protocol. For exact information on posology, refer to current protocols.

Combination therapy:
When Doxorubicin Teva is administered in combination with other cytostatics, the dosage should be reduced to 30-60 mg/m^2 every 3 to 4 weeks.

Maximal cumulative dose:

In order to avoid cardiomyopathy, it is recommended that the cumulative total lifetime dose of doxorubicin (including use with related drugs such as daunorubicin) should not exceed 450-550 mg/m^2 body surface area; extreme caution is needed when a cumulative dose of 400 mg/m^2 is exceeded in cases of previous radiation of mediastinum, previous or concomitant treatment with potentially cardiotoxic agents and in high risk patients (i.e. patients with arterial hypertension for a period exceeding 5 years; with prior coronary, valvular or myocardial heart damage; or aged over 70 years). The cardiac function of these patients should be monitored.

Special population groups:

Immunosuppressed patients: The dose should be reduced in the case of immunosuppression, an alternative dosage is 15-20 mg/m^2 body surface per week.

Patients with impaired hepatic function: In the case of decreased liver function, the dosage should be reduced according to the following table:

will be transferred to a sterile room. In case you experience any heart problems, a heart specialist (cardiologist) should investigate you.

Accidental administration outside the vein (extravasation) may cause severe side effects, including tissue death (necrosis) and inflammation of the vein involving the formation of a blood clot. A burning sensation in the region of infusion may be a sign of this, ***immediately*** warn your doctor if you suspect that this has happened.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If the following happens, tell your doctor immediately. You may need urgent medical attention:

- An allergic reaction causing swelling of the lips, face or neck leading to severe difficulty in breathing; skin rash or hives, anaphylactic shock (a severe reduction in blood pressure, pallor, agitation, weak pulse, decreased consciousness) (rare side effect: may affect up to 1 in 1,000 people)
- Severe symptoms of nausea, being sick and inflammation in the lining of the mouth or nose (rare side effect: may affect up to 1 in 1,000 people)
- Fever, infections, blood poisoning, shock (severe drop in blood pressure, pallor, restlessness, weak rapid pulse, clammy skin, reduced consciousness) as a result of blood poisoning (septic shock), bleeding, lack of oxygen in the tissues (tissue hypoxia) and tissue death. These are symptoms of damage to the bone marrow (rare side effect: may affect up to 1 in 1,000 people).
- Accidental administration outside the vein (extravasation) can cause severe skin inflammation (cellulitis), blistering, inflammation of the vein involving the formation of a blood clot (thrombophlebitis), inflammation in the glands characterised by painful, red streaks below the skin surface (lymphangitis) and localised cell death which may require surgery (including skin grafts) (rare side effect: may affect up to 1 in 1,000 people).

Other side effects

Very Common: may affect more than 1 in 10 people

- Feeling sick (nausea), being sick (vomiting), abdominal pain, problems with your digestive system, diarrhoea
- Hair loss (reversible)
- Red colouration of the urine
- Bone marrow damage (myelosupression) including a reduction in the number of white blood cells and platelets, which makes infections more likely and increases the risk of bleeding or bruising
- Anaemia (reduction in red blood cells which can make the skin pale and cause weakness or breathlessness)
- Heart muscle damage (cardiotoxicity). The risk increases if the patient is treated with radiation therapy or other medicines toxic to the heart, if the patient is elderly (over 60 years) or if the patient has high blood pressure. Effects can occur shortly after treatment or effects can be seen several years after treatment.
- Inflammation of the lining of the nose, mouth or vagina (mucositis)
- Inflammation or ulceration of the lining of the mouth (stomatitis), nose or throat (oesophagitis) e.g. mouth ulcers and cold sores
- Sensitivity of the skin to artificial or natural light (photosensitivity), flushes (reddening of the skin)
- Fever.

Common: may affect up to 1 in 10 people

- Heart rhythm disorders (irregular heartbeat, increased heart rate, decreased heart rate), contraction of the chambers of the heart, reduction in the amount of blood pumped to the body by the heart, deterioration of the function of the heart muscles (cardiomyopathy) which can be life threatening
- Bleeding problems (haemorrhage)
- Loss of appetite (anorexia)
- Allergic reactions at places where you were treated with radiation therapy (so-called radiation recall reaction)
- Itching.

Following the administration in the bladder, the following common side effects may be observed:

- Difficulty, pain or a burning sensation when passing water (urinating)
- Decreased quantity of urine
- Increased frequency of urinating
- Cramps of the bladder
- Inflammation in the bladder which sometimes causes blood in the urine
- Local side effects with administration into the bladder, such as bladder inflammation (chemical cystitis).

Uncommon: may affect up to 1 in 100 people

- Doxorubicin in combination with other cancer medicines can cause certain forms of blood cancer (leukaemia). These forms of cancer are noticeable within 1-7 years
- Blood poisoning (sepsis/septicaemia)
- Bleeding of the stomach or intestines, abdominal pain, ulcers and death of tissue cells (necrosis) of the large intestine with bleeding and infections, in particular of the large bowel. This can occur when doxorubicin is used together with cytarabine (an anti-cancer medicine)
- Loss of water (dehydration).

Rare: may affect up to 1 in 1,000 people

- Skin rash (exanthema), hives (urticaria)
- Colouring (pigmentation) of the skin and nails, detachment of the nails (onycholysis)
- Shivering, dizziness
- Injection site reactions including itching, rash and pain, inflammation of the vein (phlebitis), thickening or hardening of the walls of the vein (phlebosclerosis)
- Severe allergic reaction which causes difficulty in breathing or dizziness (anaphylactic reaction).

Very rare: may affect up to 1 in 10,000 people

- Heart rhythm disorders (unspecific ECG changes)
- Isolated cases of life-threatening irregular heart beat (arrhythmias), left sided heart failure, inflammation of the lining surrounding the heart causing chest pain and the accumulation of fluid around the heart (pericarditis), inflammation of the heart muscle and sack surrounding the heart (pericarditis-myocarditis syndrome), loss of nerve impulses in the heart (atrioventricular block, bundle branch block)
- Obstruction of a blood vessel by a blood clot
- Ulcers in the lining of the mouth, throat, gullet, stomach or intestines, colouration (pigmentation) of the mouth lining
- Swelling and numbness of the hands and feet (acral erythemas), blistering
- Tissue damage particularly of the hands and feet, leading to redness, swelling, blisters, tingling or burning sensation caused by the leakage of the medicinal product into tissues (Palmar-plantar erythrodysaesthesia syndrome)
- Condition where the kidneys stop functioning properly (acute kidney failure)
- Abnormally high levels of uric acid in the blood (hyperuricaemia) which can cause gout, kidney stones or kidney damage due to rapid tumour breakdown
- No menstrual periods (amenorrhoea)
- Fertility problems in men (decrease or lack of active sperm)
- Facial flushing.

Not known: frequency cannot be estimated from the available data

- Shortness of breath due to cramping of the muscles of the airways (bronchospasms)
- Temporary increase in liver enzymes
- Severe liver damage which can sometimes progress to permanent damage to normal liver tissue (cirrhosis)
- Inflammation of the surfaces of the eyelids, outer layer of the eye or cornea (conjunctivitis/keratitis), increased production of tears
- Severe pain and swelling in the joints
- Radiation damage (to the skin, lungs, throat, gullet, lining of the stomach and intestines, heart) that is already healing may reappear with doxorubicin treatment
- Thick, scaly, or crusty patches of skin (actinic keratosis).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Doxorubicin Teva

Keep this medicine out of the sight and reach of children.

This medicine should not be used after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Storage conditions

Before opening: Store in a refrigerator (2-8°C). Do not freeze.

After opening: The product should be used immediately after opening the vial.

After dilution:

Chemical and physical in-use stability after dilution to a concentration of 0.5 mg/ml (in sodium chloride solution for infusion 9 mg/ml or glucose solution for infusion, 50 mg/ml) has been demonstrated for 7 days when stored protected from light at room temperature (15-25°C) and at 2-8°C.

After dilution to the concentration of 0.05 mg/ml, the diluted solution should be used immediately.

From a microbiological point of view, the product should be used immediately. If it is not used immediately, in-use storage times and conditions prior to use are the responsibility of the user. Storage times of diluted product are usually no longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6 Contents of the pack and other information

What Doxorubicin Teva contains:

- The active ingredient is doxorubicin hydrochloride. Each ml of concentrate for solution for infusion contains 2 mg doxorubicin hydrochloride.
  Each vial with 5 ml contains 10 mg doxorubicin hydrochloride.
  Each vial with 10 ml contains 20 mg doxorubicin hydrochloride.
  Each vial with 25 ml contains 50 mg doxorubicin hydrochloride.
  Each vial with 100 ml contains 200 mg doxorubicin hydrochloride.
- The other ingredients are sodium chloride, hydrochloric acid (E507), sodium hydroxide (E524) and water for injections.

What Doxorubicin Teva looks like and contents of the pack

Doxorubicin Teva 2 mg/ml concentrate for solution for infusion is a clear, red solution. The solution is supplied in colourless glass vials closed with a chlorobutyl rubber stopper with an aluminium seal, covered with a coloured disc. Doxorubicin Teva 2 mg/ml is available in vials of 5 ml, 10 ml, 25 ml and 100 ml. Each package contains 1 injection bottle.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Teva Pharma B.V., Swensweg 5, 2031GA Haarlem, The Netherlands.

Manufacturer

Pharmachemie B.V., Swensweg 5, 2031 GA Haarlem, The Netherlands.

This medicinal product is authorised in the Member States of the EEA under the following names:

The Netherlands	Doxorubicine hydrochloride 2 mg/ml PCH, concentraat voor oplossing voor infusie
Belgium	Doxorubicine Teva 2mg/ml concentraat voor oplossing voor infusie
Czech Republic	Doxorubicin Teva 2 mg/ml, koncentrát pro přípravu infuzního roztoku
Denmark	Doxorubicin Teva
Estonia	Doxorubicin Teva, 2 mg/ml infusioonilahuse kontsentraat
Germany	Doxorubicinhydrochlorid Teva 2 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Ireland	Doxorubicin Teva 2 mg/ml Concentrate for Solution for Infusion
Italy	Doxorubicina Teva 2 mg/ml concentrato per soluzione per infusione
Lithuania	Doxorubicin Teva 2 mg/ml koncentratas infuziniam tirpalui
Luxembourg	Doxorubicine Teva 2 mg/ml solution à diluer pour perfusion
Latvia	Doxorubicin Teva 2 mg/ml koncentrāts infūziju šķīduma pagatavošanai
Romania	Texora 2 mg/ml concentrat pentru solutie perfuzabilă
Slovenia	Doksorubicin Teva 2 mg/ml koncentrat za raztopino za infundiranje

This leaflet was last revised in 03/2020.

Serum bilirubin	Recommended dose
20-50 µmol/L	½ normal dose
> 50-85 µmol/L	¼ normal dose
> 85 µmol/L	Stop treatment

Patients with impaired renal function:
In patients with renal insufficiency (GFR less than 10 ml/min), only 75% of the planned dose should be administered.

Patients with risk of cardiac impairment:
Patients with an increased risk of cardiac toxicity should be considered for treatment with a 24 hours continuous infusion of single dose, rather than injection. In this way, cardiac toxicity may be less frequent, without a reduction in therapeutic efficacy. In these patients, the ejection fraction should be measured before each course.

Patients with limited bone marrow reserve not related to bone marrow involvement of the disease:
The dosages may be reduced in patients with a history of treatment with myelosuppressive agents. Their bone marrow reserve may be insufficient.

Elderly:

The dosages may be reduced in elderly patients.

Paediatric population:
In view of the substantial risk of doxorubicin induced cardiotoxicity during childhood certain maximum cumulative dosages that depend on the youth of patients should be applied. In children (under 12 years of age) the maximal cumulative dose is usually considered 300 mg/m^2, whereas in adolescents (over 12 years of age) the maximal cumulative dose is set to 450 mg/m^2. For infants the maximal cumulative dosages are still indecisive, but even lower tolerability is assumed.

Dosage for children should be reduced, since they have an increased risk for cardiac toxicity, especially late. Myelotoxicity should be anticipated, with nadirs at 10 to 14 days after start of treatment. Please refer to treatment protocols and the specialist literature.

Note: Doxorubicin Teva may not be exchanged with a liposomal formulation of Doxorubicin hydrochloride.

Intravesical administration:

Doxorubicin Teva can be given by intravesical instillation for treatment of superficial cancer of the bladder and to prevent relapse after transurethral resection (T.U.R). The recommended dose for intravesical treatment of superficial cancer of the bladder is 30-50 mg in 25-50 ml of physiological saline per instillation. The optimal concentration is about 1 mg/ml. The solution should remain in the bladder for 1-2 hours. During this period the patient should be turned 90° every 15 minutes. To avoid undesired dilution with urine the patient should be informed not to drink anything for a period of 12 hours before the instillation (this should reduce the production of urine to about 50 ml/h). The instillation may be repeated with an interval of 1 week to 1 month, dependent on whether the treatment is therapeutic or prophylactic.

Treatment control

Before or during treatment with doxorubicin the following monitoring examinations are recommended (how often these examinations are done will depend on the general condition of the patient, the dose and the concomitant medication being taken):

- radiographs of the lungs and chest and ECG
- regular monitoring of heart function (LVEF by e.g. ECG, UCG and MUGA scan)
- inspection of the oral cavity and pharynx for mucosal changes
- blood tests: haematocrit, platelets, differential white cell count, SGPT, SGOT, LDH, bilirubin, uric acid, AST, ALT, ALP.

Control of the left ventricular function

Analysis of LVEF using ultrasound or heart scintigraphy should be performed in order to optimize the heart condition of the patient. This control should be made prior to the start of the treatment and after each accumulated dose of approximately 100 mg/m^2

Storage conditions after dilution

Chemical and physical in-use stability after dilution to a concentration of 0.5 mg/ml in 9 mg/ml (0.9%) sodium chloride solution for infusion or in 50 mg/ml (5%) glucose solution for infusion has been demonstrated for 7 days when stored protected from light at room temperature (15-25°C) and at 2-8°C.
After dilution to the concentration of 0.05 mg/ml, the diluted solution should be used immediately.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Disposal

Waste disposal procedures should take into account the cytotoxic nature of this substance.

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