**Package leaflet: Information for the patient**

**[Product name]**

Doxorubicin hydrochloride

**Read all of this leaflet carefully before you receive 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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 [Product name] is and what it is used for

Doxorubicin is one of a group of medicines known as anthracyclines. It works by killing tumour and blood cancer cells. Your doctor will be able to explain how doxorubicin might help in your particular condition.

This medication is used to treat:
- breast cancer
- ovarian cancer
- uterine cancer
- cancer of the bladder
- lung cancer
- thyroid cancer
- soft tissue and bone cancer (sarcoma)
- neuroblastoma (cancer of the nerve cells)
- Wilms' tumour
- malignant lymphoma (Hodgkin's and non-Hodgkin's)
- leukaemias (cancer cause abnormal production of blood cells)
- cancer of white blood cells (multiple myeloma)

## 2. What you need to know before you receive [Product name]

**You must not receive [Product name] in the following cases. Please tell your doctor**
- if you are allergic to doxorubicin or any of the other ingredients of this medicine (listed in section 6) or to other anthracyclines.
- if you have been told that your **blood is thin** (your bone marrow is not working well).
- if you have, or ever have had, any **heart problems**.
- if you have received **doxorubicin**, **other anthracyclines**, other anti-tumour medicines or immunosuppressive medicines before.
- if you tend to **bleed easily**.
- if you suffer from any kind of **infection**.
- if you suffer from **mouth ulcers**.

- if your **liver** is **not working well**.
- if you suffer from an **infection of the bladder** or if you have **blood in your urine** (in case the medicine is given to you by an administration into your bladder).
- if you are **breast-feeding**.

**Warnings and precautions**
Talk to your doctor, pharmacist or nurse before you are given [Product name].

Special care should be taken
- if you have had any radiotherapy before.
- if you are pregnant, trying to become pregnant, likely to want to try to become pregnant in the future or if you want to father a child.
- if you are on a controlled sodium diet.

If there is a burning sensation in the area of the infusion, this can be a sign of an injection error and the infusion must be stopped immediately.

You should avoid contact to persons recently vaccinated against polio when you are under treatment with [Product name].

**Other medicines and [Product name]**
Tell your doctor if you are taking, have recently taken or might take any other medicines.

*The following medications can interact with [Product name]:*
- Other cytostatics (medication against cancer) e.g. anthracyclines (daunorubicin, epirubicin, idarubicin), cisplatin, cyclophosphamide, cyclosporine, cytarabine, dacarbazine, dactinomycin, fluorouracil, mitomycin C, taxanes (e.g. paclitaxel), mercaptopurine, methotrexate, streptozocin and sorafenib
- Cardioactive medicines (medications for heart diseases), e.g. calcium channel blockers, verapamil, digoxin
- Inhibitors of cytochrome P-450 (medicines that stop the substance cytochrome P-450, which is important for the detoxification of your body, from working; e.g. cimetidine)
- Medicine inducing cytochrome P-450 (e.g. rifampicin, barbiturates)
- Antiepileptic medicines (e.g. carbamazepine, phenytoin, valproate)
- Heparin (prevents the clotting of the blood)
- Amidopyrine derivatives (pain-killers)
- Antiretroviral medicines (medications against special forms of viruses, e.g. ritonavir against AIDS)
- Chloramphenicol
- Sulphonamides (medications against bacteria)
- Progesterone (e.g. at threatening miscarriage)
- Amphotericin (used to treat fungal infections)
- Live vaccines (e.g. against polio myelitis, malaria)
- Trastuzumab (used in the treatment of breast cancer) which can take up to 7 months to be removed from the body. As trastuzumab may affect the heart, you should not use doxorubicin for up to 7 months after you have stopped taking trastuzumab. If doxorubicin is used before this time, then your heart function should be carefully monitored.
- Clozapine (antipsychotic medicine)
- Dose adjustment of uric acid lowering agents may be necessary

Please note that these statements may also apply to products used some time ago or at some time in the future.

**Pregnancy, breast-feeding and fertility**

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy
If you are a woman, you should not get pregnant during treatment with doxorubicin and for at least 7 months after the last dose.
If there is a desire to have children after completion of the therapy, genetic counselling is recommended in advance.

Contraception in males and females
If you are a man, you should take adequate precautions to ensure that your partner does not become pregnant during your treatment with doxorubicin and for at least 4 months after the last dose.

**Doxorubicin is not recommended if you are pregnant.**

Breast-feeding
You should not breastfeed during therapy with [Product name] and for at least 2 weeks after the last dose.

Fertility
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).

Ask your doctor or pharmacist for advice before taking any medicine.

**Driving and using machines**
Due to the frequent occurrence of drowsiness, nausea and vomiting, you are not advised to drive cars and operate machinery.

**[Product name] contains sodium**
Please tell your doctor if you are on a low-sodium diet. He/she will take into account that this medicine contains 0.154 mmol (or 3.54 mg) sodium per ml of solution. The different pack sizes of [Product name] contain the following amounts of sodium:

| | |
|---|---|
| 5 ml vial: | This pack size contains less than 1 mmol sodium (23 mg), that is to say essentially 'sodium-free'. |
| 10 ml vial: | This pack size contains 35.42 mg sodium (main component of cooking/table salt). This is equivalent to 1.77% of the recommended maximum daily dietary intake of sodium for an adult. |
| 25 ml vial: | This pack size contains 88.55 mg sodium (main component of cooking/table salt). This is equivalent to 4.43% of the recommended maximum daily dietary intake of sodium for an adult. |
| 75 ml vial: | This pack size contains 265.65 mg sodium (main component of cooking/table salt). This is equivalent to 13.28% of the recommended maximum daily dietary intake of sodium for an adult. |
| 100 ml vial: | This pack size contains 354.20 mg sodium (main component of cooking/table salt). This is equivalent to 17.71% of the recommended maximum daily dietary intake of sodium for an adult. |

## 3. How [Product name] is administered

**Method and routes of administration**
Do not administer the medicine yourself. Your medicine will be given to you as part of an intravenous infusion, into a blood vessel, under the direction of specialists. You will be monitored regularly both during and after your treatment.
If you suffer from superficial bladder cancer it is possible that you may receive your medicine into your bladder (intravesical use).

**Dosage**
The dosage is usually calculated on the basis of your body surface area. 60 – 75 mg per square metre of body surface area may be given every three weeks when used alone. The dosage may need to be reduced to 30 – 40 mg per square metre of body surface area when given in combination with other anti-tumour medicines. The dosage may be given as either a single dose every three weeks or divided over three consecutive days (20 – 25 mg per square metre of body surface area on each day). If given weekly, the recommended dose is 20 mg per square metre of body surface area.
Your doctor will advise you of how much you will need.

**Patients with reduced liver or kidney function**
If your liver or kidney function is reduced, the dosage should be decreased. Your doctor will advise you of how much you need.

**Use in children/obese patients/elderly/patients after radiotherapy**
The dosage may need to be reduced in children, in obese patients and the elderly or if you have received any radiotherapy. Your doctor will advise you of how much you need.

**If you received more [Product name] than you should**
During and after treatment you will be carefully monitored by your doctor or nurse. The symptoms of an overdose are an extension of doxorubicin´s possible side effects, particularly the blood changes, gastrointestinal and heart problems. Heart disorders may even occur up to six months after you received the overdose.
In case of an overdose your doctor will take appropriate measures, such as a blood transfusion and/or treatment with antibiotics.
Please tell your doctor if any of the symptoms occur.

**If treatment with [Product name] is interrupted or stopped**
Your doctor will decide on the duration of your treatment with [Product name]. If the treatment is stopped before the advised course of treatment is finished, the effects of the doxorubicin therapy might be reduced.
Ask your doctor for advice if you wish to stop the treatment.

## 4. Possible side effects

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

**Contact your doctor straight away if you notice any of the following serious side effects:**
They have been ranked according to their potential seriousness.

- You may develop **hives**, **fever**, **chills**, **severe hypersensitivity**. This type of allergic reaction can be life-threatening.
- Heart problems – for example you may notice your **heart beating abnormally quickly**, with an increase in pulse rate. In case of heart problems, routine ECG monitoring is commonly applied. If you have suffered from heart problems (even a long time ago) before treatment with [Product name] make sure to tell your doctor about this.
- Blood changes: decrease in certain kind of white blood cells (your **vulnerability for infections** may increase), decrease in platelets (you may suffer from **unusual bleedings)** and you may observe **signs of anaemia** (weakness, tiredness, laboured breathing with a feeling of

apprehension).

Your urine may be coloured red, particularly the first time that you pass urine after each injection of [Product name]. This is nothing to worry about and your urine will soon return to its normal colour.

Information on frequency of the side effects is provided below.

The potential side effects are classified as follows:

*Very common*: may affect more than 1 in 10 patients
*Common:* may affect up to 1 in 10 patients
*Uncommon:* may affect up to 1 to 10 out of 1,000 patients
*Rare:* may affect up to 1 to 10 out of 10,000 patients
*Very rare:* may affect less than 1 in 10,000 patients
*Not known:* the frequency cannot be estimated from the available data

**Very common (may affect more than 1 in 10 people)**
- infections
- decreased activity in bone marrow (myelosuppression), lack of white blood cells (leukopenia), reduction in the number of certain white blood cells and platelets (neutropenia and thrombocytopenia), decreased number of red blood cells (anaemia), lack of oxygen in the tissues (tissue hypoxia) or death
- reduced number of certain white blood cells accompanied by fever (febrile neutropenia)
- inflammation in a vein leading to a blood clot (thrombophlebitis)
- feeling and/or being sick (nausea and/or vomiting)
- inflammation of membranes in digestive tract, starts with burning sensations in mouth or pharynx (mucositis)
- inflammation of the mouth lining (stomatitis)
- diarrhoea – may result in dehydration
- hand-foot syndrome (painful reddening with swelling of the palms and soles of the feet)
- separation of nail plates
- hair loss (alopecia)
- localised injury of the skin, reddening of the skin
- increased sensitivity of skin to the sunlight
- skin rashes
- shivering, fever, feeling of weakness (asthenia)
- abnormal results of heart examinations (asymptomatic decrease in left ventricular ejection fraction (LVEF)), abnormal electrocardiogram (ECG), abnormal liver values (transaminases)
- weight gain.

**Common (may affect up to 1 in 10 people):**
- cardiac damage such as disease of the heart muscle (cardiomyopathy), fast heartbeat (tachycardia), heart rhythm disorder with fast heartbeat (tachyarrhythmia), slowed heartbeat (bradycardia), heart failure, heart weakness
- eating disorder (anorexia)
- bladder inflammation sometimes with painful urination, need to urinate more often or during night or blood in urine and urinary bladder spasms (following administration into the bladder)
- serious infection of the whole body (sepsis)
- bacterial infection of the blood (septicaemia)
- skin and nails may appear darker than usual
- itchy skin
- hives
- local hypersensitivity reaction of the field of radiation
- conjunctivitis (usually causing red watery eyes)
- vein inflammation (phlebitis)
- bleeding
- inflammation of the foodpipe, abdominal pain or burning sensation.

**Uncommon (may affect up to 1 in 100 people):**
- dehydration
- induration or stiffening of the vein wall (phlebosclerosis)
- inflammation in the large bowel (colitis)
- inflammation of the colon (also in severe form with sometimes serious infections) in combination with doxorubicin and cytarabine (anti-cancer drugs)
- inflammation of the stomach with possible bleeding (erosive gastritis)
- bleeding in stomach or bowel
- ulceration and necrosis (death of cells of the tissue) of the digestive tract
- blood poisoning with impairment of organ functions and low blood pressure (septic shock)
- blood cancer arisen from combined treatment with a special kind of other anti-cancer medicines (secondary leukaemia, i.e. acute lymphocytic leukaemia)
- clot formation in a vessel (thromboembolism).

**Rare (may affect up to 1 in 1,000 people):**
- rapid break down of cancer cells causing metabolic imbalances (tumour lysis syndrome)
- tissue death (tissue necrosis)
- acute and potentially life-threatening general allergic reaction including skin rash, itching, fever, chills, allergic painful swelling of the eyelids and tongue and breathing difficulties (anaphylactic reactions)
- rash-like symptoms (erythematous reactions) along the vein used for the injection
- dizziness
- inflammation of the lung after radiation
- breathing disorders, swelling of the nasal lining, rapid breathing and difficult breathing
- increased flow of tears.

**Very rare (may affect up to 1 in 10,000 people):**
- high uric acid level in blood (hyperuricaemia)
- certain heart rhythm disorder (atrioventricular block)
- low blood pressure and circulation (shock)
- mucosal injuries of the gastrointestinal tract (erosions), discolouration inside the mouth
- general muscle weakness
- absence of menstruation
- low sperm volume or lack of sperm
- general malaise.

**Not known (cannot be estimated from the available data):**
- hot flushes
- severe heart failure (loss of cardiac function)
- irregular heart beat
- coughing or difficulty in breathing (bronchospasm)
- liver disorder
- red colouration of the urine 1 – 2 days after administration
- loss of renal function may lead to renal failure
- infertility in men
- inflamed cornea (keratitis)
- joint pain
- a stinging or burning sensation at the infusion site.

Burning, redness and swelling at the administration site may occur. If this is the case during an infusion you should inform the doctor or nurse, because the injection should be stopped immediately and restarted at another site.

**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 the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store [Product name]

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.
Store the unopened vials in a refrigerator (2 – 8 °C). Keep the vial in the outer carton in order to protect from light.
The product should be used immediately after opening the vial.
For single dose use only. Any unused solution should be discarded immediately after initial use.

Do not use this medicine if you notice that the solution is not clear, red and free of particles.

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

Remnants of the medicinal product as well as all materials that have been used for dilution and administration must be destroyed according to hospital standard procedures applicable to cytotoxic agents with due regard to current laws related to the disposal of hazardous waste.

## 6. Contents of the pack and other information

**What [Product name] contains**
1 ml contains 2 mg doxorubicin hydrochloride.

Each 5 ml vial contains a total content of doxorubicin hydrochloride of 10 mg.
Each 10 ml vial contains a total content of doxorubicin hydrochloride of 20 mg.
Each 25 ml vial contains a total content of doxorubicin hydrochloride of 50 mg.
Each 75 ml vial contains a total content of doxorubicin hydrochloride of 150 mg.
Each 100 ml vial contains a total content of doxorubicin hydrochloride of 200 mg.

The other ingredients are sodium chloride, hydrochloric acid (for pH adjustment) and water for injections.

**What [Product name] looks like and contents of the pack**
[Product name] is a clear, red solution which is practically free of particles.

Pack sizes:
The solution is available in packs of 1 or 5 vials containing 5/10/25/75 or 100 ml solution.
This corresponds to 10/20/50/150 or 200 mg of the active substance, doxorubicin hydrochloride, per vial.

Not all pack sizes may be marketed.

**Marketing Authorisation Holder and Manufacturer**
medac
Gesellschaft für klinische Spezialpräparate mbH
Theaterstr. 6
22880 Wedel

Germany

**This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:**

{Name of the Member State} {Name of the medicine}
{Name of the Member State} {Name of the medicine}
United Kingdom (Northern Ireland) {Name of the medicine}

**This leaflet was last revised in 03/2023**

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The following information is intended for healthcare professionals only:

**Incompatibilities**
Doxorubicin should not be mixed with heparin as a precipitate may form and it should not be mixed with 5-fluorouracil as degradation may occur. Prolonged contact with any solution of an alkaline pH should be avoided as it will result in hydrolysis of the medicine.

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

**Opened vials**
The product should be used immediately after opening the vial.

**Prepared infusion solutions**
Chemical and physical in-use stability at a concentration of 0.5 mg/ml has been demonstrated in sodium chloride 0.9 % and glucose 5 % for up to 7 days at 2 °C to 8 °C or room temperature (20 °C to 25 °C) when prepared in PE-bags and protected from light.
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 °C to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

**Special precautions for disposal and other handling**
For single use only.
Any unused product or waste material should be disposed of in accordance with local requirements.

Observe guidelines for handling cytotoxic medicines.

The following protective recommendations are given due to the toxic nature of this substance:
- Personnel should be trained in good technique for handling.
- Pregnant staff should be excluded from working with this medicine.
- Personnel handling doxorubicin should wear protective clothing: goggles, gowns, 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 and absorbent paper.
- All items used for administration or cleaning, including gloves, should be placed in high risk waste disposal bags for high temperature (700 °C) incineration.
- In case of skin contact, thoroughly wash the affected area with soap and water or sodium bicarbonate solution. However, do not graze the skin by using a scrubbing brush.
- In case of contact with eye(s), hold back the eyelid(s) and flush the affected eyes with copious amounts of water for at least 15 minutes. Then seek medical evaluation by a physician.
- Spillage or leakage should be treated with dilute sodium hypochlorite (1 % available chlorine) solution, preferably soaking overnight and then rinse with water.

- All cleaning materials should be disposed of as indicated previously.
- Always wash hands after removing gloves.