PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: **S4**

DOXORUBICIN 10 mg/5 mL FRESENIUS

concentrate for solution for infusion

DOXORUBICIN 50 mg/25 mL FRESENIUS

concentrate for solution for infusion

Doxorubicin hydrochloride

Sugar free

Read all of this leaflet carefully before you are given DOXORUBICIN FRESENIUS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet

1. What DOXORUBICIN FRESENIUS is and what it is used for

Doxorubicin is one of a group of medicines known as anthracyclines. Doxorubicin works by killing tumour and blood cancer cells.

DOXORUBICIN FRESENIUS is used in the treatment of various cancers to slow or stop the growth of cancer cells. A combination of different types of cancer medicines will often be used to achieve better results and minimise side effects.

Your doctor will be able to explain how DOXORUBICIN FRESENIUS might help in your particular condition.

2. What you need to know before you use DOXORUBICIN FRESENIUS

Do not use DOXORUBICIN FRESENIUS

- if you are hypersensitive (allergic) to doxorubicin hydrochloride, or any of the other ingredients of DOXORUBICIN FRESENIUS (listed in section 6)
- if you are allergic to any other anthracycline
- if you have been told your blood is thin (your bone marrow is not working well)
- if your liver is not working well
- if you suffer from heart disease
- if you had a recent heart attack
- serious abnormality of the heartbeat (dysrhythmia)
- if you have previously been treated with doxorubicin or similar chemotherapy medicines like, idarubicin, epirubicin or daunorubicin, as previous treatment with these similar medicines can increase the risk of side effects with DOXORUBICIN FRESENIUS

- if you are pregnant or breastfeeding (see Pregnancy and breastfeeding).

Warnings and precautions

DOXORUBICIN FRESENIUS will only be used in specialised departments of oncology (cancer) and will be administered under the supervision of doctor experienced in cancer chemotherapy.

Tell your doctor or healthcare provider before being given the injection:

- if you suffer from liver disease
- if you suffer from mouth ulcers
- if you have secondary acute myelogenous leukaemia (AML), a type of cancer of the blood cells

Site of administration:

Avoid any contact with your skin and mucous membranes.

Tell your doctor as soon as you experience stinging or redness at the site of injection. The infusion will immediately be stopped and restarted in another vein.

Skin reactions due to previous cancer therapy may recur with administration of DOXORUBICIN FRESENIUS.

DOXORUBICIN FRESENIUS irritates the skin and thrombophlebitis (inflammation of the vein with formation of a clot) and streaking of the skin over the vein used for infusion may occur and it should not be confused with extravasation (stinging or burning at injection site).

Cardiac risk with administration of DOXORUBICIN FRESENIUS:

Your doctor will monitor your heart function carefully during the treatment because:

DOXORUBICIN FRESENIUS may damage the heart muscle and may lead to heart failure after a certain cumulative dose (adding up of single doses). The risk for heart muscle damage is higher if you have previously received medicines that may damage the heart or radiotherapy of the upper body.

If you are on this treatment, you will undergo frequent ECG monitoring and if your doctor finds any abnormalities, he/she will discontinue treatment or do further evaluation tests.

Myelosuppression with the administration of DOXORUBICIN FRESENIUS:

You may suffer from myelosuppression (a reduction in bone marrow activity that leads to a lower concentration of platelets, red blood cells and white blood cells). This may make you more prone to infections or bleeding.

Your doctor will conduct blood tests regularly to monitor your blood cells.

Other safety information

DOXORUBICIN FRESENIUS may enhance the toxicity of other anticancer therapies. Your doctor will ensure that the necessary tests are done to monitor these effects.

The levels of uric acid (showing that cancer cells are destroyed) in your blood may be high during treatment. Your doctor will tell you if you need to take any medicine to control this.

Existing infections should be treated before DOXORUBICIN FRESENIUS therapy is started.

DOXORUBICIN FRESENIUS is generally not recommended in combination with live, attenuated vaccines. Contact with persons recently vaccinated against polio should be avoided.

You may experience changes in your menstrual cycle and your ability to conceive may be affected.

DOXORUBICIN FRESENIUS may give a red colour to your urine, which should not be mistaken for blood. This is a normal effect of the medicine that does not pose any health hazards.

Other medicines and DOXORUBICIN FRESENIUS

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

The following medicines may interact with DOXORUBICIN FRESENIUS:

- other cancer medicines e.g. trastuzumab, anthracyclines (daunorubicin, epirubicin, idarubicin), cisplatin, cyclophosphamide, ciclosporin, cytarabine, dacarbazine, dactinomycin, fluorouracil, mitomycin C, taxanes (e.g. paclitaxel), mercaptopurine, methotrexate, streptozocin, 6- mercaptopurine
- medicines for heart disease e.g. calcium channel blockers, verapamil, and digoxin
- ciclosporin (an immune suppressant medicine)
- ritonavir (a medicine used for HIV treatment)
- clozapine (an antipsychotic medicine used in schizophrenia)
- amphotericin B (medicines used against fungal diseases)
- uric acid lowering medicines (one example is allopurinol), as their dose may need adjustment
- radiotherapy: any radiotherapy treatment before, during and after DOXORUBICIN FRESENIUS may increase the toxic effects on the heart and liver
- live vaccines (e.g. polio (myelitis), malaria)

- phenytoin (a medicine used to prevent and control seizures).

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before receiving DOXORUBICIN FRESENIUS.

Pregnancy

Your doctor will not administer DOXORUBICIN FRESENIUS if you are pregnant (see "Do not use DOXORUBICIN FRESENIUS").

Breastfeeding

Do not breastfeed while you are treated with DOXORUBICIN FRESENIUS. The medicine can be passed on to the baby through the breast milk.

Fertility

If you are a woman, you should not get pregnant during treatment with DOXORUBICIN FRESENIUS or up to 7 months after treatment.

If you are a man, you should take adequate precautions to ensure that your partner does not become pregnant during your treatment with DOXORUBICIN FRESENIUS or up to 6 months after treatment and to seek advice on cryo-conservation (or cryo-preservation) of sperm prior to treatment because of the possibility of irreversible infertility due to therapy with DOXORUBICIN FRESENIUS. If you are considering becoming parents after the treatment, please discuss this with your doctor.

Driving and using machines

Nausea and vomiting frequently occur. If you experience these adverse effects, you should avoid driving and operating machinery while on therapy with DOXORUBICIN FRESENIUS.

DOXORUBICIN FRESENIUS contains sodium

DOXORUBICIN FRESENIUS contains 0,15 mmol (3,5 mg) sodium per mL. This should be considered if you are on a controlled sodium diet.

3. How to use DOXORUBICIN FRESENIUS

You will not be expected to give yourself DOXORUBICIN FRESENIUS. It will be given to you by a person who is qualified to do so.

DOXORUBICIN FRESENIUS can only be given under supervision by a doctor with experience in cancer treatment.

Your doctor will calculate your dosage according to your body surface area, your condition and the cancer to be treated.

DOXORUBICIN FRESENIUS will be administered intravenously (injected into a vein). The dose will be repeated at intervals determined by your doctor. Your doctor will tell you how long your treatment with DOXORUBICIN FRESENIUS will last.

If you have the impression that the effect of DOXORUBICIN FRESENIUS is too strong or too weak, tell your doctor.

If you receive more DOXORUBICIN FRESENIUS than you should:

Since a healthcare provider will administer DOXORUBICIN FRESENIUS, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

The symptoms of overdosage will be an extension of the side effects. Please tell your doctor if you experience a worsening of any of the side effects.

If you forget to use DOXORUBICIN FRESENIUS

Since a healthcare provider will administer DOXORUBICIN FRESENIUS, it is unlikely that the dose will be missed.

4. Possible side effects

DOXORUBICIN FRESENIUS can have side effects.

Not all side effects reported for DOXORUBICIN FRESENIUS are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving DOXORUBICIN FRESENIUS, please consult your healthcare provider for advice.

If any of the following happens, stop using DOXORUBICIN FRESENIUS and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, face, lips or throat, which may cause difficulty breathing,
- rash or itching, hives, red swollen skin.

These are all serious side effects. If you have them, you may have a serious reaction to DOXORUBICIN FRESENIUS. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- fever (high temperature), chills, shivering and fast heartbeat (sepsis, blood poisoning)
- anaemia (a low red blood cell count) that can leave you feeling tired and lethargic
- low blood platelet count that could make you bleed or bruise more easily
- low white blood cell counts (these cells fight infection), increasing the chance of infections and raised temperature (fever)
- decreased activity in your bone marrow, affecting your immunity against infections. Your doctor should test your blood cell count during treatment
- abnormal increase in or irregular heart rate (cardiomyopathy, dysrhythmias)
- shortness of breath, swollen legs (congestive heart failure)
- intestinal perforation (blood in the stool, severe abdominal pain, nausea and vomiting blood)
- acute renal failure (decreased urine output, swelling of legs, fatigue)
- pain and swelling at the injection site.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- anorexia
- nausea
- vomiting
- swollen or sore mouth
- diarrhoea
- loss of hair
- facial flushing

Less frequent side effects

- dehydration (loss of water, feeling thirsty)
- headache
- eye infection
- excessive secretion of tears
- low blood pressure
- inflammation in vein (phlebitis)
- inflammation of the food pipe (painful swallowing)
- abdominal pain
- ulcers in the intestines and mouth
- excessive pigmentation of skin and nails
- detached nails

- urine might appear red in colour
- gout (high uric acid)
- absence of menstruation
- reduced sperm volume
- enlarged breasts
- feeling unwell
- weakness
- shivering
- dizziness

Frequency unknown:

- thromboembolism (clot formed in a blood vessel)
- excessive pigmentation of oral mucosa - feeling of intense heat (hot flushes)
- inflammation of the large intestine (colitis)
- liver disorders (yellowing of skin and eyes, increase in liver enzyme blood test results)
- tissue hypoxia (low oxygen in your tissues) (your skin may feel cold and if severe take on a bluish colour
- plantar-palmar dysaesthesia (hand-to-foot syndrome is a distinctive and relatively frequent skin toxic reaction)
- photosensitivity
- no sperm formation
- asthenia (loss or lack of bodily strength; weakness; debility)

- thrombophlebitis (vein inflammation under the skin)
- a stinging or burning sensation at the administration site in relation to extravasation. Extravasation can lead to local death of calls of the tissue which may require surgical measures.

If you notice any of side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of DOXORUBICIN FRESENIUS.

Patients are asked to report any suspected adverse drug reactions to their healthcare provider or Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicine's regulatory authority in the country where the product is marketed.

5. How to store DOXORUBICIN FRESENIUS

Store all medicines out of reach of children.

Store at or below 2 - 8 °C. Do not freeze. Keep vial in carton to protect from light. Store in upright position.

Infusion preparation:

DOXORUBICIN FRESENIUS is for single use only. Any unused solution should be discarded.

After dilution with 0,9 % sodium chloride or dextrose 5 % in water the diluted solution should be used immediately. Any unused solution should be discarded.

6. Contents of the pack and other information

What DOXORUBICIN FRESENIUS contains

- The active substance is doxorubicin hydrochloride. Each mL of the concentrate for solution for infusion contains 2 mg doxorubicin hydrochloride.

Each 5 mL vial contains 10 mg doxorubicin hydrochloride.

Each 25 mL vial contains 50 mg doxorubicin hydrochloride.

- The inactive ingredients are sodium chloride and water for injection.

What DOXORUBICIN FRESENIUS looks like and contents of the pack

DOXORUBICIN FRESENIUS is a clear red solution, filled in clear glass vial when examined under suitable conditions of visibility it should be free from particles.

DOXORUBICIN 10 mg/5 mL FRESENIUS**:** 10 mg is packed in 5 mL clear colourless type I moulded glass vial with 5 mL fill, plugged with bromobutyl grey rubber stoppers with aluminium flip off seal.

Each vial may be shrink wrapped along with a plastic bottom and packaged in a mono-carton.

Not all pack sizes may be marketed.

DOXORUBICIN 50 mg/25 mL FRESENIUS**:** 50 mg is packed in 30 mL clear colourless type I, moulded glass vial with 25 mL fill, plugged with bromobutyl grey rubber stoppers with aluminium flip off seal.

Each vial may be shrink wrapped along with a plastic bottom and packaged in a mono-carton.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

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DOXORUBICIN 50 mg/25 mL FRESENIUS: 48/26/0938

Access to the corresponding Professional Information

The professional information will be printed and packaged with the product.