INSTRUCTION LEAFLET

DOXEL 20 mg concentrate for i.v. infusion vial

Administered intravenously.

Sterile-Apyrogenic

- ***Active ingredient:*** Docetaxel
  Each vial contains 20 mg docetaxel concentrate solution.
- ***Excipients:*** Polysorbate 80, Citric acid
  Solvent: 203.6 mg alcohol 96% (v/v) (alcohol equivalent 191.1 mg) and 1.5 ml sufficient amount of water for injection

Read this INSTRUCTION LEAFLET carefully before you start using this medicine, because it contains important information for you.

- *Keep this instruction leaflet. You may need to read it again later.*
- *If you have additional questions, please consult your doctor or pharmacist.*
- *This medicine has been prescribed for you personally, do not give it to others.*
- *If you visit a doctor or hospital during the use of this medicine, tell your doctor that you are using this medicine.*
- *Follow the instructions written in this leaflet exactly. Do not use **high or low doses** other than the recommended dose for the medicine.*

In this Instruction Leaflet:

1. What is DOXEL and what is it used for?

2. Things to consider before using DOXEL

3. How to use DOXEL?

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are included.

1. What is DOXEL and what is it used for?

- DOXEL contains the active ingredient docetaxel. Docetaxel is a substance obtained from the needle-like leaves of the yew tree.
- Each vial of DOXEL contains 20 mg docetaxel. It also contains a solvent vial of 96% ethanol solution in water for injection.
- It is a clear viscous solution, colorless to yellow-brown, administered by intravenous infusion. It is packaged in a protective blister with its solvent, which is a colorless, clear ethanol solution in water for injection.
- DOXEL belongs to a group of medicines called taxoids, used in cancer treatment.
- Your doctor may have prescribed DOXEL for the treatment of breast cancer, specific forms of lung cancer (non-small cell lung cancer), ovarian cancer, head and neck cancer, prostate cancer, and stomach cancer.
- DOXEL can be administered alone or in combination with doxorubicin, trastuzumab, or capecitabine for the treatment of advanced breast cancer.
- DOXEL can be administered in combination with, simultaneously or sequentially after, anthracycline and cyclophosphamide for the treatment of early-stage breast cancer with or without lymph node involvement.
- DOXEL can be administered alone or in combination with cisplatin for the treatment of lung cancer. DOXEL can be administered alone or in combination with platinum-group drugs for the treatment of ovarian cancer.
- DOXEL can be used in combination with prednisone or prednisolone for the treatment of prostate cancer.
- DOXEL can be administered in combination with cisplatin and 5-fluorouracil for the treatment of metastatic stomach cancer.
- DOXEL can be administered alone or in combination with cisplatin and 5-fluorouracil for the treatment of head and neck cancers.

2. Things to consider before using DOXEL

DO NOT USE DOXEL in the following situations:

If;

- You have previously had an allergy to the active substance docetaxel or other excipients contained in the medicine,
- Your white blood cell count is very low,
- You have severe liver disease.

USE DOXEL CAREFULLY in the following situations:

During your treatment with DOXEL, you may experience white blood cell disorders, and associated infection and fever may occur. Therefore, before each DOXEL treatment, blood tests will be performed to determine if you have a sufficient number of blood cells to receive this medicine and if your liver functions are adequate.

Your doctor will take precautions to minimize certain undesirable effects that may occur after DOXEL administration, especially allergic reactions and fluid retention (such as swelling in hands, feet, and legs or weight gain). For this reason, you will be asked to start pre-treatment with an orally administered corticosteroid such as dexamethasone one day before DOXEL administration and to continue taking this medicine for one or two days after DOXEL administration.

During your treatment with DOXEL, your doctor may consider it necessary for you to use another medicine (e.g., G-CSF) to maintain your blood cell count.

If vision impairment occurs during your treatment, contact your doctor immediately. If a complete eye examination reveals that you have developed an eye problem called "cystoid macular edema," your doctor may decide to discontinue DOXEL treatment.

During your treatment, swelling, peeling, and redness may appear on your palms and soles. In this case, your doctor may decide to discontinue treatment or temporarily interrupt treatment.

During your treatment, respiratory problems may arise or existing problems may worsen. In this case, your doctor will perform the necessary examinations and treatments and may decide to discontinue treatment or temporarily interrupt treatment.

Before starting and during your DOXEL treatment, regular blood tests will be performed to assess your liver functions. If the values are above a certain limit, your doctor may reduce your treatment dose or stop the treatment.

DOXEL can affect nerves (peripheral sensory neuropathy). During your treatment, you may experience taste disturbance, tingling, and numbness in your fingers and/or toes, around your mouth, or in your throat, sometimes accompanied by cramps. Report such symptoms to your doctor; the dose of the medicine may need to be reduced.

During your treatment, heart failure may occur. Since your risk of heart failure increases when your medicine is used with trastuzumab, your doctor will want to regularly monitor your heart functions.

During your treatment, gastrointestinal problems such as abdominal pain and tenderness, fever, and diarrhea may occur, especially in the early stages. Immediately report such symptoms to your doctor so that necessary evaluation and treatment can be provided.

If these warnings apply to you at any time in the past, please consult your doctor.

Using DOXEL with food and drink

Insufficient data.

Pregnancy

Consult your doctor or pharmacist before using the medicine. If you are pregnant, DOXEL should not be administered to you unless specified by your doctor.

Since DOXEL can harm the unborn baby, you should not become pregnant during your treatment and should use an appropriate method of contraception.

If you are a male receiving DOXEL treatment, it is recommended that you do not father a child for up to 6 months after treatment and that you obtain information about sperm preservation methods before treatment, as docetaxel may affect male reproductive ability.

If you realize that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Breastfeeding

Consult your doctor or pharmacist before using the medicine. You should not breastfeed your baby while you are receiving DOXEL treatment.

Driving and using machines

There is no harm in driving between DOXEL courses. However, if you feel dizzy/light-headed or unsure of yourself, do not drive.

Important information about some excipients in DOXEL

This medicinal product contains approximately 12% v/v ethanol (alcohol) in its premix solution; for example, each 1 ml solution contains 0.096 g (0.12 ml) ethanol. This amount is equivalent to the alcohol in 2.4 ml of beer or 1 ml of wine. It may be harmful for those suffering from alcoholism. This should be taken into account for pregnant or breastfeeding women, children, and high-risk patients such as those with liver disease or epilepsy.

Using with other medicines

Since there may be interactions between DOXEL and other medicines, do not use any other medical treatment without consulting your doctor, as DOXEL or other medicines you are taking may not show the expected effect or your likelihood of experiencing side effects may increase.

If you are currently using or have recently used any prescription or over-the-counter medicine, please inform your doctor or pharmacist about them.

3. How to use DOXEL?

DOXEL will be administered to you by specialist healthcare personnel.

Instructions for proper use and dose/frequency of administration

The administered dose will vary according to your weight and general condition. Your doctor will calculate your body surface area in square meters (m^2) and determine the dose you need to receive.

Route and method of administration

DOXEL will be given to you by infusion into one of your veins. The infusion will last approximately one hour and will be administered in the hospital.

Frequency of administration:

The usual frequency of your DOXEL infusions will be once every 3 weeks.

Your doctor may change your DOXEL dose and frequency of administration based on your blood test results, general condition, and response to the medicine.

Please inform your doctor, especially if you have symptoms such as diarrhea, mouth sores, drowsiness or tingling sensation, and fever, and provide your blood test results to your doctor. This information will help your doctor decide whether a dose reduction is necessary. If you have any other questions about the use of this product, ask your doctor or pharmacist.

Different age groups

Use in children:

DOXEL is not used in children under 18 years of age.

Use in the elderly:

There are no specific instructions for the use of DOXEL in the elderly.

Special use cases:

Use in patients with liver failure:

Your physician may adjust the dose if deemed necessary, based on the results of liver function tests.

Use in patients with kidney failure: Insufficient data available.

If you have the impression that the effect of DOXEL is too strong or too weak, talk to your doctor or pharmacist.

If you have used more DOXEL than you should:

Since DOXEL will be administered to you in a hospital by specialist healthcare personnel, it is unlikely that you will use more than you should.

If you forget to use DOXEL:

Since DOXEL will be administered to you in a hospital by specialist healthcare personnel, it is unlikely that you will forget to use it.

Effects that may occur when treatment with DOXEL is discontinued

Since DOXEL will be administered to you in a hospital by specialist healthcare personnel, it is not possible for you to discontinue it.

4. What are the possible side effects?

Like all medicines, DOXEL may cause side effects in individuals sensitive to the ingredients it contains.

Your doctor will discuss these with you and explain the risks and benefits of your treatment.

Very common: May be seen in more than 1 in 10 patients.
Common: May be seen in 1 to 10 out of 100 patients.
Uncommon: May be seen in 1 to 10 out of 1000 patients.
Rare: May be seen in 1 to 10 out of 10000 patients.
Very rare: May be seen in less than 1 in 10000 patients.
Unknown (cannot be estimated from the available data)

Very common side effects reported with DOXEL administered alone are:

- Decrease in red blood cells or white blood cells
- Hair loss
- Nausea
- Vomiting
- Mouth sores
- Diarrhea
- Fatigue.

The severity of DOXEL's side effects may increase when administered with other chemotherapy drugs.

The following allergic reactions may occur during infusion administered in the hospital. Very common:

- Hot flashes, skin reactions, itching,
- Feeling of tightness in the chest, difficulty breathing,
- Fever or chills,
- Back pain,
- Low blood pressure.

More severe reactions may occur.

Your condition will be closely monitored by hospital staff during treatment. If you experience any of these effects, notify your doctor or nurse immediately.

If you notice any of the following, tell your doctor:

Between DOXEL infusions, any of the following may occur, and their frequency may vary depending on which medicines are co-administered to you.

Very common:

- Infections, decrease in red blood cells (anemia), decrease in white blood cells important for fighting infections, or platelets (thrombocytes) involved in blood clotting
- Fever: If your fever rises, inform your doctor immediately
- Allergic reactions described above
- Loss of appetite (anorexia)
- Insomnia
- Pain in joints or muscles, feeling of numbness or tingling
- Headache
- Change in taste sensation
- Eye inflammation or increased tear secretion
- Swelling due to impaired lymph flow
- Shortness of breath
- Runny nose, inflammation of the throat and nose, cough
- Nosebleed
- Mouth sores
- Stomach disorders including nausea, vomiting, and diarrhea, constipation
- Abdominal pain
- Indigestion
- Temporary hair loss (in most people, hair grows back normally)

- Redness and swelling in the palms or soles; this condition may cause your skin to peel in these areas (this reaction may also occur on the arms, face, or body)
- Discoloration of your nails and separation from the nail bed
- Muscle aches and pains; back pain or bone pain
- Changes in menstrual bleeding or cessation of menstrual bleeding
- Swelling in hands, feet, legs
- Fatigue or flu-like symptoms
- Weight gain or weight loss

Common:

- Oral thrush
- Excessive dehydration (loss of body water)
- Dizziness
- Hearing loss
- Decrease in blood pressure; irregular or fast heartbeats
- Heart failure
- Esophagitis
- Dry mouth
- Difficulty swallowing or pain when swallowing
- Bleeding
- Increase in liver enzymes (regular blood tests are required for this reason)

Uncommon:

- Weakness
- Pain at the injection site, skin reactions, phlebitis (inflammation of the vein) or swelling
- Colitis, enteritis, bowel perforation
- Blood clots

Rare:

- Convulsions, temporary loss of consciousness
- Vision disorders (glare, seeing flashing lights)
- Hearing disorders
- Difficulty breathing due to lung diseases (pneumonia, lung tissue disorders, respiratory failure, pneumonia due to radiotherapy)

Very rare:

- Jaundice
- Chest tightness (may be a symptom of a heart attack)
- Skin rashes with blistering

Unknown:

- Decrease in blood sodium levels, often with dehydration, vomiting, and pneumonia
- Edema occurring inside the eye causing vision impairment (cystoid macular edema)
- Kidney dysfunction, kidney failure (when used with drugs toxic to the kidneys)

If any of these side effects worsen, inform your doctor or pharmacist.

If you experience any side effects not mentioned in this instruction leaflet, inform your doctor or pharmacist.

Reporting of side effects

If you experience any side effects, whether listed in this leaflet or not, talk to your doctor, pharmacist or nurse. You can also report side effects directly to the Turkish Pharmacovigilance Centre (TÜFAM) by clicking on the "Drug Side Effect Notification" icon on www.titck.gov.tr or by calling the side effect notification line 0 800 314 00 08. By reporting side effects, you will contribute to obtaining more information about the safety of the medicine you are using.

5. How to store DOXEL?

Keep DOXEL out of the sight and reach of children, and in its packaging.

Do not use medicines that show precipitation or crystals.

Store DOXEL at room temperature below 25°C. Store in its packaging, protected from light. After reconstitution (premix solution), it can remain in the refrigerator at 2°C - 8°C and at room temperature below 25°C for 8 hours. The infusion solution should be used within 4 hours at room temperature below 25°C.

Use in accordance with the expiry date.

Do not use DOXEL after the expiry date on the packaging.

Do not use DOXEL if you notice any defects in the product and/or its packaging.

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This instruction leaflet was approved on ../../....

You can access detailed and up-to-date information about this medicine by scanning the QR code with a smartphone/tablet or a QR code reader.

THE FOLLOWING INFORMATION IS FOR HEALTHCARE PROFESSIONALS WHO WILL ADMINISTER THIS MEDICINE

DOXEL is an antineoplastic agent, and like other potentially toxic compounds, care must be taken during the manual handling and preparation of DOXEL solutions. Wearing gloves during the procedure is recommended.

If DOXEL concentrate, premix solution, or infusion solution comes into contact with the skin, it should be immediately and thoroughly washed with soap and water. If DOXEL concentrate, premix solution, or infusion solution comes into contact with mucous membranes, it should be immediately and thoroughly washed with water.

Preparation for intravenous administration

a) Preparation of DOXEL Premix Solution (10 mg docetaxel/ml)

If stored in the refrigerator, the required number of DOXEL injectable concentrate vials and diluent vials are removed. The vials are allowed to stand at room temperature below 25°C for 5 minutes.

The entire content of the diluent vial is drawn into a syringe under aseptic conditions by tilting the vial partially and transferred to the DOXEL injectable concentrate vial to prepare the premix solution.

Each premix solution vial is manually rotated for approximately 45 seconds to ensure complete mixing of the concentrate and diluent. Do not shake.

The DOXEL premix solution is allowed to stand for 5 minutes at room temperature below 25°C and checked for homogeneity and clarity (foam may form even after 5 minutes due to Polysorbate 80 in the formulation). The premix solution contains 10 mg/ml docetaxel and should be used immediately after preparation. However, the premix solution is stable for 8 hours in the refrigerator at 2°C and 8°C and at room temperature below 25°C.

b) Preparation of Infusion Solution

More than one premix vial may be required to obtain the dose needed for the patient. Based on the dose required for the patient, expressed in mg, the premix containing 10 mg/ml docetaxel is withdrawn from the necessary number of premix vials using a syringe with an attached needle. For example, for a dose containing 140 mg docetaxel, 14 ml of docetaxel premix solution will be required.

The required amount of DOXEL premix solution is injected into an infusion bag (PVC-free) or bottle containing 250 ml of 0.9% sodium chloride solution or 5% glucose solution.

If a dose higher than 200 mg docetaxel is required, a larger volume of infusion carrier should be used to avoid exceeding a docetaxel concentration of 0.9 mg/ml.

The infusion bag (PVC-free) or bottle is mixed by manual rotation.

The DOXEL infusion solution should be administered aseptically as a 1-hour infusion at room temperature below 25°C and under normal lighting conditions.

As with all parenteral products, DOXEL premix solution or infusion solution should be inspected before use; if precipitation is present, the solution should be discarded.

The infusion solution should be used within 4 hours at room temperature below 25°C. Unused product or waste material should be disposed of in accordance with the "Regulation on the Control of Medicinal Products" and "Regulations on the Control of Packaging and Packaging Waste."