PACKAGE LEAFLET

Package leaflet: Information for the patient

Savene 20 mg/ml powder and solvent for concentrate for solution for infusion
Dexrazoxane

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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See Section 4.

What is in this leaflet

1. What Savene is and what it is used for

Savene contains the active substance dexrazoxane, which acts as an antidote to anti-cancer medicines called anthracyclines.

Most anti-cancer medicines are administered intravenously (into a vein). Occasionally an accident occurs and the medicine is infused outside the vein and into the surrounding tissue or leaks from the vein into the surrounding tissue. This event is called extravasation. It is a serious complication as it can cause severe tissue damage.

Savene is used to treat anthracyline extravasation in adults. It can reduce the amount of tissue damage caused by anthracycline extravasation.

2. What you need to know before you use Savene

Do not use Savene:
- If you are allergic to dexrazoxane or any of the other ingredients of this medicine (listed in section 6)
- If you are planning to become pregnant and do not use adequate contraceptive measures
- If you are breast-feeding
- If you are given yellow-fever vaccine

Warnings and precautions
Talk to your doctor or nurse before using Savene:
- Savene should only be given to you if you have an extravasation in connection with anthracycline-containing chemotherapy.
- During treatment with Savene the area where the extravasation has occurred will be examined on a regular basis and you will have blood tests taken regularly to check your blood cells.
- If you have liver problems, your doctor will monitor your liver function during treatment.
- If you have kidney problems, your doctor will monitor for signs of changes to your blood cells.

Children and adolescents
Savene should not be administered to children below the age of 18 years.

Other medicines and Savene
Tell your doctor or nurse if you are taking, have recently taken, or might take any other medicines.

In particular, tell your doctor or nurse if you are taking or may take any of the following medicines:
- Vaccines: you must not use Savene if you are going to receive yellow fever vaccine and it is not recommended that you use Savene if you are going to receive a vaccine containing live virus particles.
- A product called DMSO (which is a cream to treat some skin diseases).
- Phenytoin (a treatment against seizures) (Savene may reduce the effectiveness of this medicine).
- Anticoagulants (blood thinners) (your blood may need to be monitored more frequently).
- Ciclosporin or tacrolimus (both treatments lower the body's immune system and are used to prevent organ rejection after an organ transplant).
- Myelosuppressive medicines (decrease production of red, white, or coagulating blood cells).

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 for advice before taking this medicine.
Savene should not be administered if you are pregnant.
You must not breast-feed while you are treated with Savene.
If you are sexually active, you are advised to use effective birth control to prevent pregnancy during and for six months after treatment, whether you are male or female (see section 2 'Do not use Savene').
There is limited information about the effect of Savene on fertility – if you have a concern about this speak to you doctor.

Driving and using machines
Dizziness, tiredness and sudden fainting have been reported in a few patients treated with Savene. The treatment is considered to have a limited influence on the ability to drive and use machines.

Savene contains potassium and sodium
The Savene solvent contains 98 mg potassium in each 500 ml bottle which may be harmful to people on a low-potassium diet or who have kidney problems. If you are at risk of high potassium levels in your blood, your doctor will monitor this.
Savene solvent also contains 1.61 g sodium (main component of cooking/table salt) in each 500 ml bottle. This is equivalent to 81% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Savene

Savene will be given to you under the control of a doctor experienced in the use of anti-cancer treatments.

Recommended dose
The dose will depend on your height, weight and kidney function. Your doctor will calculate your body surface area in square meter (m^2) to determine the dose you should receive. The recommended adult dose (with normal kidney function) is:

Day 1: 1000 mg/m^2
Day 2: 1000 mg/m^2
Day 3: 500 mg/m^2

Your doctor may reduce your dose if you have kidney problems.
Savene will be given by infusion into one of your veins. The infusion will last 1-2 hours.

Frequency of administration
You will receive your infusion once daily for 3 consecutive days. The first infusion will be given as soon as possible and within the first six hours after extravasation of an anthracycline medicine. Savene infusion will be given at the same time every day of your treatment.
Savene will not be used again at the time of your next anthracycline cycle, except if extravasation occurs again.

If you receive more Savene than you should
If you receive more Savene than you should, you will be closely monitored with specific attention to your blood cells, potential gastro-intestinal signs, skin reactions and hair loss.

If Savene comes into contact with the skin, the affected area should immediately be rinsed thoroughly with water.

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.

Some side effects can be serious and need immediate medical attention.
The following serious side effect has been reported in patients during treatment with Savene (frequency not known):
- Allergic reactions, symptoms of which could be itching (pruritis), rash, facial/throat swelling, wheezing, breathlessness or difficult breathing, changes in levels of consciousness, hypotension, sudden fainting

If you get any of the above symptoms, seek medical advice immediately.

Other possible side effects are listed below:

Very common: may affect more than 1 in 10 people
- Nausea
- Reactions at the site of injection (pain at the site, red, swollen or painful skin at the site or hardening of the skin at the site)
- Reduction in the number of white blood cells and platelets
- Infection (after an operation or other infections)

Common: may affect up to 1 in 10 people
- Vomiting
- Diarrhoea
- Feeling tired, feeling sleepy, feeling dizzy, sudden fainting
- Reduction in any of your senses (sight, smell, hearing, touch, taste)
- Fever
- Inflammation of the blood vessel where the treatment is given (phlebitis)
- Inflammation of a blood vessel just under the skin, often with a small blood clot
- Blood clot in the vein, usually in an arm or leg
- Inflammation in the mouth
- Dry mouth
- Hair loss
- Itching (pruritus)
- Weight loss, loss of appetite
- Muscle pain, tremor (uncontrolled muscle movement)
- Vaginal bleeding
- Difficulties in breathing

- Pneumonia (lung infection)
- Swelling in arms or legs (oedema)
- Wound complications
- Changes in liver function (these may be seen in test results)

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Savene

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 carton, powder vial label, and solvent bottle label after 'EXP'. The expiry date refers to the last day of that month.

Store below 25 °C.
Keep the powder vials and solvent bottles in the outer carton in order to protect from light.

6. Contents of the pack and other information

What Savene contains
- The active substance is dexrazoxane. Each vial contains 500 mg dexrazoxane as 589 mg dexrazoxane hydrochloride.
- The other ingredient(s) are: The solvent which contains sodium chloride, potassium chloride, magnesium chloride hexahydrate, sodium acetate trihydrate, sodium gluconate, sodium hydroxide and water for injections.

What Savene looks like and contents of the emergency kit
The Savene kit consists of Savene powder for concentrate (white to off-white powder) and Savene solvent. One emergency kit contains 10 vials of Savene powder and 3 bottles of Savene solvent supplied with 3 bottle hangers.

The concentration of dexrazoxane following reconstitution with 25 ml Savene solvent is 20 mg/ml. The concentrate is slightly yellow.

Marketing Authorisation Holder and Manufacturer

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The following information is intended for healthcare professionals only.

Preparation guide for use with Savene 20 mg/ml powder and solvent for concentrate for solution for infusion

It is important that you read the entire content of this procedure prior to the preparation of Savene.

1. FORMULATION

Savene is supplied as:
1. Savene powder for concentrate
2. Solvent for Savene

Savene powder must be reconstituted in 25 ml Savene solvent to obtain a concentrate that must be further diluted in the remaining Savene solvent prior to administration.

2. RECOMMENDATION FOR THE SAFE HANDLING

Savene is an anti-cancer agent and the normal procedures for proper handling and disposal of anti-cancer medicines should be adopted, namely:
- Personnel should be trained to reconstitute the medicine
- Pregnant staff should be excluded from working with this medicine
- Personnel handling this medicine during reconstitution should wear protective clothing including mask, goggles and gloves
- Accidental contact with the skin or eyes should be treated immediately and thoroughly with copious amounts of water

3. PREPARATION FOR THE INTRAVENOUS ADMINISTRATION

3.1 Reconstitution of Savene powder to prepare a concentrate

3.1.1 Using a syringe fitted with a needle, withdraw aseptically 25 ml from the Savene solvent bottle.
3.1.2 Inject the entire contents of the syringe into the vial containing the Savene powder.
3.1.3 Remove the syringe and needle and mix manually by repeated inversions until the powder is fully dissolved. Do not shake.
3.1.4 Allow the vial with the concentrate to stand for 5 minutes at room temperature and check if the solution is homogenous and clear. The concentrate is slightly yellow.
The concentrate contains 20 mg dexrazoxane per ml and should be used immediately for further dilution. It contains no antibacterial preservative.
3.1.5 Keep and store the opened solvent bottle under aseptic conditions because it is needed for dilution of the concentrate.

3.2 Dilution of the concentrate

3.2.1 Up to four vials containing Savene concentrate may be necessary to obtain the required dose for the patient. Based on the required dose for the patient expressed in mg, withdraw aseptically the corresponding volume containing 20 mg dexrazoxane per ml from the appropriate number of vials containing concentrate. Use a graduated syringe filled with a needle.
3.2.2 Inject the required volume back into the opened Savene solvent bottle (see point 3.1.5). The solution must not be mixed with any other medicines.
3.2.3 Mix the solution by agitating gently the infusion bottle.
3.2.4 Savene should be administered aseptically as a 1-2 hours infusion under room temperature and normal light conditions.
3.2.5 As with all parenteral products, Savene concentrate and infusion solution should be inspected visually for particulate matter and discoloration prior to administration. Solutions containing a precipitate should be discarded.

4. STORAGE

4.1 Before reconstitution and dilution:

- Store below 25 °C.
- Keep the powder vials and solvent bottles in the outer carton in order to protect from light.

4.2 After reconstitution and dilution:

- Chemical and physical in-use stability after reconstitution and subsequent dilution in the solvent has been demonstrated for 4 hours when stored at 2 to 8 °C.
- In order to avoid the potential contamination of the medicine by microbes, the product should be used immediately.
- If the medicine is not used immediately, it should be kept at a temperature of 2 to 8 °C (in the refrigerator) and no longer than 4 hours.

5. DISPOSAL

All items for preparation, administration or cleaning, including gloves, as well as liquid waste should be disposed of in accordance with local requirements.