Package leaflet: Information for the user

Doxorubicin pegylated liposomal SUN 2 mg/ml concentrate for solution for infusion
pegylated liposomal 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.
- 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 Doxorubicin pegylated liposomal SUN is and what it is used for

Doxorubicin pegylated liposomal SUN is an antitumour agent.

Doxorubicin pegylated liposomal SUN is used to treat cancer of the breast in patients at risk for heart problems. Doxorubicin pegylated liposomal SUN is also used to treat cancer of the ovary. It is used to kill cancer cells, shrink the size of the tumour, delay the growth of the tumour, and extend your survival. Doxorubicin pegylated liposomal SUN is also used in combination with another medicine, bortezomib, to treat multiple myeloma (a cancer of the blood) in patients who have received at least 1 prior therapy. Doxorubicin pegylated liposomal SUN is also used to produce an improvement in your Kaposi's sarcoma including flattening, lightening and even shrinkage of the cancer. Other symptoms of Kaposi's sarcoma, such as swelling around the tumour, may also improve or disappear.

Doxorubicin pegylated liposomal SUN contains a medicine which is able to interact with cells in such a way as to selectively kill cancer cells. The doxorubicin hydrochloride in Doxorubicin pegylated liposomal SUN is enclosed in tiny spheres called pegylated liposomes which help to deliver the medicinal product from the blood stream to the cancerous tissue rather than healthy normal tissue.

2. What you need to know before you use Doxorubicin pegylated liposomal SUN

Do NOT use Doxorubicin pegylated liposomal SUN
- if you are allergic to doxorubicin hydrochloride, peanut or soya, or any of the ingredients of this medicine (listed in section 6).

Warnings and precautions
You should tell your doctor about any of the following
- if you are receiving any treatment for heart disease or liver disease
- if you are diabetic, because Doxorubicin pegylated liposomal SUN contains sugar which may require an adjustment to the treatment of your diabetes
- if you have Kaposi's sarcoma and have had your spleen removed

- if you notice sores, discolouration or any discomfort in your mouth.

Children and adolescents
Doxorubicin pegylated liposomal SUN should not be used in children and adolescents, because it is not known how the medicine will affect them.

Other medicines and Doxorubicin pegylated liposomal SUN
Tell your doctor or pharmacist
- if you are taking or have recently taken any other medicines, including medicines obtained without a prescription
- about any other cancer treatments you are on or have been taking, as particular care needs to be taken with treatments which reduce the number of white blood cells, as this may cause further reduction in the number of white blood cells. If you are unsure about what treatments you have received or any illnesses you have had, discuss these with your doctor.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.

Because the active ingredient doxorubicin hydrochloride in Doxorubicin pegylated liposomal SUN may cause birth defects, it is important to tell your doctor if you think you are pregnant. Avoid becoming pregnant while you or your partner are taking Doxorubicin pegylated liposomal SUN and in the six months following discontinuation of Doxorubicin SUN treatment.

Because doxorubicin hydrochloride may be harmful to nursing infants, women must discontinue breast-feeding before starting treatment with Doxorubicin pegylated liposomal SUN. Health experts recommend that HIV infected women do not breast-feed their infants under any circumstances in order to avoid transmission of HIV.

Driving and using machines
Do not drive or use any tools or machines if you feel tired or sleepy from treatment with Doxorubicin pegylated liposomal SUN.

Doxorubicin pegylated liposomal SUN contains soya oil and sodium
This medicinal product contains soya oil. If you are allergic to peanut or soya, do not use this medicine.
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How to use Doxorubicin pegylated liposomal SUN

Doxorubicin pegylated liposomal SUN is a unique formulation. It must not be used interchangeably with other formulations of doxorubicin hydrochloride.

How much Doxorubicin pegylated liposomal SUN is given
If you are being treated for breast cancer or ovarian cancer, Doxorubicin pegylated liposomal SUN will be administered at a dose of 50 mg per square meter of your body surface area (based on your height and weight). The dose is repeated every 4 weeks for as long as the disease does not progress and you are able to tolerate the treatment.

If you are being treated for multiple myeloma, and have already received at least 1 prior therapy, Doxorubicin pegylated liposomal SUN will be administered at a dose of 30 mg per square meter of your body surface area (based on your height and weight) as a 1 hour intravenous infusion on day 4 of the bortezomib 3-week regimen immediately after the bortezomib infusion. The dose is repeated as long as you respond satisfactorily and tolerate treatment.

If you are being treated for Kaposi'sarcoma, Doxorubicin pegylated liposomal SUN will be administered at a dose of 20 mg per square meter of your body surface area (based on your height and weight). The dose is repeated every 2 to 3 weeks for 2-3 months, then as often as necessary to maintain an improvement in your condition.

How Doxorubicin pegylated liposomal SUN is given
Doxorubicin pegylated liposomal SUN will be given to you by your doctor in a drip (infusion) into a vein. Depending on the dose and indication, this may take from 30 minutes to more than one hour (i.e., 90 minutes).

If you use more Doxorubicin pegylated liposomal SUN than you should
Acute overdosing worsens side effects like sores in the mouth or decreases the number of white blood cells and platelets in the blood. Treatment will include administration of antibiotics, platelet cell transfusions, use of factors which stimulate production of white blood cells and symptomatic treatment of mouth sores.

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

4. Possible side effects

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

During the infusion of Doxorubicin pegylated liposomal SUN, the following reactions may occur:
- severe allergic reaction that may include a swollen face, lips, mouth, tongue or throat, difficulty swallowing or breathing, itchy rash (hives)
- inflamed and narrowed airways in the lungs, causing coughing, wheezing and shortness of breath (asthma)
- flushing, sweating, chills or a fever
- chest pain or discomfort
- back pain
- high or low blood pressure
- fast heart beat
- fits (seizures)

Leaking of the injection fluid from the veins into the tissues under the skin may occur. If the drip stings or hurts while you are receiving a dose of Doxorubicin pegylated liposomal SUN, **tell your doctor immediately.**

Your doctor should be contacted immediately if any of the following serious side effects are noticed**:**
- you develop fever, feel tired, or if you have signs of bruising or bleeding (very common)
- redness, swelling, peeling or tenderness, mainly on the hands or feet ('hand-foot' syndrome). These effects have been seen very commonly and are sometimes severe. In severe cases, these effects may interfere with certain daily activities, and may last for 4 weeks or longer before resolving completely. The doctor may wish to delay the start and/or reduce the dose of the next treatment (see Strategies to prevent and treat hand foot syndrome, below)
- sores in mouth, severe diarrhoea or vomiting or nausea (very common)
- infections (common), including lung infections (pneumonia) or infections that may affect your vision
- being short of breath (common)
- severe stomach pain (common)
- severe weakness (common)
- severe allergic reaction that may include a swollen face, lips, mouth, tongue or throat; difficulty swallowing or breathing; itchy rash (hives) (uncommon)

- cardiac arrest (heart stops beating); heart failure, in which the heart does not pump enough blood to the rest of the body, which makes you short of breath and may lead to swollen legs (uncommon)
- blood clot that moves to the lungs, causes chest pain and makes you short of breath (uncommon)
- swelling, warmth, or tenderness in the soft tissues of your leg, sometimes with pain which gets worse when you stand or walk (rare)
- severe or life-threatening rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome) or over most of the body (toxic epidermal necrolysis) (rare).

Other side effects
Between infusions, the following may occur:

Very common side effects (may affect more than 1 in 10 people)
- decrease in the number of white blood cells, which can increase the chances of infections. In rare cases, having low white blood cells may lead to severe infection. Anaemia (reduction in red blood cells) may cause tiredness, and decreased platelets in the blood may increase the risk of bleeding. It is because of the potential changes in your blood cells that you will have regular blood tests.
- decreased appetite;
- constipation;
- skin rashes, including redness of the skin, allergic skin rash, red or raised rash on the skin
- hair loss
- pain including in the muscles and chest muscle, joint, arm, or leg
- feeling very tired

Common side effects (may affect up to 1 in 10 people)
- infections, including severe infection throughout the body (sepsis), lung infections, herpes zoster virus infections (shingles), a type of bacterial infection (mycobacterium avium complex infection), urinary tract infection, fungal infections (including thrush and oral thrush in the mouth) infection of the hair roots, infected or irritated throat, infected nose, sinuses or throat (cold)
- low number of a type of white blood cell (neutrophils), with a fever
- severe weight loss and muscle wasting, not enough water in the body (dehydration), low level of potassium, sodium, or calcium in the blood
- feeling confused, feeling anxious, depression, difficulty sleeping
- nerve damage that may cause tingling, numbness, pain or loss of pain sensation, nerve pain, unusual feeling in the skin (such as tingling or a crawling feeling), decreased feeling or sensitivity, especially in the skin
- change in sense of taste, headache, feeling very sleepy with low energy, feeling dizzy;
- inflamed eyes (conjunctivitis)
- fast heart beat
- high or low blood pressure, flushing
- shortness of breath that may be brought on by physical activity, nose bleeds, cough
- inflamed stomach lining or foodpipe, ulcers (sores) in the mouth, indigestion, difficulty swallowing, mouth pain, dry mouth
- skin problems, including flaky or dry skin, redness of the skin, blister or ulcer (sore) on the skin, itching, dark skin patches
- excessive sweating
- muscle spasms or aches
- pain including in the muscles, bone, or back
- pain when passing urine

- allergic reaction to infusion of the medicine, flu-like illness, chills, inflamed lining of the cavities and passages in the body, such as the nose, mouth or windpipe, feeling weak, generally feeling unwell, swelling caused by fluid build up in the body, swollen hands, ankles or feet
- weight loss.

When Doxorubicin pegylated liposomal SUN is used alone, some of these effects are less likely to occur, and some have not occurred at all.

Uncommon side effects (may affect up to 1 in 100 people)
- herpes simplex virus infections (cold sores or genital herpes), fungal infection
- low number of all types of blood cells, increased number of 'platelets' (cells that help blood to clot)
- allergic reaction
- high level of potassium in the blood, low level of magnesium in the blood
- nerve damage affecting more than one area of the body
- fits (seizures), fainting
- unpleasant or painful sensation, especially to touch, feeling sleepy
- blurred vision, watery eyes
- heart beat feels fast or uneven (palpitations), heart muscle disease, heart damage
- tissue damage (necrosis) where the injection is given, inflamed veins that cause swelling and pain, feeling dizzy upon sitting up or standing up
- chest discomfort
- passing wind, inflamed gums (gingivitis)
- skin problems or rashes, including flaky or peeling skin, allergic skin rash, ulcer (sore) or hives on the skin, discoloured skin, change in the natural colour (pigment) of the skin, small red or purple spots caused by bleeding under the skin, nail problems, acne
- muscle weakness
- breast pain
- irritation or pain where the injection is given
- swollen face, high body temperature
- symptoms (such as inflammation, redness or pain) come back at a part of the body that previously received radiation therapy or was previously damaged by a chemotherapy injection into a vein.

Rare side effects (may affect up to 1 in 1,000 people)
- infection that occurs in people with a weak immune system
- low number of blood cells made in the bone marrow
- inflamed retina, which may cause changes in vision or blindness
- abnormal heart rhythm, abnormal heart tracing on an ECG (electrocardiogram) and may be with a slow heart beat, problem with the heart that affects the heart beat and rhythm, blue colour to the skin and mucosa caused by low oxygen in the blood
- widening of blood vessels
- tight feeling in the throat
- sore and swollen tongue, ulcer (sore) on the lip
- skin rash with fluid-filled blisters
- vaginal infection, redness of the scrotum
- problems with the lining of the cavities and passages in the body, such as the nose, mouth or windpipe
- abnormal liver blood test results, increased level of 'creatinine' in the blood.

Not known (frequency cannot be estimated from the available data)
- cancer of the blood that develops quickly and affects the blood cells (acute myeloid leukaemia), bone marrow disease that affects the blood cells (myelodysplastic syndrome), cancer of the mouth or lip.

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 the Yellow Card Scheme at: 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.

Strategies to prevent and treat hand-foot syndrome include:
- soaking hands and/or feet in basins of cold water when possible (e.g., while watching television, reading, or listening to the radio)
- keeping hands and feet uncovered (no gloves, socks, etc.)
- staying in cool places
- taking cool baths during hot weather
- avoiding vigorous exercise that might cause trauma to the feet (e.g., jogging)
- avoiding exposure of the skin to very hot water (e.g., jacuzzis, saunas)
- avoiding tight fitting footwear or high-heeled shoes

Pyridoxine (Vitamin B6):
- vitamin B6 is available without prescription;
- take 50-150 mg daily beginning at the first signs of redness or tingling.

5. How to store Doxorubicin pegylated liposomal SUN

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

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

After dilution:
Chemical and physical in-use stability has been demonstrated for 24 hours at 2°C to 8°C. 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 should not be longer than 24 hours at 2°C to 8°C. Partially used vials must be discarded.

Do not use this medicine after the expiry date which is stated on the label and carton.

Do not use this medicine if you notice that it shows evidence of precipitation or any other particulate matter.

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 pegylated liposomal SUN contains
- The active substance is doxorubicin hydrochloride. One ml of Doxorubicin pegylated liposomal SUN contains 2 mg of doxorubicin hydrochloride in a pegylated liposomal formulation.
- The other ingredients are α-(2-[1.2 distearoyl-*sn*-glycero(3)phosphooxy]ethylcarbamoyl)-ω-methoxypoly(oxyethylen)-40 sodium salt (MPEG-DSPE), fully hydrogenated soy phosphatidylcholine (HSPC), cholesterol, sucrose, histidine, water for injection, hydrochloric acid (E507) (for pH adjustment), sodium hydroxide (E524) (for pH adjustment).

What Doxorubicin pegylated liposomal SUN looks like and contents of the pack

Doxorubicin pegylated liposomal SUN concentrate for solution for infusion: vials which provide 10 ml (20 mg) or 25 ml (50 mg).
The solution for infusion is sterile, translucent and red. Doxorubicin pegylated liposomal SUN is available in glass vials as a single pack or packs of ten vials. Vials are with or without a plastic protection (e.g. sleeving, oncosafe).

Not all pack sizes may be marketed.

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This leaflet was last revised in 09/2024.

The following information is intended for medical or healthcare professionals only

INFORMATION FOR THE HEALTHCARE PROFESSIONALS

Please see the Summary of Product Characteristics for more information.

Caution must be exercised in handling Doxorubicin pegylated liposomal SUN solution for infusion. The use of gloves is required. If Doxorubicin pegylated liposomal SUN comes into contact with skin or mucosa, wash immediately and thoroughly with soap and water. Doxorubicin SUN must be handled and disposed of in a manner consistent with that of other anticancer medicinal products.

Determine the dose of Doxorubicin pegylated liposomal SUN to be administered (based upon the recommended dose and the patient's body surface area). Take the appropriate volume of Doxorubicin pegylated liposomal SUN up into a sterile syringe. Aseptic technique must be strictly observed since no preservative or bacteriostatic agent is present in Doxorubicin pegylated liposomal SUN. The appropriate dose of Doxorubicin pegylated liposomal SUN must be diluted in 5% (50 mg/ml) glucose solution for infusion prior to administration. For doses < 90 mg, dilute Doxorubicin pegylated liposomal SUN in 250 ml, and for doses ≥ 90 mg, dilute Doxorubicin pegylated liposomal SUN in 500 ml.

To minimise the risk of infusion reactions, the initial dose is administered at a rate no greater than 1 mg/minute. If no infusion reaction is observed, subsequent Doxorubicin pegylated liposomal SUN infusions may be administered over a 60-minute period.

In the breast cancer trial program, modification of the infusion was permitted for those patients experiencing an infusion reaction as follows: 5% of the total dose was infused slowly over the first 15 minutes. If tolerated without reaction, the infusion rate was doubled for the next 15 minutes. If tolerated, the infusion was completed over the next hour for a total infusion time of 90 minutes.

If the patient experiences early symptoms or signs of infusion reaction, immediately discontinue the infusion, give appropriate premedications (antihistamine and/or short acting corticosteroid) and restart at a slower rate.

The use of any diluent other than 5% (50 mg/ml) glucose solution for infusion, or the presence of any bacteriostatic agent such as benzyl alcohol may cause precipitation of Doxorubicin pegylated liposomal SUN.

It is recommended that the Doxorubicin pegylated liposomal SUN infusion line be connected through the side port of an intravenous infusion of 5% (50 mg/ml) glucose. Infusion may be given through a peripheral vein. Do not use with in-line filters.