Package Leaflet: Information for the patient

Gemcitabine 1000 mg, powder for solution for infusion

gemcitabine

Read all of this leaflet carefully before you start taking 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 Gemcitabine is and what it is used for

Gemcitabine belongs to a group of medicines called "cytotoxics". These medicines kill dividing cells, including cancer cells.

Gemcitabine may be given alone or in combination with other anti-cancer medicines, depending on the type of cancer.

Gemcitabine is used in the treatment of the following types of cancer:
- non-small cell lung cancer (NSCLC), alone or together with cisplatin
- pancreatic cancer
- breast cancer, together with paclitaxel
- ovarian cancer, together with carboplatin
- bladder cancer, together with cisplatin.

2. What you need to know before you are given Gemcitabine

You should not be given Gemcitabine
- if you are allergic to gemcitabine or any of the other ingredients of this medicine (listed in section 6)
- if you are breast-feeding

Warnings and precautions
Talk to your doctor before you are given Gemcitabine.
Before the first infusion you will have samples of your blood taken to evaluate if you have sufficient kidney and liver function. Before each infusion you will have samples of your blood taken to evaluate if you have enough blood cells to receive Gemcitabine. Your doctor may decide to change the dose or delay treating you depending on your general condition and if your blood cell counts are too low. Periodically you will have samples of your blood taken to evaluate your kidney and liver function.

Please tell your doctor if
- you have, or have previously had liver disease, heart disease, vascular disease or problems with your kidneys as you may not be able to receive Gemcitabine
- you have recently had, or are going to have radiotherapy as there may be an early or late radiation reaction
- you have been vaccinated recently
- you get symptoms such as headache with confusion, seizures (fits) or changes in vision, call your doctor right away. This could be a very rare nervous system side effect named posterior reversible encephalopathy syndrome
- you develop breathing difficulties or feel very weak and are very pale (may be a sign of kidney failure or problems with your lungs)
- you develop generalised swelling, shortness of breath or weight gain, as this may be a sign of fluid leaking from your small blood vessels into the tissue
- you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using gemcitabine.

Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis and acute generalized exanthematous pustulosis (AGEP) have been reported in association with gemcitabine treatment. Seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section.

Children and adolescents
This medicine is not recommended for use in children under 18 years of age due to insufficient data on safety and efficacy.

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

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. The use of Gemcitabine should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking Gemcitabine during pregnancy.

You must discontinue breast-feeding during Gemcitabine treatment.

Men are advised not to father a child during and up to 6 months following treatment with Gemcitabine. If you would like to father a child during the treatment or in the 6 months following treatment, seek advice from your doctor or pharmacist. You may want to seek counselling on sperm storage before starting your therapy.

Driving and using machines
Gemcitabine may make you feel sleepy, particularly if you have consumed any alcohol. Do not drive a car or use machinery until you are sure that Gemcitabine treatment has not made you feel sleepy.

Gemcitabine contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially ‘sodium-free’.

3. How Gemcitabine is given

The recommended dose of Gemcitabine is 1000-1250 mg for every square metre of your body's surface area. Your height and weight are measured to work out the surface area of your body. Your doctor will

use this body surface area to work out the right dose for you. This dosage may be adjusted, or treatment may be delayed depending on your blood cell counts and on your general condition.

How frequently you receive your Gemcitabine infusion depends on the type of cancer that you are being treated for.

A hospital pharmacist or doctor will have dissolved the Gemcitabine powder before it is given to you.

You will always receive Gemcitabine by infusion into one of your veins. The infusion will last approximately 30 minutes.

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

4. Possible side effects

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

You must contact your doctor immediately if you notice any of the following:

Extreme tiredness and weakness, purpura or small areas of bleeding in the skin (bruises), acute renal failure (low urine output or no urine output), and signs of infection. These may be features of thrombotic microangiopathy (clots forming in small blood vessels) and haemolytic uraemic syndrome, which may be fatal.

A red, scaly widespread rash with bumps under the swollen skin (including your skin folds, trunk, and upper extremities) and blisters accompanied by fever (Acute Generalized Exanthematous Pustulosis (AGEP)) (frequency not known).

Tell your doctor about any of the following serious side-effects straight away

Very common: may affect more than 1 in 10 users
- allergic reactions: if you develop mild to moderate skin rash, or fever
- tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have less haemoglobin than normal which is very common)
- bleeding from the gums, nose or mouth or any bleeding that would not stop, reddish or pinkish urine, unexpected bruising (since you might have less platelets than normal which is very common).

Common: may affect up to 1 in 10 users
- temperature of 38°C or greater, sweating or other signs of infection (since you might have less white blood cells than normal accompanied by fever also known as febrile neutropenia)
- pain, redness, swelling or sores in your mouth (stomatitis)
- allergic reactions: if you develop itching
- difficulty breathing (it is common to have mild breathing difficulty soon after the Gemcitabine infusion which soon passes).

Uncommon: may affect up to 1 in 100 users
- difficulty breathing (more severe lung problems)
- irregular heart rate (arrhythmia).

Rare: may affect up to 1 in 1,000 users
- difficulty breathing (more severe lung problems)
- severe chest pain (myocardial infarction).

Very rare: may affect up to 1 in 10,000 users

- severe hypersensitivity/allergic reaction with severe skin rash including red itchy skin, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), wheezing, fast beating heart and you may feel you are going to faint (anaphylactic reaction)
- generalised swelling, shortness of breath or weight gain, as you might have fluid leakage from small blood vessels into the tissues (capillary leak syndrome)
- headache with changes in vision, confusion, seizures or fits (posterior reversible encephalopathy syndrome)
- severe rash with itching, blistering or peeling of the skin (Stevens-Johnson syndrome, toxic epidermal necrolysis).

Tell your doctor about any of the following side effects as soon as possible

Very common: may affect more than 1 in 10 users
- low white blood cells
- difficulty breathing
- vomiting
- nausea
- hair loss
- liver problems: found through abnormal blood test results
- blood in urine
- abnormal urine tests: protein in urine
- flu like symptoms including fever
- swelling of ankles, fingers, feet, face (oedema).

Common: may affect up to 1 in 10 users
- poor appetite (anorexia)
- headache
- insomnia
- sleepiness
- cough
- runny nose
- constipation
- diarrhoea
- itching
- sweating
- muscle pain
- back pain
- fever
- weakness
- chills
- infections.

Uncommon: may affect up to 1 in 100 users
- scarring of the air sacs of the lung (interstitial pneumonitis)
- wheeze (spasm of the airways)
- scarring of the lungs (abnormal chest X ray/scan)
- heart failure
- kidney failure
- serious liver damage, including liver failure
- stroke.

Rare: may affect up to 1 in 1,000 users
- low blood pressure
- skin scaling, ulceration or blister formation

- sloughing of skin and severe skin blistering
- injection site reactions
- severe lung inflammation causing respiratory failure (adult respiratory distress syndrome)
- a skin rash like severe sunburn which can occur on skin that has previously been exposed to radiotherapy (radiation recall)
- fluid in the lungs
- scarring of the air sacs of the lung associated with radiation therapy (radiation toxicity)
- gangrene of fingers or toes
- inflammation of the blood vessels (peripheral vasculitis).

Very rare: may affect up to 1 in 10,000 users
- increased platelet count
- inflammation of the lining of the large bowel, caused by reduced blood supply (ischaemic colitis)
- low haemoglobin level (anaemia), low white blood cells and low platelet count will be detected by a blood test
- clots forming in small blood vessels (thrombotic microangiopathy).

Not known (cannot be estimated from the available data)
- sepsis: when bacteria and their toxins circulate in the blood and start to damage the organs
- skin redness with swelling (pseudocellulitis)
- a condition where eosinophils, a type of cell ordinarily found in the blood, accumulate in the lungs (pulmonary eosinophilia).

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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.

5. How to store Gemcitabine

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 vial and carton. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

After reconstitution:
Chemical and physical in-use stability has been demonstrated for 24 hours at 15-30°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 would normally not be longer than 24 hours at 30°C.

The reconstituted solution should not be refrigerated.

Do not use this medicine if you notice a cloudy solution or an insoluble precipitate.

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 **Gemcitabine 1000 mg Powder for Solution for Infusion contains**

- The active substance is: gemcitabine (as hydrochloride)
- The other ingredients are: mannitol, sodium acetate trihydrate, sodium hydroxide, hydrochloric acid.

One vial contains 1 g gemcitabine (as hydrochloride).

One ml of the reconstituted solution for infusion contains 38 mg gemcitabine (as hydrochloride).

What Gemcitabine 1000 mg Powder for Solution for Infusion looks like and contents of the pack

Powder for solution for infusion

White to off-white lyophilized cake.

1 vial of 50 ml.

Marketing Authorisation Holder and Manufacturer
Sun Pharmaceutical Industries Europe BV
Polarisavenue 87
2132 JH Hoofddorp
The Netherlands

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

Germany:	Gemcitabine SUN 1 g Pulver zur Herstellung einer Infusionslösung
Spain:	Gemcitabina SUN 1000 mg polvo para solución para perfusión EFG
Italy:	Gemcitabina SUN 1 g polvere per soluzione per infusione
Netherlands:	Gemcitabine SUN 1000 mg poeder voor oplossing voor infusie
Romania:	Gemcitabină SUN 1 g, pulbere pentru soluţie perfuzabilă
United Kingdom (Northern Ireland):	Gemcitabine 1 g, powder for solution for infusion

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The following information is intended for healthcare professionals only

Instructions for use, handling and disposal.

- Use aseptic techniques during the reconstitution and any further dilution of gemcitabine for intravenous infusion administration.
- Calculate the dose and the number of Gemcitabine vials needed.
- Reconstitute 1000 mg vials with 25 ml sterile sodium chloride solution for injection, without preservative. Shake to dissolve. The total volume after reconstitution is 26.3 ml respectively. This dilution yields a gemcitabine concentration of 38 mg/ml, which includes accounting for the displacement volume of the lyophilised powder. Further dilution with sterile sodium chloride 9 mg/ml (0.9%) solution for injection, without preservative may be done. The resulting solution is clear and ranges in colour from colourless to light straw-coloured.
- Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.
- Solutions of reconstituted gemcitabine should not be refrigerated, as crystallisation may occur. Chemical and physical in-use stability has been demonstrated for 24 hours at 30°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 would normally not be longer than 24 hours at room temperature, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.
- Gemcitabine solutions are for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

Preparation and administration precautions

The normal safety precautions for cytostatic agents must be observed when preparing and disposing of the infusion solution. Handling of the solution for infusion should be done in a safety box and protective coats and gloves should be used. If no safety box is available, the equipment should be supplemented with a mask and protective glasses.
If the preparation comes into contact with the eyes, this may cause serious irritation. The eyes should be rinsed immediately and thoroughly with water. If there is lasting irritation, a doctor should be consulted. If the solution is spilled on the skin, rinse thoroughly with water.

Disposal

Any unused product should be disposed of in accordance with local requirements.