Package leaflet: Information for the patient

Gemcitabine 10 mg/ml, solution for infusion

gemcitabine

Read all of this leaflet carefully before you are given 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, pharmacist or nurse.
- If you get any side effects talk to your doctor, pharmacist or nurse. 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
Before the first infusion you will have samples of your blood taken to check if you have sufficient kidney and liver function. Before each infusion you will have samples of your blood taken to check 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 check your kidney and liver function.

Talk to your doctor before you are given Gemcitabine 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.

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

Pregnancy
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before this medicine is given to you. The use of Gemcitabine should be avoided during pregnancy. Your doctor will discuss with you the potential risk of treatment with Gemcitabine during pregnancy.

Breast-feeding
Tell your doctor if you are breast-feeding. You must discontinue breast-feeding during Gemcitabine treatment.

Fertility
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. 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
One ml of the solution for infusion contains 4.575 mg sodium.

This medicine contains 549.00 mg (23.88 mmol) of sodium (main component of cooking/table salt) in each 120 ml infusion bag. This is equivalent to 27.5% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 594.65 mg (25.87 mmol) of sodium (main component of cooking/table salt) in each 130 ml infusion bag. This is equivalent to 29.7% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 640.50 mg (27.86 mmol) of sodium (main component of cooking/table salt) in each 140 ml infusion bag. This is equivalent to 32% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 686.25 mg (29.85 mmol) of sodium (main component of cooking/table salt) in each 150 ml infusion bag. This is equivalent to 34.3% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 732.00 mg (31.84 mmol) of sodium (main component of cooking/table salt) in each 160 ml infusion bag. This is equivalent to 36.6% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 777.75 mg (33.83 mmol) of sodium (main component of cooking/table salt) in each 170 ml infusion bag. This is equivalent to 38.8% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 823.50 mg (35.82 mmol) of sodium (main component of cooking/table salt) in each 180 ml infusion bag. This is equivalent to 41.2% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 915.00 mg (39.80 mmol) of sodium (main component of cooking/table salt) in each 200 ml infusion bag. This is equivalent to 45.8% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 1006.50 mg (43.78 mmol) of sodium (main component of cooking/table salt) in each 220 ml infusion bag. This is equivalent to 50.3% of the recommended maximum daily dietary intake of sodium for an adult.

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 dose 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.

You will always receive Gemcitabine by infusion (a drip) 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, pharmacist or nurse.

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.

Serious side effects
You must tell your doctor immediately about any of the following serious side effects:

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

Common (may affect up to 1 in 10 people)
- temperature of 38°C or greater, sweating or other signs of infection (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
- mild breathing difficulty (it is common to have mild breathing difficulty soon after the Gemcitabine infusion which soon passes).

Uncommon (may affect up to 1 in 100 people)
- difficulty breathing due to more severe lung problems (interstitial pneumonitis, bronchospasm)
- irregular heart rate (arrhythmia).

Rare (may affect up to 1 in 1,000 people)
- difficulty breathing due to more severe lung problems (pulmonary oedema, adult respiratory distress syndrome)
- severe chest pain (myocardial infarction).

Very rare (may affect up to 1 in 10,000 people)
- 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).

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

Very common (may affect more than 1 in 10 people)
- 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 people)
- 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 people)
- 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 people)
- low blood pressure
- skin scaling, ulceration or blister formation
- sloughing of skin and severe skin blistering
- injection site reactions
- 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 people)
- increased platelet count
- inflammation of the lining of the large bowel, caused by reduced blood supply (ischaemic colitis)
- clots forming in small blood vessels (thrombotic microangiopathy).

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

Low haemoglobin level (anaemia), low white blood cells and low platelet count will be detected by a blood test.

Reporting of side effects

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

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 infusion bag and the outer packaging after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions. Do not refrigerate or freeze.

After opening the infusion bag:
From a microbiological point of view, the solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

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 solution for infusion contains
- The active substance is: gemcitabine (as hydrochloride)
- The other ingredients are: sodium chloride, water for injection, sodium hydroxide and/or hydrochloric acid (for pH adjustment).

One 120 ml infusion bag contains 1200 mg gemcitabine (as hydrochloride).
One 130 ml infusion bag contains 1300 mg gemcitabine (as hydrochloride).
One 140 ml infusion bag contains 1400 mg gemcitabine (as hydrochloride).
One 150 ml infusion bag contains 1500 mg gemcitabine (as hydrochloride).
One 160 ml infusion bag contains 1600 mg gemcitabine (as hydrochloride).
One 170 ml infusion bag contains 1700 mg gemcitabine (as hydrochloride).
One 180 ml infusion bag contains 1800 mg gemcitabine (as hydrochloride).
One 200 ml infusion bag contains 2000 mg gemcitabine (as hydrochloride).
One 220 ml infusion bag contains 2200 mg gemcitabine (as hydrochloride).

One ml of the solution for infusion contains 10 mg gemcitabine.
One ml of the solution for infusion contains 4.575 mg sodium.

What Gemcitabine solution for infusion looks like and contents of the pack

Gemcitabine solution for infusion is a clear, colourless, sterile solution free from visible particulate matter.
Gemcitabine solution for infusion is supplied in carton boxes each containing 1, 5 or 10 single-dose infusion bags of 120 ml, 130 ml, 140 ml, 150 ml, 160 ml, 170 ml, 180 ml, 200 ml or 220 ml.

Not all pack sizes may be marketed.

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

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The following information is intended for healthcare professionals only

Instructions for use, handling and disposal

Handling

- Calculate the dose, and decide which size of the Gemcitabine infusion bags is needed. If the required dose cannot be achieved with the available presentations, use of an alternative gemcitabine product, including gemcitabine as a concentrate or gemcitabine as powder for solution for infusion, is recommended.
- Inspect the product pack for any damage. Do not use if there are signs of tampering.
- Apply patient-specific label on the overwrap.

Removal of infusion bag from overwrap and infusion bag inspection
- Tear overwrap at notch. Do not use if overwrap has been previously opened or damaged.
- Remove infusion bag from overwrap.
- Use only if infusion bag and seal are intact. Prior to administration check for minute leaks by squeezing bag firmly. If leaks are found, discard the bag and solution as sterility may be impaired.
- Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.

Administration
- Break the Minitulipe stopper seal by applying pressure on one side with hand.
- Using aseptic technique, attach sterile administration set.
- Refer to directions for use accompanying the administration set.

Precautions
- Do not use in series connection.
- Do not introduce additives into the infusion bag.
- The solution for infusion is ready to use and must not be mixed with other medicinal products.
- *After opening the infusion bag*:
  From a microbiological point of view, the solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.
- Gemcitabine solution for infusion is for single use only.

Personnel must be provided with appropriate handling materials, notably long sleeved gowns, protection masks, caps, protective goggles, sterile single-use gloves, protective covers for the work area and collection bags for waste.

Cytotoxic preparations should not be handled by pregnant staff.

If the product comes into contact with the eyes, severe irritation may result. In such an event, the eyes should be washed thoroughly and immediately. Consult a doctor if irritation persists. If the solution should come into contact with skin, rinse the affected area thoroughly with water. Excreta and vomit must be handled with care.

Disposal
Any unused medicinal product or waste material should be disposed of in accordance with local requirements for cytotoxic agents.