Package leaflet: Information for the user

Gemcitabine 200 mg Powder for Solution for Infusion
Gemcitabine 1 g Powder for Solution for Infusion
Gemcitabine 2 g Powder for Solution for Infusion

gemcitabine

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, pharmacist or nurse.
- 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, 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 use Gemcitabine

Do not take 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 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.

Talk to your doctor before using Gemcitabine if:
- you have, or have previously had liver disease, heart disease, vascular disease or problems with your kidneys
- you have recently had, or are going to have radiotherapy
- you have been vaccinated recently
- you develop breathing difficulties or feel very weak and are very pale (may be a sign of kidney failure or problems with your lungs).
- during this treatment with this medicine you experience headaches, confusion, seizures (fits), visual disturbances 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 generalised swelling, shortness of breath or weight gain as these may be a sign of fluid leaking from your blood vessels into the tissues.

Children and adolescents
This medicinal product 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 hospital pharmacist if you are taking, have recently taken or might take any other medicines, including vaccinations and medicines obtained without a prescription; or if you have recently undergone radiotherapy or are going to have radiotherapy.

Pregnancy, breast-feeding and fertility
Pregnancy
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. The use of Gemcitabine should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking Gemcitabine during pregnancy.

Breast-feeding
If you are breast-feeding, tell your doctor.
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 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
Gemcitabine contains 3.56 mg (< 1 mmol) of sodium in each 200 mg vial and 17.81 mg (< 1 mmol) sodium in each 1 g vial and 35.62 mg (1.54 mmol) sodium in each 2 g vial. To be taken into consideration by patients on a controlled sodium diet.

3. How to use Gemcitabine

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 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.

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

- Fever or infection (common, may affect up to 1 in 10 people): if you have a temperature of 38ºC or greater, sweating or other signs of infection (since you might have less white blood cells than normal which is very common).
- Irregular heart rate (arrhythmia) (uncommon, may affect up to 1 in 100 people).
- Pain, redness, swelling or sores in your mouth (common, may affect up to 1 in 10 people).
- Allergic reactions: if you develop skin rash (very common, may affect more than 1 in 10 people) / itching (common, may affect up to 1 in 10 people), or fever (very common, may affect more than 1 in 10 people).
- Anaphylactic reaction (severe hypersensitivity/ allergic reaction): 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 (tachycardia) and you may feel you are going to faint (a spontaneous loss of consciousness caused by insufficient blood to the brain) (very rare (may affect up to 1 in 10,000 people)).
- Tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have less haemoglobin than normal which is very common, may affect more than 1 in 10 people).
- 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, may affect more than 1 in 10 people).
- Difficulty breathing (it is very common to have mild breathing difficulty soon after the Gemcitabine infusion which soon passes, however uncommonly or rarely there can be more severe lung problems).
- Heart attack (myocardial infarction) (rare (may affect up to 1 in 1,000 people))
- Haemolytic uraemic syndrome: 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. It may be fatal (uncommon (may affect up to 1 in 100 people)).
- Potentially life-threatening cutaneous reactions (Toxic epidermal necrolysis (TEN), Stevens-Johnson Syndrome (SJS)): severe rash with itching, blistering or peeling of the skin. Skin rashes are often accompanied by flu-like symptoms (very rare, may affect up to 1 in 10,000 people).
- Headaches with changes in vision, confusion, seizures or fits (posterior reversible encephalopathy syndrome) (very rare, may affect up to 1 in 10,000 people).
- Generalised swelling, shortness of breath or weight gain, since you may have fluid leakage from your blood vessels into the tissues (capillary leak syndrome) (very rare, may affect up to 1 in 10,000 people).

Other side effects with Gemcitabine may include:

Very common side effects (may affect more than 1 in 10 people)
Low haemoglobin level (anaemia)
Low white blood cells
Low platelet count
Difficulty breathing
Vomiting
Nausea
Skin rash- allergic skin rash, frequently itchy
Hair loss
Liver problems: found through abnormal blood test results
Blood in urine
Abnormal urine tests: protein in urine
Flu like symptoms including fever
Oedema (swelling of ankles, fingers, feet, face)

Common side effects (may affect up to 1 in 10 people)
Fever accompanied by low white blood cell count (febrile neutropaenia)
Anorexia (poor appetite)
Headache
Insomnia
Sleepiness
Cough
Runny nose
Constipation
Diarrhoea
Pain, redness, swelling or sores in the mouth
Itching
Sweating
Muscle pain
Back pain
Fever
Weakness
Chills

Uncommon side effects (may affect up to 1 in 100 people)
Stroke
Irregular heart beat (arrhythmia)
Heart failure
Interstitial pneumonitis (scarring of the air sacs of the lung)
Spasm of the airways (wheeze)
Abnormal chest X ray/scan (scarring of the lungs)
Serious liver damage, including liver failure which could be life-threatening
Kidney failure
Haemolytic uraemic syndrome (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, it may be fatal)

Rare side effects (may affect up to 1 in 1,000 people)
Heart attack (myocardial infarction)
Low blood pressure
Gangrene of fingers or toes
Fluid in the lungs
Adult Respiratory Distress Syndrome (severe lung inflammation causing respiratory failure)
Skin scaling, ulceration or blister formation
Injection site reactions
Radiation toxicity- scarring of the air sacs of the lung associated with radiation therapy
Radiation recall-(a skin rash like severe sunburn) which can occur on skin that has previously been exposed to radiotherapy.

Very rare side effects (may affect up to 1 in 10,000 people)
Increased platelet count
Anaphylactic reaction (severe hypersensitivity/ allergic reaction)
Ischemic colitis (inflammation of the lining of the large bowel, caused by reduced blood supply)
Sloughing of skin and severe skin blistering (Toxic epidermal necrolysis, Stevens-Johnson Syndrome).
Capillary leak syndrome (leakage of fluid from the blood vessels into the tissue)
Posterior reversible encephalopathy syndrome (a neurologic condition with symptoms including seizures, headache, confusion and changes in vision.

You might have any of these symptoms and/or conditions. You must tell your doctor as soon as possible when you start experiencing any of these side effects.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.
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.

Unopened container
Do not refrigerate or freeze.

Opened container
After opening, the contents should be reconstituted, and if appropriate further diluted, and used immediately. Reconstituted solutions should not be refrigerated, as crystallisation may occur.

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice any signs of particles.

6. Contents of the pack and other information

What Gemcitabine contains

- The active substance is gemcitabine (as hydrochloride). After reconstitution one ml of Gemcitabine contains 38 mg gemcitabine. One vial Gemcitabine contains 200 mg, 1 g or 2 g gemcitabine.

- The other ingredients are mannitol E421, sodium acetate trihydrate and sodium hydroxide 1 N (for pH adjustment)

What Gemcitabine looks like and contents of the pack

Gemcitabine powder for solution for infusion is a white to off-white compact aggregate powder. After reconstitution in 0.9% sodium chloride solution, the solution is clear to pale opalescent and colourless to pale yellow.

Gemcitabine is in colourless glass vials with bromobutylic rubber stopper and sealed with aluminium seals with plastic caps. Each vial will be packed with or without a protective plastic overwrap.

Pack sizes
One vial containing 200 mg gemcitabine.
One vial containing 1 g gemcitabine.
One vial containing 2 g gemcitabine.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Actavis Group PTC ehf.
Reykjavikurvegi 76-78
220 Hafnarfjordur
Iceland

Manufacturers

S.C. Sindan-Pharma S.R.L.
11 Ion Mihalache Blvd.
Bucharest, 011171
Romania

Actavis Italy S.p.A. – Nerviano Plant
Viale Pasteur 10
20014 Nerviano (MI)
Italy

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Gemcitabin Actavis 38 mg/ml Pulver zur Herstellung einer Infusionslösung
Greece	Gemcitabine / Actavis
Ireland	Gemcitabine 200mg powder for solution for infusion
	Gemcitabine 1g powder for solution for infusion
	Gemcitabine 2g powder for solution for infusion
Sweden	Gemcitabin Actavis

This leaflet was last revised in January 2019

The following information is intended for healthcare professionals only:

Instruction for use

Cytotoxic

Handling

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.

Instructions for reconstitution (and further dilution, if performed)

The only approved diluent for reconstitution of gemcitabine sterile powder is sodium chloride 9 mg/ml (0.9%) solution for injection (without preservative). Due to solubility considerations, the maximum concentration for gemcitabine upon reconstitution is 40 mg/ml. Reconstitution at concentrations greater than 40 mg/ml may result in incomplete dissolution and should be avoided.

- Use aseptic technique during the reconstitution and any further dilution of gemcitabine for intravenous infusion administration.

- To reconstitute, add the appropriate volume of sterile sodium chloride 9 mg/ml (0.9%) solution for injection without preservative (as stated in the table below) and shake to dissolve:

Presentation	Volume of sterile sodium chloride 9 mg/ml (0.9%) solution for injection (without preservative) to be added	Total volume after reconstitution	Final concentration
200 mg	5 ml	5.26 ml	38 mg/ml
1 g	25 ml	26.3 ml	38 mg/ml
2 g	50 ml	52.6 ml	38 mg/ml

  Further dilution with sterile sodium chloride 9 mg/ml (0.9 %) solution for injection, without preservative can be done. Reconstituted solution is a clear colourless to light straw-coloured solution.

- Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.

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