Package leaflet: Information for the user

Gemcitabine 38 mg/mL concentrate for solution for infusion

gemcitabine

Read all of this leaflet carefully, before you start receiving this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please 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 – ATC code: L01BC05

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

Gemcitabine may be given on its own or in combination with other anti-cancer medicines (e.g. cisplatin, paclitaxel, carboplatin), depending on the type of cancer you have.

Gemcitabine is used in the treatment of the following types of cancer:

- Non-small cell lung cancer (NSCLC), when given alone or together with cisplatin
- Pancreatic cancer
- Breast cancer, when given together with paclitaxel
- Ovarian cancer, when given together with carboplatin
- Bladder cancer, when given 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).
- you are breast-feeding

Warnings and precautions

Before your first infusion, you will have samples of your blood taken to check how well your kidneys and liver are working. Before each infusion, you will also have blood tests to check if you have enough blood cells to receive gemcitabine.

Your doctor may decide to change your dose or delay treating you, based on your general health or 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 or nurse before you are given gemcitabine if:
- you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using gemcitabine
- you have, or have previously had liver disease, heart disease, or vascular disease
- you have recently had, or are going to have radiotherapy
- you have recently been vaccinated
- you develop breathing difficulties, or feel very weak and look very pale (this may be a sign of kidney failure).

Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis and acute generalised 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 4.

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, pharmacist or nurse if you are taking, have recently taken or might take any other medicines, including vaccinations.

Pregnancy, breast-feeding and fertility
Pregnancy
If you are pregnant, or thinking about becoming pregnant, tell your doctor. The use of gemcitabine should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking gemcitabine during pregnancy. Women of childbearing age must use effective contraception during treatment with gemcitabine and up to 6 months after the last dose.

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 3 months following treatment with gemcitabine. Men are advised to use effective contraception during treatment with gemcitabine and for 3 months after the last dose. If you would like to father a child during the treatment or in the 3 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 operate machinery until you are sure that gemcitabine treatment has not made you feel sleepy.

Gemcitabine contains sodium

Gemcitabine 200 mg concentrate for solution for infusion
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

Gemcitabine 1 g concentrate for solution for infusion
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

Gemcitabine 2 g concentrate for solution for infusion
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3. How Gemcitabine is given

Your initial dose of gemcitabine will be calculated by your doctor and will depend on the type of cancer you have and the surface area of your body in square meters (m^2).

Your height and weight are measured to work out the surface area of your body. Your doctor will use this information to work out the right dose for you. The usual dose of gemcitabine is between 1 000 mg/m^2 and 1 250 mg/m^2.

This dosage may be adjusted, or treatment may be delayed depending on your blood cell counts, your general health and any side effects you experience.

How frequently you receive your gemcitabine infusion will depend on what type of cancer you are being treated for.

You will always receive gemcitabine as an infusion (a slow injection via a drip) into one of your veins. The infusion will last approximately 30 minutes.

As gemcitabine will be given to you under the supervision of a doctor, it is unlikely that you will receive the wrong dose. However, if you have any concerns about the dose you receive or if you have any further questions about the use of this medicine, please talk to your doctor, pharmacist or nurse.

4. Possible side effects

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

You must contact your doctor immediately if you notice any of the following:
- 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).
- Tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have less haemoglobin than normal which is very common).

- Mild to moderate skin rash (very common) / itching (common), or fever (very common); (allergic reactions).
- Temperature of 38 ºC 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) (common).
- Pain, redness, swelling or sores in your mouth (stomatitis) (common).
- Irregular heart rate (arrhythmia) (uncommon)
- 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) (very rare) and haemolytic uraemic syndrome (uncommon), which may be fatal.
- Difficulty breathing (it is 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)
- Severe chest pain (myocardial infarction) (rare).
- 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) (very rare).
- Generalised swelling, shortness of breath or weight gain, as you might have fluid leakage from small blood vessels into the tissues (capillary leak syndrome) (very rare)
- Headache with changes in vision, confusion, seizures or fits (posterior reversible encephalopathy syndrome) (very rare)
- Severe rash with itching, blistering or peeling of the skin (Stevens-Johnson syndrome, toxic epidermal necrolysis) (very rare).
- 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 Generalised Exanthematous Pustulosis (AGEP)) (frequency not known).

Other side effects with Gemcitabine may include:

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 the 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 people
- 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: frequency cannot be estimated from the available data
- A condition where eosinophils, a type of cell ordinarily found in the blood, accumulate in the lungs (pulmonary eosinophilia)
- Skin redness with swelling (Pseudocellulitis)
- When bacteria and their toxins circulate in the blood and starts to damage the organs (sepsis)

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.

If you are concerned about any side effects, talk to your doctor.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not mentioned 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

Gemcitabine will be stored and administered by healthcare professionals, who will follow this guidance:

- 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 after EXP. The expiry date refers to the last day of that month.
- Store in a refrigerator (2 °C-8 °C).
- This medicine is for single use only; any unused solution should be discarded according to local procedures.

6. Contents of the pack and other information

What Gemcitabine contains
- The active substance in Gemcitabine is gemcitabine (in the form of gemcitabine hydrochloride). The concentrated solution has a strength of 38 mg/mL, which means that every millilitre of the concentrate contains 38 milligrams of gemcitabine (in the form of gemcitabine hydrochloride).
- The other ingredients in this medicine are Water for Injections, hydrochloric acid (for pH adjustment) and sodium hydroxide (for pH adjustment).

What Gemcitabine looks like and contents of the pack
- Gemcitabine is a clear, colourless or light straw-coloured solution
- Gemcitabine is packaged in glass vials
- Three sizes of glass vial are available, containing either
    - 200 mg gemcitabine (as hydrochloride) in 5.3 mL solution
    - 1 g gemcitabine (as hydrochloride) in 26.3 mL solution
    - 2 g gemcitabine (as hydrochloride) in 52.6 mL solution
- Each vial is packed into a single outer carton

Marketing Authorisation Holder and Manufacturer
The marketing authorisation holder is Hospira UK Limited, Horizon, Honey Lane, Hurley, Maidenhead, SL6 6RJ, UK.

The manufacturer is Pfizer Service Company BVBA, Hoge Wei 10, 1930 Zaventem, Belgium.

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

Belgium:	Gemcitabine Hospira 38 mg/mL Concentraat voor oplossing voor infusie Gemcitabine Hospira 38 mg/mL Solution à diluer pour perfusion

	Gemcitabine Hospira 38 mg/mL Konzentrat zur Herstellung einer Infusionslösung
France:	Gemcitabine Hospira 38 mg/mL, Solution à diluer pour perfusion
Luxembourg:	Gemcitabine Hospira 38 mg/mL Solution à diluer pour perfusion
Malta:	Gemcitabine 38 mg/mL Concentrate for Solution for Infusion
Spain:	Gemcitabina Hospira 1 000 mg Concentrado Para Solucion Para Perfusion Gemcitabina Hospira 200 mg Concentrado Para Solucion Para Perfusion Gemcitabina Hospira 2 000 mg Concentrado Para Solucion Para Perfusion
United Kingdom (Northern Ireland):	Gemcitabine 38 mg/mL concentrate for solution for infusion

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The following information is intended for healthcare professionals only:

Gemcitabine 38 mg/mL concentrate for solution for infusion

Instructions for use, handling and disposal

Use

- Refer to the SPC to calculate the dose and the number of vials required.
- Dilution of the solution is required: An approved diluent for Gemcitabine Concentrate for Solution for Infusion is sodium chloride 9 mg/mL (0.9%) solution for injection (without preservative). Use the aseptic technique during any further dilution of the Gemcitabine concentrate, prior to administration.
- Parenteral products should be visually inspected for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.
- After dilution, chemical and physical in-use stability has been demonstrated for:

Diluent	**Target Concentration**	**Storage Conditions**	**Time period**
0.9% sodium chloride solution for infusion	0.1 mg/mL and 26 mg/mL	2-8 °C in the absence of light in non-PVC (polyolefin) infusion bags	84 days
0.9% sodium chloride solution for infusion	0.1 mg/mL and 26 mg/mL	2-8 °C in the absence of light in PVC infusion bags	24 hours
0.9% sodium chloride solution for infusion	0.1 mg/mL and 26 mg/mL	25 °C under normal lighting conditions in PVC infusion bags	24 hours
5% glucose solution for infusion	0.1 mg/mL and 26 mg/mL	25 °C under normal lighting conditions in PVC infusion bags	24 hours

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 2 °C to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Handling

- The normal safety precautions for cytostatic agents must be observed when preparing and disposing of the infusion solution. Handling of the concentrate 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

- Gemcitabine is for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.