**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.
- If you get any side effects, talk to your doctor, or 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 Powder for Solution for Infusion 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 you have.

Gemcitabine Infusion is used in the treatment of a number of types of cancer including:
- 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 Powder for Solution for Infusion

**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.

Tell the doctor if you think any of the above applies to you.

**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 also have samples of your blood taken to check if you have enough blood cells to receive gemcitabine. Your doctor may decide to change your 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 or pharmacist or nurse before using 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, vascular disease or problems with your kidneys talk to your doctor or hospital pharmacist as you may not be able to receive Gemcitabine.
- you have recently had, or are going to have radiotherapy, please tell your doctor as there may be an early or late radiation reaction with Gemcitabine.
- you have been vaccinated recently, please tell your doctor as this can possibly cause bad effects with Gemcitabine.
- during treatment with this medicine, 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, please tell your doctor as this may be a sign of kidney failure or problems with your lungs.
- you develop generalised swelling, shortness of breath or weight gain, please tell your doctor as this may be a sign of fluid leaking from your small blood vessels into the tissue.

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**
Please tell your doctor if you are taking, have recently taken or might take any other medicines, including vaccinations and medicines obtained without a prescription.

**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 if pregnant. 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 treatment with Gemcitabine.

**Fertility**
Men are advised not to father a child during, and up to 6 months after treatment with gemcitabine. If you would like to father a child during the treatment or in the 6 months following treatment, please 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 treatment can make you feel drowsy. Alcohol can make this worse. Do not drive or operate machinery until you are sure that Gemcitabine has not made you feel sleepy.

**Gemcitabine contains sodium**

*Gemcitabine 200 mg Powder 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 Powder for Solution for Infusion*
This medicine contains 29 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.45% of the recommended maximum daily dietary intake of sodium for an adult.

*Gemcitabine 2 g Powder for Solution for Infusion*
This medicine contains 58.5 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.93% of the recommended maximum daily dietary intake of sodium for an adult.

## 3. How Gemcitabine Powder for Solution for Infusion is given

The usual dose of Gemcitabine is between 1 000 mg/m$^2$ and 1 250 mg/m$^2$. 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 infusion will depend on the type of cancer 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:

- 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).
- Sudden weakness or numbness of your face, arms or legs, especially on one side, or slurred speech, even for a short period of time. These may be signs of a stroke (uncommon).
- 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 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
- Feeling sick (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
- Difficulty sleeping (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

**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):

- Skin redness with swelling (Pseudocellulitis)
- When bacteria and their toxins circulate in the blood and starts to damage the organs (sepsis)
- A condition where eosinophils, a type of cell ordinarily found in the blood, accumulate in the lungs (pulmonary eosinophilia)

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 or 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 Powder for Solution for Infusion

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.

This medicinal product does not require any special storage conditions.

After reconstitution:

This medicine may be stored for 35 days at 25 °C. From a microbiological point of view however, it is advised that the product is used immediately.

The reconstituted solution should not be refrigerated.

The prepared solution for infusion should not be used if it contains particles or if it is strongly coloured.

This medicine will be prepared and administered to you by healthcare staff. Any unused medicine will be disposed of by healthcare staff, according to local procedures.

## 6. Contents of the pack and other information

**What Gemcitabine contains**

- The active substance is gemcitabine (as hydrochloride)
- Vials contain either 200 mg, 1 g or 2 g gemcitabine (as hydrochloride)
- The other ingredients are mannitol, sodium acetate trihydrate, hydrochloric acid (for pH adjustment) and sodium hydroxide (for pH adjustment) [see section 2 “Gemcitabine Powder for Solution for Infusion contains sodium”]
- One mL of the reconstituted solution for infusion contains 38 mg gemcitabine (as hydrochloride)

**What Gemcitabine looks like and contents of the pack**

This medicinal product is a powder for solution for infusion (a powder which is dissolved before being injected slowly via a drip into a vein). It can also be referred to as a ‘powder for infusion’.

The powder is white to off-white and when dissolved ready for infusion, it produces a colourless or slightly yellow solution.

The 200 mg, 1 g and 2 g vials are sold separately as single packs or packs of 5. Not all pack sizes may be marketed. Vials may be sheathed in protective ONCO-TAIN® sleeves.

**Marketing Authorisation Holder and Manufacturer**

The marketing authorisation holder and manufacturer is Hospira UK Limited, Horizon, Honey Lane, Hurley, Maidenhead, SL6 6RJ, UK.

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**The following information is intended for healthcare professionals only:**

**Instructions for use, handling and disposal**

For single use only

This medicinal product has only been shown to be compatible with sodium chloride 9 mg/mL (0.9%) solution for injection. Accordingly, only this diluent should be used for reconstitution. Compatibility with other active substances has not been studied. Therefore, it is not recommended to mix this medicinal product with other active substances when reconstituted.

Reconstitution at concentrations greater than 38 mg/mL may result in incomplete dissolution, and should be avoided.
mL (0.9%) solution for injection (as stated in the table below) and shake to dissolve.

| Presentation | Volume of sodium chloride 9 mg/mL (0.9%) solution for injection to be added | Displacement volume | Final concentration |
|---|---|---|---|
| 200 mg | 5 mL | 0.26 mL | 38 mg/mL |
| 1 g | 25 mL | 1.3 mL | 38 mg/mL |
| 2 g | 50 mL | 2.6 mL | 38 mg/mL |

The appropriate amount of drug may be further diluted with sodium chloride 9 mg/mL (0.9%) solution for injection.

Chemical and physical in-use stability has been demonstrated for 35 days at 25 °C.

From a microbiological point of view, the product should be used immediately.

Solutions should not be refrigerated, as crystallisation may occur.

Parenteral drugs should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit.

Any unused solution should be discarded as described below.

**Guidelines for the Safe Handling of Cytotoxic Medicinal Products**

Local guidelines on safe preparation and handling of cytotoxic medicinal products must be adhered to. Cytotoxic preparations should not be handled by pregnant staff. The preparation of injectable solutions of cytotoxic agents must be carried out by trained specialist personnel with knowledge of the medicines used. This should be performed in a designated area. The work surface should be covered with disposable plastic-backed absorbent paper.

Suitable eye protection, disposable gloves, face mask and disposable apron should be worn. Precautions should be taken to avoid the drug accidentally coming into contact with the eyes. If accidental contamination occurs, the eye should be washed with water thoroughly and immediately.

Syringes and infusion sets should be assembled carefully to avoid leakage (use of Luer lock fittings is recommended). Large bore needles are recommended to minimise pressure and the possible formation of aerosols. The latter may also be reduced by the use of a venting needle.

Actual spillage or leakage should be mopped up wearing protective gloves. Excreta and vomit must be handled with care.

**Disposal**

Adequate care and precaution should be taken in the disposal of items used to reconstitute this medicinal product. Any unused dry product or contaminated materials should be placed in a high-risk waste bag. Sharp objects (needles, syringes, vials, etc) should be placed in a suitable rigid container. Personnel concerned with the collection and disposal of this waste should be aware of the hazard involved. Waste material should be destroyed by incineration. Any unused product or waste material should be disposed of in accordance with local requirements.