**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 receiving this medicine.**
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist. See section 4

**In this leaflet**:


## 1. WHAT GEMCITABINE POWDER FOR SOLUTION FOR INFUSION IS AND WHAT IT IS USED FOR

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

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

Gemcitabine powder for solution for infusion 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. BEFORE YOU ARE GIVEN GEMCITABINE POWDER FOR SOLUTION FOR INFUSION

**You should not be given Gemcitabine powder for solution for infusion:**
- if you are allergic (hypersensitive) to gemcitabine or any of the other ingredients of Gemcitabine powder for solution for infusion (listed in section 6).
- if you are breast-feeding

**Take special care with Gemcitabine powder for solution for infusion**:
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 powder for solution for infusion. 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 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 or problems with your kidneys, as you may not be able to be treated with Gemcitabine powder for solution for infusion.
- you have recently had, or are going to have radiotherapy, as early or late reactions due to radiation can sometimes occur with Gemcitabine powder for solution for infusion

- you have been vaccinated recently, as this could cause harmful effects with Gemcitabine powder for solution for infusion.
- you develop breathing difficulties or feel very weak and are very pale (may be a sign of kidney failure or a problem 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, and symptoms of a serious condition called Capillary Leak Syndrome (CLS).
- you during treatment with this medicine get symptoms such as headache with confusion, seizures (fits) or changes in vision. You should contact your doctor right away, as this could be a very rare nervous system side effect named posterior reversible encephalopathy syndrome (PRES).

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 4.

**Children and adolescents**
This medicine should not be used in children and adolescents under 18 years of age due to the lack of data on safety and efficacy.

**Other medicines and Gemcitabine powder for solution for infusion**
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.

**Pregnancy**
If you are pregnant, or thinking about becoming pregnant, tell your doctor. The use of Gemcitabine powder for solution for infusion should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking Gemcitabine powder for solution for infusion during pregnancy Women of childbearing potential must use effective contraception during treatment with Gemcitabine powder for solution for infusion and for 6 months after the last administration.

**Fertility**
Men are advised not to father a child during and up to 3 months following treatment with Gemcitabine powder for solution for infusion and must therefore use effective contraception during treatment for 3 months after treatment discontinuation. 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.

**Breast-feeding**
If you are breast-feeding, tell your doctor.
You must discontinue breast-feeding during Gemcitabine powder for solution for infusion treatment.

**Driving and using machines**
Gemcitabine powder for solution for infusion 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 powder for solution for infusion treatment has not made you feel sleepy.

**Important information about some of the ingredients of Gemcitabine powder for solution for infusion**
Gemcitabine powder for solution for infusion contains 3.5 mg (< 1 mmol) of sodium in each 200 mg vial, 17.5 mg (< 1 mmol) sodium in each 1000 mg vial and 35 mg (1.52 mmol) sodium in each 2000 mg vial. This should be taken into consideration by patients on a controlled sodium diet.

## 3. HOW GEMCITABINE POWDER FOR SOLUTION FOR INFUSION IS GIVEN

The usual 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 powder for solution for 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, Gemcitabine powder for solution for infusion can cause side effects, although not everybody gets them.

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

- 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 accompanied by fever, also known as febrile neutropenia which is common).
- Irregular heart rate (arrhythmia) (uncommon).
- Pain, redness, swelling or sores in your mouth (stomatitis) (common).
- Allergic reactions: if you develop mild to moderately severe skin rash (very common) / itching (common), or fever (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).
- 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).
- 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)
- Generalised swelling, shortness of breath or weight gain, as you might have fluid leakage from small blood vessels into tissues (capillary leak syndrome) (very rare).
- Headache with changes in vision, confusion, seizures or fits (posterior reversible encephalopathy syndrome) (very rare).
- Extreme fatigue and a feeling of weakness, purpura or small areas of bleeding in the skin (ecchymosis), acute kidney failure (low urine output or no urine output), and signs of infection (haemolytic uraemic syndrome). This can be fatal (uncommon).
- Severe chest pain (myocardial infarction) (rare).
- A severe hypersensitivity/allergic reaction with severe skin rash, including reddening of the skin and itching, swelling of the hands, feet, ankles, face, lips, mouth or throat (which can cause swallowing or breathing difficulties), wheezing, rapid heartbeat and feeling faint (anaphylactic reaction) (very rare).
- A severe skin rash with itching, bullous lesions or peeling of the skin (Stevens-Johnson syndrome, toxic epidermal necrolysis) (very rare).
- Extreme fatigue and weakness, purpura or small areas of bleeding in the skin (bruises), acute kidney failure (low or absent urine production) and signs of infection. These may be features of thrombotic microangiopathy (formation of clots in small blood vessels) and of haemolytic uraemic syndrome, which can 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).

**Other side effects with Gemcitabine powder for solution for infusion may include:**

**Very common side effects (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
- Oedema (swelling of ankles, fingers, feet, face)

**Common side effects (may affect up to 1 in 10 people)**

- Anorexia (poor appetite)
- Headache
- Insomnia
- Sleepiness
- Cough
- Runny nose
- Constipation
- Diarrhoea
- Itching
- Excessive sweating

- Muscle pain
- Back pain
- Fever
- Weakness
- Chills
- Infections

**Uncommon side effects (may affect up to 1 in 100 people)**
- Interstitial lung disease (scarring of the air sacs of the lung)
- Spasm of the airways (wheeze)
- Abnormal chest X ray/scan (scarring of the lungs)
- Heart failure
- Kidney failure
- Severe liver damage, including liver failure.
- Cerebrovascular accident

**Rare side effects (may affect up to 1 in 1,000 people)**
- Low blood pressure
- Skin scaling, ulceration or blister formation on the skin
- Formation of large blisters on the skin and oozing of the skin
- Injection site reactions
- Severe lung inflammation resulting in respiratory failure (adult respiratory distress syndrome)
- Skin rash resembling severe sunburn that may occur on skin previously exposed to radiotherapy (recall reactions)
- Fluid in the lungs
- Alveolar lung damage associated with radiotherapy (toxicity associated with radiation)
- Gangrene in the fingers or toes
- Inflammation of blood vessels (peripheral vasculitis).

**Very rare side effects (may affect up to 1 in 10,000 people)**

- Increased platelet count
- Inflammation of the wall of the large intestine due to reduced blood supply (ischaemic colitis)
- A low haemoglobin level (anaemia) and low white blood cell and platelet counts will be detected by blood sampling
- Thrombotic microangiopathy: formation of clots in small blood vessels.

**Frequency not known (cannot be estimated from the available data)**
- Sepsis: when bacteria and their toxins circulate in the blood and begin to damage organs
- Pseudo-cellulitis: redness of the skin with swelling.

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 or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via
HPRA Pharmacovigilance
Website: www.hpra.
By reporting side effects you can help provide more information on the safety of this medicine.
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## 5. HOW TO STORE GEMCITABINE POWDER FOR SOLUTION FOR INFUSION

Keep out of the reach and sight of children.
Do not use Gemcitabine powder for solution for infusion after the expiry date, which is stated on the carton and vial. The expiry date refers to the last day of that month.

Unopened vial: This medicinal product does not require any special storage conditions.

Reconstituted solution: The product should be used immediately. When prepared as directed, chemical and physical in-use stability of reconstituted solutions of gemcitabine were demonstrated for 21 days at 25°C. Further dilution by a healthcare provider may be done. Solutions of reconstituted gemcitabine should not be refrigerated, as crystallisation may occur.

This medicine is for single use only; any unused solution should be discarded under the local requirements.

## 6. FURTHER INFORMATION

**What Gemcitabine powder for solution for infusion contains**
The active substance is gemcitabine. Each vial contains 200, 1000 mg, 2000 mg of gemcitabine (as gemcitabine hydrochloride).
The other ingredients are mannitol (E421), sodium acetate, hydrochloric acid and sodium hydroxide.

**What Gemcitabine powder for solution for infusion looks like and contents of the pack**
Gemcitabine powder for solution for infusion is a white to off-white powder, for solution for infusion in a vial. Each vial contains 200 mg, 1000 mg or 2000 mg of gemcitabine. Each pack of Gemcitabine powder for solution for infusion contains 1 vial.

The 200 mg, 1 g and 2 g vials are sold separately in single packs.
Not all pack sizes may be marketed.

**Marketing authorisation holder:**
Accord Healthcare Ireland Ltd.
Euro House
Euro Business Park
Little Island
Cork T45 K857
Ireland

**Manufacturers:**
Accord Healthcare Polska Sp.z o.o.,
ul. Lutomierska 50,95-200 Pabianice, Poland

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

| **Name of the Member State** | **Name of the medicine** |
|---|---|
| Spain | Gemcitabina Accord 200 mg / 1 g / 2 g Polvo para solución para infusión EFG |
| Ireland | Gemcitabine 200 mg / 1g / 2g Powder for Solution for Infusion |
| Poland | Gemcitabine Accord |
| Portugal | Gemcitabina Accord |
| Greece | Gemcitabine Accord 200 mg /1 g Κόνις για διάλυμα προς έγχυση |
| United Kingdom (Northern Ireland) | Gemcitabine 200 mg / 1 g / 2 g Powder for Solution for Infusion |
| Cyprus | Gemcitabine Accord 200mg / 1 g Powder for Solution for Infusion |

**The leaflet was last revised in 03/2024**

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

**Instructions for use, handling and disposal.**

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

2. Calculate the dose and the number of Gemcitabine powder for solution for infusion vials needed.

3. Reconstitute 200 mg vials with 5 ml of 9 mg/ml (0.9 %) sterile sodium chloride solution for injection, without preservative, or 25 ml sterile sodium chloride solution for injection, without preservative to the 1000 mg vial, or 50 ml sterile sodium chloride solution for injection, without preservative to the 2000 mg vial. Shake to dissolve. The total volume after reconstitution is 5.26 ml (200 mg vial) or 26.3 ml (1000 mg vial) or 52.6 ml (2000 mg vial) 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.

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

5. Solutions of reconstituted gemcitabine should not be refrigerated, as crystallisation may occur. Chemical and physical in-use stability has been demonstrated for 21 days at 25°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.

6. 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.