

Gemcitabine Lyophilized Powder for Solution for Infusion 200 mg and 1000 mg

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further question, ask your doctor or your 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.

What is in this leaflet:

1. What Gemsiban® is and what it is used for
2. What you need to know before you are given Gemsiban®
3. How Gemsiban® is used
4. Possible side effects
5. How to store Gemsiban®
6. Contents of the pack and other information

1. What Gemsiban® is and what it is used for

Gemcitabine, the active substance of Gemsiban®, is a nucleoside analog that exhibits antitumor activity.

Gemsiban® is used for:

- First-line treatment for locally advanced or metastatic non-small cell lung cancer (as monotherapy in elderly patients and in palliative treatment; otherwise in combination with cisplatin)
- Treatment of locally advanced or metastatic pancreatic cancer
- Treatment of advanced or metastatic bladder cancer (in combination with cisplatin)
- Treatment of locally advanced or metastatic epithelial ovarian cancer which has relapsed after a recurrence-free interval of at least 6 months following previous platinum-based therapy (in combination with carboplatin)
- Treatment of metastatic breast cancer which has relapsed after previous chemotherapy including an anthracycline (in combination with paclitaxel)

2. What you need to know before you are given Gemsiban®

You should not be given Gemsiban®:

- if you are allergic (hypersensitive) 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 your kidneys and liver are working well enough for to receive this medicine. Before each infusion you will have samples of your blood taken to check if you have enough blood cells to receive Gemsiban®. 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 how well your kidneys and liver are working.

Please tell your doctor, nurse or hospital pharmacist before using Gemsiban®:

If 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 Gemsiban®.

If 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 Gemsiban®.

If you have been vaccinated recently, please tell your doctor as this can possibly cause bad effects with Gemsiban®.

If 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.

If 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.

If you develop generalized 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.

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 Gemsiban®

Please tell your doctor or hospital pharmacist if you are taking or have recently taken 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 Gemsiban® should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking Gemsiban® during pregnancy.

Breast-feeding

If you are breast-feeding, tell your doctor. You must discontinue

breast-feeding during Gemsiban® treatment.

Fertility

Men are advised not to father a child during and up to 6 months following treatment with Gemsiban®. 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

Gemsiban® 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 Gemsiban® treatment has not made you feel sleepy.

3. How Gemsiban® is used

The usual dose of Gemsiban® is 1000-1250 mg for every square meter 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 Gemsiban® infusion depends on the type of cancer that you are being treated for.

You will always receive Gemsiban® 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.

Usual dosage:

In the treatment of **pancreatic cancer**, an initial course of Gemsiban® 1 g/m² once weekly for up to 7 weeks may be given, followed after a one-week recovery period by a regimen of infusions once weekly for 3 consecutive weeks out of 4.

In **non-small cell lung cancer**, Gemsiban® may be given as a single agent; 1 g/m² once weekly for 3 consecutive weeks out of 4 is recommended. Alternatively, it may be given before cisplatin. Two schedules have been used; Gemsiban® 1.25 g/m² is given on days 1 and 8 of a 21-day cycle, or Gemsiban® 1 g/m² is given on days 1, 8 and 15 of a 28-day cycle.

In the treatment of **bladder cancer**, Gemsiban® is given before cisplatin. The recommended dose of Gemsiban® is 1 g/m² on days 1, 8, and 15 of a 28-day cycle.

In **breast cancer**, Gemsiban® is usually given after a taxane such as paclitaxel. A dose of Gemsiban® 1.25 g/m² is given on days 1 and 8 of a 21-day cycle.

In **ovarian cancer**, Gemsiban® is given before carboplatin. The recommended dose of Gemsiban® is 1 g/m² on days 1 and 8 of a 21-day cycle.

4. Possible side effects

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 hemoglobin than normal which is very common).
- Mild to moderate skin rash (very common) / itching (common), or fever (very common); (allergic reaction).
- Temperature of 38°C 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) and hemolytic uremic syndrome, which may be fatal.
- Difficulty breathing (it is common to have mild breathing difficulty soon after the Gemsiban® 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).

- Generalized 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).

Other side effects with Gemsiban® may include:

Common or very common

Alopecia, anemia, appetite decreased, asthenia, back pain, bone marrow depression, chills, constipation, cough, diarrhea, drowsiness, dyspnea, fever, hematuria (blood in urine), headache, hyperhidrosis, influenza like illness, insomnia, leucopenia,

myalgia (muscle pain), nausea, neutropenia, oedema (swelling of ankles, fingers, feet, face), oral disorders, proteinuria, rhinitis, skin reactions, thrombocytopenia, vomiting, liver problems (found through abnormal blood test results), itching, sweating

Uncommon

Respiratory disorders, interstitial pneumonitis (scarring of the air sacs of the lung), 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 or very rare

Capillary leak syndrome, hypotension, myocardial infarction, posterior reversible encephalopathy syndrome (PRES), severe cutaneous adverse reactions (SCARs), skin ulcer, thrombocytosis (increased platelet count), sloughing of skin and severe skin blistering, injection site reactions, severe lung inflammation causing respiratory failure (adult respiratory distress syndrome), gangrene of fingers or toes, inflammation of the blood vessels (peripheral vasculitis), inflammation of the lining of the large bowel, caused by reduced blood supply (ischemic colitis), thrombotic microangiopathy (clots forming in small blood vessels)

Frequency not known

Arrhythmias, hemolytic uremic syndrome, hepatic disorders, pulmonary oedema, radiation injuries, vasculitis, pseudo cellulitis (skin redness with swelling), sepsis (when bacteria and their toxins circulate in the blood and starts to damage the organs)

Further information

Gemsiban® should be discontinued if signs of microangiopathic hemolytic anemia occur.

5. How to store Gemsiban®

Keep out of the reach and sight of children.

Do not use this medicine after the expiry date (EXP) which is stated on the box and the vial.

Store below 30°C. Do not freeze. Do not refrigerate after reconstitution.

This medicine is for single use only.

Reconstituted solution: The product should be used immediately. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Gemsiban® contains:

- The active substance is Gemcitabine. Each vial contains 200 mg or 1000 mg of gemcitabine (as gemcitabine Hydrochloride). After reconstitution one ml of Gemsiban® contains 38mg Gemcitabine.
- The other ingredients are mannitol, sodium acetate and sodium hydroxide or hydrochloric acid.

What Gemsiban® looks like and contents of the pack

Gemsiban® is a white to off-white powder for solution for infusion in a vial.

Gemsiban® 200mg: Each vial contains 200mg Gemcitabine.

Gemsiban® 1000mg: Each vial contains 1000mg Gemcitabine.

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 Gemsiban® for intravenous infusion administration.
2. Calculate the dose and the number of Gemsiban® 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. Shake to dissolve. The total volume after reconstitution is 5.26 mL (200 mg vial) or 26.3 mL (1000 mg vial) respectively. This dilution yields a gemcitabine concentration of 38 mg/mL. 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 Gemsiban® should not be refrigerated, as crystallization may occur.
6. Gemsiban® 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.

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Leaflet	Gemcitabine Lyophilized
Color	PANTONE 295 U 
Size	210 mm x 295 mm Tolerance: 1±mm
Grammage	58-70 g/m ²
File Name	GEBL-0000-LF-00
date	05.07.04