Package leaflet: Information for the user

Gemcitabine 200 mg PCH, poeder voor oplossing voor infusie
Gemcitabine 1000 mg PCH, poeder voor oplossing voor infusie

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, 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 use 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, nurse or hospital pharmacist before using gemcitabine if:

- you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using gemcitabine.

If you have, or have previously had liver disease, heart disease or vascular disease or problems with your kidneys talk to your doctor or hospital pharmacist as you may not be able to receive gemcitabine.

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 gemcitabine.

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

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 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 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
There is no relevant use of gemcitabine in the paediatric population.

Other medicines and gemcitabine
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 gemcitabine should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking gemcitabine during pregnancy. Women of childbearing age should use effective contraception during treatment with gemcitabine and for 6 months after receiving 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 and should therefore use effective contraception during treatment with gemcitabine and for up to 3 months afterwards. 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 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, that is to say essentially 'sodium free'.

3. How to use gemcitabine

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 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 any further questions on the use of this medicine ask your doctor, pharmacist or nurse.

4. Possible side effects

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

Frequencies of the observed side effects are defined as:
- Very common: may affect more than 1 in 10 people
- Common: may affect up to 1 in 10 people
- Uncommon: may affect up to 1 in 100 people
- Rare: may affect up to 1 in 1,000 people
- Very rare: may affect up to 1 in 10,000 people

You must contact your doctor immediately if you notice any of the following:
- Fever or infection (common): 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)
- Pain, redness, swelling or sores in your mouth (common)
- Allergic reactions: if you develop skin rash (very common) / itching (common), or fever (very common). Contact your doctor if you get a severe rash or itching or blistering (Stevens-Johnson syndrome or Toxic epidermal necrolysis)
- 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)
- 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 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 the tissues (capillary leak syndrome) (very rare).
- Headache with changes in vision, confusion, seizures or fits (posterior reversible encephalopathy syndrome) (very rare).
- 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 haemolytic uraemic syndrome, which may be fatal.

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 neutropenia)
- 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
- Infections

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

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

Very rare side effects (may affect up to 1 in 10,000 people)
- Increased platelet count
- Anaphylactic reaction (severe hypersensitivity/ allergic reaction)
- Sloughing of skin and severe skin blistering
- Ischaemic colitis (inflammation of the lining of the large bowel, caused by reduced blood supply)
- Capillary leak syndrome (fluids from your small blood vessels leak out into the tissue).
- Thrombotic microangiopathy: clots forming in small blood vessels

Not known (frequency cannot be estimated from the available data)
- Sepsis: when bacteria and their toxins circulate in the blood and starts to damage the organs
- Pseudocellulitis: Skin redness 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.

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 listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. 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.
Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

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.

Gemcitabine should not been used if there are any signs of particles.

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

6. Contents of the pack and other information

What gemcitabine contains

- The active substance is gemcitabine (as hydrochloride).
  Each vial contains 200 mg or 1 g gemcitabine. After reconstitution one ml of gemcitabine contains 38 mg 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 sodium chloride solution 9 mg/ml (0.9%), the solution is clear to pale opalescent and colourless to pale yellow.

Gemcitabine is packed in colourless glass vials with bromobutylic rubber stoppers. 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.

Not all pack sizes may be marketed.

Houder van de vergunning voor het in de handel brengen en fabrikant
Houder van de vergunning voor het in de handel brengen
Pharmachemie B.V.
Swensweg 5
2031 GA Haarlem
Nederland

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

Actavis Italy S.p.A.
Nerviano Plant
Viale Pasteur 10
20014 Nerviano (Milan)
Italië

Pharmachemie B.V.
Swensweg 5
2031 GA Haarlem
Nederland

In het register ingeschreven onder:
Gemcitabine 200 mg PCH, poeder voor oplossing voor infusie: RVG 101088
Gemcitabine 1000 mg PCH, poeder voor oplossing voor infusie: RVG 101089

Dit geneesmiddel is geregistreerd in de lidstaten van de EEA onder de volgende namen:
Duitsland Gemcitabin-GRY 1000 mg Pulver zur Herstellung einer Infusionslösung

Nederland	Gemcitabine 200 mg PCH, poeder voor oplossing voor infusie Gemcitabine 1000 mg PCH, poeder voor oplossing voor infusie

Deze bijsluiter is voor het laatst goedgekeurd in november 2023.

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

Instruction for use, handling and disposal

Cytotoxic

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 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 1 g vial. Shake to dissolve. The total volume after reconstitution is 5.26 ml (200 mg vial) or 26.3 ml (1 g vial) respectively. This dilution yields a gemcitabine concentration of 38 mg/ml, which includes accounting for the misplacement 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. Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C. From amicrobiological 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 (and further dilution, if applicable) has taken place in controlled and validated aseptic conditions.

   Solutions of reconstituted gemcitabine should not be refrigerated, as crystallisation may occur.

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.