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 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, nurse or pharmacist.
- 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 (e.g. cisplatin, paclitaxel, carboplatin), 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 check if your liver and kidneys are working well enough for you 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 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 check how well your kidneys and liver are working.

Talk to your doctor, nurse or hospital pharmacist before using gemcitabine.

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 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.

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 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, breast-feeding and fertility
Pregnancy
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine. The use of gemcitabine should be avoided during pregnancy. 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 gemcitabine treatment.

Fertility
Men are advised not to father a child during and up to 6 months following treatment with gemcitabine. 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
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 200 mg concentrate for solution for infusion contains a maximum of 4.9 mg sodium (<1 mmol) in each vial, that is to say essentially "sodium-free".

Gemcitabine 1000 mg concentrate for solution for infusion contains a maximum of 24.2 mg (1.05 mmol) sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.2% of the recommended maximum daily dietary intake of sodium for an adult.

Gemcitabine 2000 mg Concentrate for Solution for Infusion contains a maximum of 48.4 mg (2.10 mmol) sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.4% of the recommended maximum daily dietary intake of sodium for an adult.

3. HOW TO USE GEMCITABINE

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 (m2).

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 1g/m2 and 1.25g/m2.

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, nurse or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

The following information is intended for healthcare professionals only:

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 (PP and polyolefin) infusion bags	84 days
0.9% sodium chloride solution for infusion	0.1 mg/ml and 26 mg/ml	25°C under normal lighting conditions non-PVC (PP and polyolefin) infusion bags	24 hours
5% glucose solution for infusion	0.1 mg/ml and 26 mg/ml	25°C under normal lighting conditions non-PVC (PP and polyolefin) infusion bags	24 hours

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 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) (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 haemolytic uraemic syndrome, 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).

Other side effects with Gemcitabine 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
- Swelling of ankles, fingers, feet, face (oedema)

Common side effects (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 side effects (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 side effects (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 side effects (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.
- 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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search MHRA Yellow Card at 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 (EXP) which is stated on the carton. 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 is gemcitabine (as 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 (as gemcitabine hydrochloride).
- The other ingredients are water for injections, hydrochloric acid (for pH adjustment) and sodium hydroxide (for pH adjustment).

What Gemcitabine looks like and contents of the pack
Clear colourless to pale yellow solution.

Gemcitabine is packaged in glass vials.

Three sizes of glass vial are available, containing either
200 mg gemcitabine (as hydrochloride) in 5.26 ml solution
1000 mg gemcitabine (as hydrochloride) in 26.3 ml solution
2000 mg gemcitabine (as hydrochloride) in 52.6 ml solution
Each vial is packed into a single outer carton

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Hikma Farmacêutica (Portugal), S.A., Estrada do Rio da Mó 8, 8A e 8B, Fervença, 2705-906 Terrugem SNT, Portugal.

Manufacturer
Thymoorgan Pharmazie GmbH, Schiffgraben 23, 38690 Goslar, Germany.

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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 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.