

## Package leaflet: Information for the user

### Gemcitabine 40 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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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
2. What you need to know before you use Gemcitabine
3. How to use Gemcitabine
4. Possible side effects
5. How to store Gemcitabine
6. Contents of the pack and other information

#### **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 take 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 before using Gemcitabine if:

- you have, or have previously had liver disease, heart disease, vascular disease or problems with your kidneys

- you have recently had, or are going to have radiotherapy
- you have been vaccinated recently
- you develop breathing difficulties or feel very weak and are very pale (may be a sign of kidney failure or problems with your lungs)
- you are suffering from alcoholism, as this medicinal product contains ethanol (alcohol)
- you are suffering from epilepsy, as this medicinal product contains ethanol (alcohol)
- during treatment with this medicine you experience headaches, confusion, seizures, visual disturbances 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 generalised swelling, shortness of breath or weight gain as these may be a sign of fluid leaking from your blood vessels into the tissues.

Instructions for dilution should be strictly followed in order to avoid adverse events.

### **Children and adolescents**

This medicinal product is not recommended for use in children under 18 years of age due to insufficient data on safety and efficacy.

### **Other medicines and Gemcitabine**

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; or if you have recently undergone radiotherapy or are going to have radiotherapy.

### **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 for advice before taking 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**

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.

The amount of alcohol in this medicinal product may impair your ability to drive or use machines.

Do not drive a car or use machinery until you are sure that Gemcitabine treatment is not affecting your alertness.

### **Gemcitabine contains ethanol**

This medicinal product contains 395 mg ethanol (alcohol) per ml concentrate, equivalent to 500 ml beer, 200 ml wine per dose of 2 g. Harmful for those suffering from alcoholism. To be taken into account in high-risk groups such as patients with liver disease or epilepsy. The amount of alcohol in this medicinal product may alter the effects of other medicines. The amount of alcohol in this medicinal product may impair your ability to drive or use machines.

### **Gemcitabine contains sodium**

Gemcitabine contains 3.95 mg (< 1 mmol) of sodium per ml concentrate. To be taken into consideration by patients on a controlled sodium diet.

### **3. How to use Gemcitabine**

The recommended 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 diluted the Gemcitabine concentrate 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:**

- Fever or infection (common (may affect up to 1 in 10 people)): if you have a temperature of 38°C 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 (may affect up to 1 in 100 people)).
- Pain, redness, swelling or sores in your mouth (common (may affect up to 1 in 10 people)).
- Allergic reactions: if you develop skin rash (very common (may affect more than 1 in 10 people)) / itching (common (may affect up to 1 in 10 people)), or fever (very common (may affect more than 1 in 10 people)).
- Anaphylactic reactions (severe hypersensitivity / allergic reaction): 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 (tachycardia) and you may feel you are going to faint (a spontaneous loss of consciousness caused by insufficient blood to the brain) (very rare (may affect up to 1 in 10,000 people)).
- Tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have less haemoglobin than normal which is very common (may affect more than 1 in 10 people)).
- 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 (may affect more than 1 in 10 people)).
- 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).
- Heart attack (myocardial infarction) (rare (may affect up to 1 in 1,000 people)).
- Haemolytic uraemic syndrome: 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. It may be fatal (uncommon (may affect up to 1 in 100 people)).
- Potentially life-threatening cutaneous reactions (Toxic epidermal necrolysis (TEN), Stevens-Johnson Syndrome (SJS)): severe rash with itching, blistering or peeling of the skin. Skin rashes are often accompanied by flu-like symptoms (very rare (may affect up to 1 in 10,000 people)).
- Headaches with changes in vision, confusion, seizures or fits (posterior reversible encephalopathy syndrome) (very rare (may affect up to 1 in 10,000 people)).
- Generalised swelling, shortness of breath or weight gain, since you may have fluid leakage from your blood vessels into the tissues (capillary leak syndrome) (very rare (may affect up to 1 in 10,000 people)).

**Other 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 neutropaenia)  
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

**Uncommon side effects (may affect up to 1 in 100 people)**

Stroke  
Irregular heart beat (arrhythmia)  
Heart failure  
Interstitial pneumonitis (scarring of the air sacs of the lung)  
Spasm of the airways (wheeze)  
Abnormal chest X ray/scan (scarring of the lungs)  
Serious liver damage, including liver failure which could be life-threatening  
Kidney failure  
Haemolytic uraemic syndrome (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, it may be fatal)

**Rare side effects (may affect up to 1 in 1,000 people)**

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

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

Anaphylactic reaction (severe hypersensitivity / allergic reaction)  
Increased platelet count  
Ischemic colitis (inflammation of the lining of the large bowel, caused by reduced blood supply)  
Sloughing of skin and severe skin blistering (Toxic epidermal necrolysis, Stevens-Johnson Syndrome)  
Capillary leak syndrome (leakage of fluid from the blood vessels into the tissue)  
Posterior reversible encephalopathy syndrome (a neurologic condition with symptoms including seizures, headache, confusion and changes in vision)

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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); e-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

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.

### *Unopened container*

Store below 25°C.

Do not refrigerate or freeze.

### *After first opening*

Chemical and physical in-use stability has been demonstrated for 28 days at 25°C.

From a microbiological point of view, once opened, the product may be stored for a maximum of 28 days at 25°C. Other in-use storage times and conditions are the responsibility of the user.

### *Solution for infusion*

Chemical and physical in-use stability after dilution in 0.9% sodium chloride solution (5.2 mg/ml gemcitabine) has been demonstrated for 5 days at 2°C to 8°C and about 30°C.

From a microbiological point of view, the solution for infusion 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°C to 8°C unless dilution has taken place in controlled and validated aseptic conditions.

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice any signs of particles.

## **6. Contents of the pack and other information**

### **What Gemcitabine contains**

- The active substance is gemcitabine (as gemcitabine hydrochloride). Each ml of concentrate for solution for infusion contains 40 mg gemcitabine (as gemcitabine hydrochloride). Each 5 ml vial contains 200 mg gemcitabine (as gemcitabine hydrochloride). Each 25 ml vial contains 1 g gemcitabine (as gemcitabine hydrochloride). Each 50 ml vial contains 2 g gemcitabine (as gemcitabine hydrochloride).
- The other ingredients are disodium phosphate anhydrous, sodium hydroxide, hydrochloric acid, ethanol anhydrous, water for injections.

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

Gemcitabine concentrate for solution for infusion is a clear, colourless or pale yellow solution.

Gemcitabine is in colourless glass vials with rubber stopper and sealed with aluminium caps with polypropylene disc. Each vial will be packed with or without a protective plastic overwrap.

### *Pack sizes*

1 x 5 ml vial

1 x 25 ml vial

1 x 50 ml vial

Not all pack sizes may be marketed.

### **Marketing Authorisation Holder and Manufacturer**

**Marketing Authorisation Holder**

Actavis Group PTC ehf.  
Reykjavíkurvegi 76-78  
220 Hafnarfjörður  
Iceland

**Manufacturers**

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

Actavis Italy S.p.A. – Nerviano Plant  
Viale Pasteur 10  
20014 Nerviano (MI)  
Italy

**This medicinal product is authorised in the Member States of the EEA under the following names:**

Netherlands: Gemcitabine Actavis 40 mg/ml concentraat voor oplossing voor infusie

Austria: Gemcitabin Actavis 40 mg/ml Konzentrat zur Herstellung einer Infusionslösung

Bulgaria, Estonia, Iceland, Italy, Poland: Gembin

Cyprus: Gitrabin

Germany: Gemcitabin-Actavis 40 mg/ml Konzentrat zur Herstellung einer Infusionslösung

Denmark, Malta, Norway, Sweden: Gemcitabin Actavis

Spain: Gemcitabina Actavis 40 mg/ml concentrado para solución para perfusion EFG

Hungary: Gitrabin 40mg/ml injekció

Ireland: Gemcitabine 40mg/ml Concentrate for solution for Infusion

Lithuania: Gembin 40 mg/ml koncentratas infuziniam tirpalui

Latvia: Gembin 40 mg/ml koncentrāts infūziju šķīduma pagatavošanai, 200 mg/ 5 ml; Gembin 40 mg/ml koncentrāts infūziju šķīduma pagatavošanai, 1000 mg/ 25 ml; Gembin 40 mg/ml koncentrāts infūziju šķīduma pagatavošanai, 2000 mg/ 50 ml

Portugal: Gemcitabina Actavis

Romania: Gitrabin 40 mg/ ml concentrate for solution for infusion (200 mg/ 5 ml, 1000 mg/ 25 ml, 2000 mg/ 50 ml)

Slovenia: Gitrabin 40mg/ml koncentrat za raztopino za infundiranje

**This leaflet was last revised in September 2014.**

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

### **Instruction for use**

Cytotoxic

#### ***Handling***

The normal safety precautions for cytostatic agents must be observed when preparing and disposing of the infusion solution. Pregnant personnel should not handle the product. 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.

#### ***Instructions for dilution***

**Instructions for dilution should be strictly followed in order to avoid adverse events.**

The only approved diluent for dilution of Gemcitabine concentrate for solution for infusion is sodium chloride 9 mg/ml (0.9%) solution for injection (without preservative).

1. Use aseptic technique during dilution of gemcitabine for intravenous infusion administration.
2. The total quantity of the gemcitabine 40 mg/ml concentrate for solution for infusion required for an individual patient should be diluted into at least 500 ml of sterile sodium chloride 9 mg/ml (0.9%) solution for injection (without preservative) and infused over 30 min. Further dilution with the same diluent can be done. Diluted solution is a clear colourless or light straw-coloured solution.
3. Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.

Any unused product or waste material should be disposed of in accordance with local requirements.

#### ***Storage conditions***

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