Package leaflet: Information for the user

Gemcitabine Actavis 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.
- 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 Actavis is and what it is used for

Gemcitabine Actavis belongs to a group of medicines called “cytotoxics”. These medicines kill dividing cells, including cancer cells.

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

Gemcitabine Actavis 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 Actavis

Do not use Gemcitabine Actavis:
- 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 Actavis. 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 Actavis
- 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 Actavis
- 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 Actavis.
- If you have been vaccinated recently, please tell your doctor as this can possibly cause bad effects with Gemcitabine Actavis.
- 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 these may be a sign of fluid leaking from your small blood vessels into the tissues.

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 Actavis
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 or pharmacist for advice before taking this medicine. The use of Gemcitabine Actavis should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking Gemcitabine Actavis during pregnancy.

Breast-feeding
If you are breast-feeding, tell your doctor.
You must discontinue breast-feeding during Gemcitabine Actavis treatment.

Fertility
Men are advised not to father a child during and up to 6 months following treatment with Gemcitabine Actavis 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 Actavis may make you feel sleepy.
Do not drive a car or use machinery until you are sure that Gemcitabine Actavis treatment is not affecting your alertness.

3. How to use Gemcitabine Actavis

The recommended dose of Gemcitabine Actavis 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 Actavis infusion depends on the type of cancer that you are being treated for.

A hospital pharmacist or doctor will have diluted the Gemcitabine Actavis concentrate before it is given to you.

You will always receive Gemcitabine Actavis by infusion into one of your veins. The infusion will last approximately 30 minutes.

This medicinal product is not recommended for use in children under 18 years of age.

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:
- 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).
- Allergic reactions: Mild to moderate skin rash (very common); itching (common); or fever (very common).
- 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).
- Difficulty breathing (it is common to have mild breathing difficulty soon after the /…/ 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, often accompanied by flu-like symptoms (Stevens-Johnson syndrome, toxic epidermal necrolysis) (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.

Other side effects with Gemcitabine Actavis 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)
Low Haemoglobin level (anaemia)

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 which could be life-threatening
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 (ischemic 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.

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; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Gemcitabine Actavis

Keep this medicine out of the sight and reach of children.

Unopened container
Store in a refrigerator (2°C – 8°C)

After first opening
Chemical and physical in use stability has been demonstrated for 28 days at 25°C.
From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Solution for infusion
Chemical and physical in-use stability has been demonstrated for 28 days at 2ºC to 8ºC and about 25ºC upon dilution in 0.9% sodium chloride solution to a final concentration in the range between 2 – 25 mg/ml (2.0 mg/ml, 12 mg/ml and 25 mg/ml). Diluted solutions are stable when packaged into either PVC or PE infusion bags.
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 carton and the vial after EXP. 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 Actavis 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 hydrochloric acid (E-507) for pH adjustment, water for injections.

What Gemcitabine Actavis looks like and contents of the pack

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

Gemcitabine Actavis is contained in type I colourless glass vials with bromobutyl rubber stoppers 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

Actavis Group PTC ehf.
Reykjavikurvegi 76-78,
220 Hafnarfjordur,
Iceland

Manufacturer
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:

The Netherlands	Gemcitabine Actavis PTC 40 mg/ml, concentraat voor oplossing voor infusie
Bulgaria	Gemcitabine Actavis 40mg/ml Concentrate for Solution for Infusion
Estonia	Gemcitabine Actavis
Ireland	Gemcitabine Actavis 40mg/ml Concentrate for Solution for Infusion
Iceland	Gitrabin
Norway	Gitrabin
Slovenia	Gemcitabin Actavis 40 mg/ml koncentrat za raztopino za infundiranje
United Kingdom	Gemcitabine 40mg/ml Concentrate for Solution for Infusion

This leaflet was last revised in February 2019

The following information is intended for healthcare professionals only:

Instruction for use

Gemcitabine Actavis 40 mg/ml concentrate for solution for infusion

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

- Use aseptic technique during dilution of gemcitabine for intravenous infusion administration.

- Diluted solution is a clear colourless or light straw-coloured solution.

- 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
After first opening
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From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Solution for infusion
Chemical and physical in-use stability has been demonstrated for 28 days at 2ºC to 8ºC and about 25ºC upon dilution in 0.9% sodium chloride solution to a final concentration in the range between 2 – 25 mg/ml (2.0 mg/ml, 12 mg/ml and 25 mg/ml). The pH of the diluted solution is in the range of 2-3 and the osmolality is approximately 285 mOsm/kg. Diluted solutions are stable when packaged into either PVC or PE infusion bags.
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.