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 Gemcitabine Actavis before it is given to you. Take special care with Gemcitabine Actavis 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 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 evaluate your kidney and liver function. Please tell your doctor if:

- you have, or have previously had liver disease, heart disease or vascular disease
- 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).

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.

Taking other medicines Please tell your doctor or hospital pharmacist if you are taking or have recently taken any other medicines.

**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. BEFORE YOU USE GEMCITABINE ACTAVIS**

You should not be given Gemcitabine Actavis

- if you are allergic (hypersensitive) to gemcitabine or any of the other ingredients of Gemcitabine Actavis
- if you are breast-feeding

Driving and using machines Gemcitabine Actavis 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 Actavis has not made you feel sleepy. Important information about some of the ingredients of Gemcitabine Actavis contains 3.56 mg (<1 mmol) of sodium in each 200 ml vial and 17.81 mg (<1 mmol) sodium in each 1000 mg vial. To be taken into consideration by patients on a controlled sodium diet.

**3. HOW TO USE GEMCITABINE ACTAVIS**

The usual 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.
medicines, including vaccinations and medicines obtained without a prescription.

**Pregnancy and breast-feeding**
If you are pregnant, or thinking about becoming pregnant, tell your doctor. 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.

If you are breast-feeding, tell your doctor.
You must discontinue breast-feeding during Gemcitabine Actavis treatment.
You will always receive Gemcitabine Actavis 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, Gemcitabine Actavis can cause side effects, although not everybody gets them.

Frequencies of the observed side effects are defined as:
- **very common**: affects more than 1 user in 10
- **common**: affects 1 to 10 users in 100
- **uncommon**: affects 1 to 10 users in 1,000
- **rare**: affects 1 to 10 users in 10,000
- **very rare**: affects less than 1 user in 10,000
- **not known**: frequency can’t be estimated from the available data

**You must contact your doctor immediately if you notice any of the following:**
- Fever or infection (common): 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).
- Pain, redness, swelling or sores in your mouth (common).
- Allergic reactions: If you develop skin rash (very common) /Itching (common), or fever (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).

**• 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 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)**

**Side effects with Gemcitabine Actavis may include:**

**Very common side effects**
- 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**
- 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**
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

**Kidney failure**

**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. If prepared aseptically, the diluted solution can be stored for 24 hours at 25°C.
Do not use Gemcitabine Actavis after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.
Gemcitabine Actavis should not be used if there are any signs of particles.

**6. FURTHER INFORMATION**

**What Gemcitabine Actavis contains**
- The active substance is gemcitabine (as gemcitabine hydrochloride). After reconstitution one ml of Gemcitabine Actavis contains 38 mg gemcitabine. One vial Gemcitabine Actavis contains 200 mg or 1 g gemcitabine.
- The other ingredients are mannitol E421, sodium acetate trihydrate and sodium hydroxide 1 N (for pH adjustment)

**What Gemcitabine Actavis looks like and contents of the pack**
Gemcitabine Actavis is a white to off-white compact aggregate powder. After reconstitution in 0.9% sodium chloride solution, the solution is clear to pale opalescent and colourless to pale yellow.
Gemcitabine Actavis is in colourless glass vials with bromobutyl rubber stopper.
Each vial will be packed with or without a protective plastic overwrap or vial shield.

**Pack sizes**
One vial containing 200 mg Gemcitabine.
One vial containing 1 g Gemcitabine.

**Marketing Authorisation Holder**
Actavis Group PTC ehf., Reykjavikurvegur 76-78, 220 Hafnarfjordur, Iceland

**Manufacturer**
Actavis Italy S.p.A., Via Pasteur 10, 20014 Nerviano (MI), Italy
<table>
<thead>
<tr>
<th>This leaflet was last approved in</th>
<th>May 2011.</th>
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<tbody>
<tr>
<td><strong>For any inquiries:</strong> Please forward to</td>
<td><a href="mailto:meeainfo@actavis.com">meeainfo@actavis.com</a></td>
</tr>
<tr>
<td><strong>The following information is intended for medical or healthcare professionals only:</strong></td>
<td></td>
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<tr>
<td><strong>Instruction for use</strong></td>
<td></td>
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<tr>
<td>Gemcitabine Actavis 200 mg</td>
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<td>Gemcitabine Actavis 1 g</td>
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<tr>
<td>Lyophilisate for solution for infusion</td>
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<tr>
<td><strong>Cytotoxic</strong></td>
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<tr>
<td><strong>Handling</strong></td>
<td>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.</td>
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<td><strong>Instructions for dilution</strong></td>
<td>The only approved diluent for reconstitution of Gemcitabine sterile powder is sodium chloride 9 mg/ml (0.9%) solution for injection (without preservative). Due to solubility considerations, the maximum concentration for gemcitabine upon reconstitution is 40 mg/ml. Reconstitution at concentrations greater than 40 mg/ml may result in incomplete dissolution and should be avoided.</td>
</tr>
<tr>
<td>1. Use aseptic technique during the reconstitution and any further dilution of Gemcitabine for intravenous infusion administration.</td>
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<tr>
<td>2. To reconstitute, add 5 ml of sterile sodium chloride 9 mg/ml (0.9%) solution for injection, to the 200 mg vial or 25 ml sterile sodium chloride 9 mg/ml (0.9%) solution for injection, to the 1000 mg vial. The total volume after reconstitution is 5.26 ml (200 mg vial) or 26.3 ml (1000 mg vial) respectively. This yields a Gemcitabine concentration of 38 mg/ml, which includes accounting for the displacement volume of the lyophilized powder. Shake to dissolve. Further dilution with sterile sodium chloride 9 mg/ml (0.9%) solution for injection can be done. Reconstituted solution is a clear colourless to light straw-coloured solution.</td>
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<tr>
<td>3. Parenteral medicinal products should be inspected visually for particulate matter and discoloration prior to administration. If particulate matter is observed, do not administer. Reconstituted solutions should be used immediately or may be stored for 24 hours at 25°C if prepared in an appropriately controlled aseptic condition. Reconstituted solutions should not be refrigerated, as crystallisation may occur.</td>
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<tr>
<td><strong>Disposal</strong></td>
<td>Gemcitabine solutions are for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.</td>
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