Ppackage leaflet: Iinformation for the user

[National approved name] 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, nurse or and pharmacist.
- If you get any side effects, talk to your doctor, pharmacist and 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

[National approved name] belongs to a group of medicines called "cytotoxics". These medicines kill dividing cells, including cancer cells.

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

This medicine 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 Pprecautions:
Before the first infusion you will have samples of your blood taken to evaluate check if your have sufficient kidney and liver and kidneys function are working well enough for you to receive this medicine. Before each infusion you will have samples of your blood taken to evaluate 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 evaluate check how well your kidneys and liver function are working.

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

~~Please tell your doctor if:~~

- 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 ~~(may be a sign of kidney failure).~~ , 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.

- If you are suffering from alcoholism, as this medicinal product contains ethanol (alcohol)
- If you are suffering from epilepsy, as this medicinal product contains ethanol (alcohol)

~~Men are advised not to father a child during and up to 6 months following treatment with Gemciatbine. 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.~~

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 ~~T~~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.

The amount of alcohol in this medicinal product may alter the effects of other medicines.

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.

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

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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
[National approved name] 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.

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

[National approved name] contains ethanol and sodium:
This medicinal product contains 42.1% - ethanol (alcohol) which corresponds to 421 mg ethanol per ml of concentrate, i.e.:
- up to 2.1 g of ethanol per 5 ml vial, equivalent to 42 ml of beer, 18 ml of wine.
- up to 10.5 g of ethanol per 25 ml vial, equivalent to 210 ml of beer, 88 ml of wine.
- up to 21.1 g of ethanol per 50 ml vial, equivalent to 421 ml of beer, 175 ml of wine.

Harmful for those suffering from alcoholism.

To be taken into account in pregnant ~~or breast feeding~~ women, children and high-risk groups such as patients with liver disease or epilepsy.

The amounts of alcohol in this medicinal product may alter the effects of other medicines.

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

This medicine contains3.40 mg/ml to 3.70 mg/-ml (0.15 mmol/ml to 0.16 mmol/ml) sodium. This should be taken into consideration by patients on a controlled sodium diet.

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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 diluted the Gemcitabine concentrate before it is given to you.

You will always receive this medicine only after dilution 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 or 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 1 in 100 people~~
~~- Rare: may affect 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 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).
- 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)

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- 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 (haemolytic uraemic syndrome). It may be fatal (uncommon).

- ~~———~~Difficulty breathing (it is very common to have mild breathing difficulty soon after the ~~———~~[National approved name] 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 ~~S~~side effects with [National approved name] may include:

Very common~~:~~ (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

~~Kidney problems: found through abnormal blood test results~~
- Blood in urine
- Abnormal urine tests: protein in urine
- Flu like symptoms including fever,
- ~~Oedema (s~~Swelling of ankles, fingers, feet, face (oedema)

Common~~:~~ (may affect up to 1 in 10 people)

~~Fever accompanied by low white blood cell count (febrile neutropaenia)~~
- ~~Anorexia (p~~Poor appetite (anorexia)
- Headache
- Insomnia
- Sleepiness
- Cough
- Runny nose
- Constipation
- Diarrhoea

~~Pain, redness, swelling or sores in the mouth~~
- Itching
- Sweating
- Muscle pain
- Back pain
- Fever
- Weakness

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- Chills

Uncommon: (may affect up to 1 in 100 people)
- ~~Interstitial pneumonitis (s~~Scarring of the air sacs of the lung (interstitial pneumonitis)
- Wheeze (~~S~~spasm of the airways ~~(wheeze~~)
- Scarring of the lungs (~~A~~abnormal chest X ray/scan ~~(scarring of the lungs~~)
- ~~Irregular heart beat (arrhythmia)~~
- Heart failure
- Kidney failure
- Serious liver damage, including liver failure
- Stroke
- ~~Haemolytic uraemic syndrome (a disease characterized by haemolytic anaemia, acute renal failure and a low platelet count)~~

Rare: (-may affect up to 1 in 1,000 people)
- ~~Heart attack (myocardial infarction)~~
- 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).
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- ~~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~~
- Scarring of the air sacs of the lung associated with radiation therapy (radiation toxicity)

- Gangrene of fingers or toes
- ~~Clinical signs of peripheral vasculitis (inflammation of the blood vessels)~~
- ~~Sloughing of skin and severe skin blistering~~
- Inflammation of the blood vessels (peripheral vasculitis)

Very rare: (-may affect up to 1 in 10,000 people)
- Increased platelet count
- ~~Anaphylactic reaction (severe hypersensitivity/ allergic reaction)~~
- ~~Ischaemic colitis (inflammation of the lining of the large bowel, caused by reduced blood supply)~~
- ~~Potentially life-threatening cutaneous reactions with widespread purpuric macules and epidermal detachment (Toxic epidermal necrolysis, Stevens-Johnson Syndrome).~~
- 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.

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.

~~If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.~~

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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 carton and label after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage condition.

Shelf life after dilution(Solution for Infusion):
Chemical and physical in-use stability after dilution in 0.9 % w/v sodium chloride solution has been demonstrated for 3 days at 2°C to 8°C or at 30°C.

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°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

This medicine is for single use only. Discard any unused contents.

If the solution appears discoloured or contains visible particles, it should be discarded.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [National approved name] contains
The active substance is gemcitabine (as 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 hydrochloride)
Each 25 ml vial contains 1000 mg gemcitabine (as hydrochloride)
Each 50 ml vial contains 2000 mg gemcitabine (as hydrochloride).

The other ingredients are: Ethanol (96%), sodium hydroxide (E524) (for pH adjustment), hydrochloric acid (E507) (for pH adjustment) and water for injections

What [National approved name] looks like and contents of the pack
This medicinal product is a concentrate for solution for infusion.
[National approved name] is a concentrate for solution for infusion and a clear, colourless to slightly yellow solution.

Each pack contains 1 vial of 5 ml, 25 ml or 50 ml of solution.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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Fresenius Kabi Oncology Plc.
Lion Court, Farnham Road, Bordon
Hampshire, GU350NF
United Kingdom

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

Austria	Gemcitabine Kabi 40 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Belgium	Gemcitabine Fresenius Kabi 40 mg/ml concentraat voor oplossing voor infusie
Bulgaria	Gemcitabine Kabi 40 mg/ml концентрат за инфузионен разтвор
Cyprus	Gemcitabine Kabi 40 mg/ml πυκνό διάλυμα για παρασκευή διαλύματος προς έγχυση
Czech Republic	Gemcitabine Kabi 40 mg/ml koncentrát pro infuzní roztok
Germany	Gemcitabine Kabi 40 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Denmark	Gemkabi
Estonia	Gemcitabine Kabi 40 mg/ml
Greece	Gemcitabine Kabi 40 mg/ml πυκνό διάλυμα για παρασκευή διαλύματος προς έγχυση
Spain	Gemcitabina Kabi 40 mg/ml concentrado para solución para perfusión EFG
Finland	Gemcitabin Fresenius Kabi 40mg/ml infuusiokonsentraatti, liuosta varten
France	Gemcitabine Kabi 40 mg/ml solution à diluer pour perfusion
Hungary	Gemcitabin Kabi 40 mg/ml koncentrátum oldatos infúzióhoz
Ireland	Gemcitabine 40 mg/ml concentrate for solution for infusion
Iceland	Gemcitabine Fresenius Kabi
Italy	Gemcitabina Fresenius 40 mg/ml concentrato per soluzione per infusione
Latvia	Gemcitabine Kabi 40 mg/ml koncentrāts infūziju šķīduma pagatavošanai
Lithuania	Gemcitabine Kabi 40 mg/ml koncentratas infuziniam tirpalui
Luxembourg	Gemcitabine Kabi 40 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Malta	Gemcitabine 40 mg/ml concentrate for solution for infusion
The Netherlands	Gemcitabinee Fresenius Kabi 40 mg/ml concentraat voor oplossing voor infusie
Norway	Gemkabi 40 mg/ml konsentrat til infusjonsvæske
Poland	Gemcitabine Kabi
Portugal	Gemcitabina Kabi
Romania	Gemcitabina Kabi 40 mg/ml concentrat pentru soluție perfuzabilă
Sweden	Gemcitabin Fresenius Kabi 40 mg/ml koncentrat till infusionsvätska, lösning
Slovenia	Gemcitabin Kabi 40 mg/ml koncentrat za raztopino za infundiranje
Slovak Republic	Gemcitabine Kabi 40 mg/ml, infúzny koncentrát
United Kingdom	Gemcitabine 40 mg/ml concentrate for solution for infusion

This leaflet was last revised in 01/2015~~{MM/YYYY}~~

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The following information is intended for 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 [National approved name] 40 mg/ml 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

Shelf life after dilution:

Chemical and physical in-use stability after dilution in 0.9 % sodium chloride solution has been demonstrated for 3 days at 2°C to 8°C or at 30°C.

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°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

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