PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

GEMCITABINE 200 mg RTU FRESENIUS

GEMCITABINE 1 g RTU FRESENIUS

GEMCITABINE 2 RTU FRESENIUS

Concentrate for solution for infusion

Sugar-free.

Read all of this leaflet carefully before you are given GEMCITABINE FRESENIUS RTU

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- **GEMCITABINE FRESENIUS RTU** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What GEMCITABINE FRESENIUS RTU is and what it is used for

GEMCITABINE FRESENIUS RTU belongs to a group of medicines called “cytotoxic medicines”. These medicines kill dividing cells, including cancer cells.

GEMCITABINE FRESENIUS RTU may be given alone, or in combination with other anti-cancer medicines, depending on the type of cancer. **GEMCITABINE FRESENIUS RTU** is used in the treatment of various types of

cancer.

2. What you need to know before you use GEMCITABINE FRESENIUS RTU

GEMCITABINE FRESENIUS RTU should not be administered to you:

- if you are hypersensitive (allergic) to gemcitabine or any of the other ingredients of **GEMCITABINE FRESENIUS RTU** (listed in section 6).
- if you are pregnant or breastfeeding;
- if you are a child.

Warnings and precautions

Tell your doctor or health care provider before being given the injection:

- if you have, or have previously had liver disease;
- if you have heart disease or vascular disease;
- if you have kidney disease;
- if you have recently had, or are going to have radiotherapy;
- if you have recently been vaccinated (for example, against yellow fever);
- if you develop breathing difficulties or feel very weak and are very pale (may be a sign of kidney failure);
- if you develop generalised swelling, shortness of breath or weight gain, as this may be a sign of fluid leaking from your small blood vessels into the tissue, and symptoms of a serious condition called Capillary Leak Syndrome (CLS);
- if during treatment with this medicine you get symptoms such as headache with confusion, seizures (fits) or changes in vision. You should contact your doctor right away, as this could be a less frequent nervous system side effect name posterior reversible encephalopathy syndrome (PRES);
- if you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using gemcitabine.

Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis and acute generalized exanthematous pustulosis (AGEP) have been reported in association with gemcitabine treatment. Seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.
Before the first infusion, samples of your blood will be taken to evaluate if you have sufficient kidney and liver function.

Before each infusion samples of your blood will be taken to evaluate if you have enough blood cells to receive **GEMCITABINE FRESENIUS RTU**. 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.

Other medicines and GEMCITABINE FRESENIUS RTU

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

- If you receive **GEMCITABINE FRESENIUS RTU** together with radiotherapy, or up to 7 days apart, you have a higher chance for toxic side effects. *See "Warnings and special precautions".*
- You should not receive yellow fever and/or other live vaccines together with **GEMCITABINE FRESENIUS RTU**. You may become seriously ill, because your immune system is affected by the treatment with **GEMCITABINE FRESENIUS RTU.**

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist or other health care provider for advice before taking this medicine.

Pregnancy

The use of **GEMCITABINE FRESENIUS RTU** should be avoided during pregnancy. Your doctor will discuss with you the potential risk of **GEMCITABINE FRESENIUS RTU** during pregnancy.

It is advised that contraception should continue 6 months after receiving the last dose of **GEMCITABINE FRESENIUS RTU**

Breastfeeding

If you are breastfeeding, tell your doctor. You must discontinue breastfeeding during **GEMCITABINE FRESENIUS RTU** treatment.

Fertility

Men are advised not to father a child during and up to 6 months following treatment with **GEMCITABINE FRESENIUS RTU**. 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

It is not always possible to predict to what extent **GEMCITABINE FRESENIUS RTU** may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which **GEMCITABINE FRESENIUS RTU** affects them.

GEMCITABINE FRESENIUS RTU may make you feel sleepy. Do not drive a car or use machinery until you are sure that treatment with **GEMCITABINE FRESENIUS RTU** has not made you feel sleepy.

GEMCITABINE FRESENIUS RTU contains sodium

GEMCITABINE 200 mg FRESENIUS RTU contains a maximum of 2,4 mg (<1 mmol) sodium per vial.

GEMCITABINE 1 g FRESENIUS RTU contains a maximum of 12,1 mg (<1 mmol) sodium per vial.

GEMCITABINE 2 g FRESENIUS RTU contains a maximum of 24,2 mg sodium per vial. This should be taken into consideration if you are on a sodium-controlled diet.

3. How to use GEMCITABINE FRESENIUS RTU

You will not be expected to give yourself **GEMCITABINE FRESENIUS RTU**. It will be given to you by a person who is qualified to do so.

You should only receive treatment with **GEMCITABINE FRESENIUS RTU** if prescribed and overseen by a doctor who specialises in the use of anti-cancer chemotherapy

Your doctor will tell you how long your treatment with **GEMCITABINE FRESENIUS RTU** will last. Do not stop treatment early unless advised by your doctor.

The usual dose of **GEMCITABINE FRESENIUS RTU** is between 1 g/m2 and 1,25 g/m2. 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.

A hospital pharmacist or doctor will dilute the **GEMCITABINE FRESENIUS RTU** concentrate in sodium chloride infusion solution before it is given to you.

You will always receive **GEMCITABINE FRESENIUS RTU** by infusion into one of your veins. The infusion will last approximately 30 minutes.

How frequently you receive your **GEMCITABINE FRESENIUS RTU** depends on the type of cancer that you are being treated for.

GEMCITABINE FRESENIUS RTU is not recommended for use in children.

If you have further questions on the use of this product ask your doctor or pharmacist.

If you receive more GEMCITABINE FRESENIUS RTU than you should

Since a healthcare provider will administer **GEMCITABINE FRESENIUS RTU**, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If GEMCITABINE FRESENIUS RTU is not administered to you

Since a healthcare provider will administer **GEMCITABINE FRESENIUS RTU**, it is unlikely that the dose will be missed. If you have the impression that the effect of **GEMCITABINE FRESENIUS RTU** is too strong or too weak, tell your doctor or pharmacist.

4. Possible side effects

GEMCITABINE FRESENIUS RTU can have side effects.

Not all side effects reported for **GEMCITABINE FRESENIUS RTU** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **GEMCITABINE FRESENIUS RTU**, please consult your health care provider for advice.

If any of the following happens, tell your doctor immediately; he/she will decide whether they will stop the administration of **GEMCITABINE FRESENIUS RTU**:

- swelling of the face, tongue and/or throat causing difficulty in swallowing, breathing with difficulty, wheezing, severe dizziness, very fast heartbeat and heavy sweating (anaphylactoid reaction);
- a severe allergic skin reaction with peeling, itching, fever, hives (nettle rash), chills, swelling, blistering of the skin, mouth or genitals (‘Stevens-Johnson syndrome’ or ‘toxic epidermal necrolysis’).

These are all very serious side effects. If you have them, you may have had a serious reaction to **GEMCITABINE FRESENIUS RTU**. You may need urgent medical attention.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- bleeding that will not stop, reddish or pinkish urine, bleeding from gums, nose or mouth or any bleeding that

would not stop, reddish or pinkish urine, unexpected bruising (as you might have thrombocytopenia, a less than normal platelet count, which occurs frequently);

- unusual tiredness or weakness; you may have too few red blood cells, or their haemoglobin content is too low (anaemia);
- numbness or weakness, confusion or trouble understanding other people, trouble speaking, visual loss, severe headache that comes on for no known reason. You may have developed posterior reversible encephalopathy syndrome or had a stroke;
- irregular heartrate (dysrhythmia) or shortness of breath with swollen ankles (congestive heart failure);
- severe chest pain (myocardial infarction);
- yellowing of the skin and whites of the eyes (liver problems);
- swelling in the legs, ankles and feet, due to a build-up of fluid (oedema), swelling in your abdomen, due to a build-up of fluid;
- death of tissue caused by loss of blood flow and usually followed by infection (gangrene) in fingers or toes;
- problems with breathing, which do not improve soon after you have received your dose of **GEMCITABINE FRESENIUS RTU**. You may have a severe lung reaction, with scarring of the air sacs of the lung (your doctor will see this on a chest x-ray or scan);
- decreased urination or blood in the urine, abdominal pain, vomiting and occasionally fever (haemolytic uremic syndrome).
- a red, scaly widespread rash with bumps under the swollen skin (including your skin folds, trunk, and upper extremities) and blisters accompanied by fever (Acute Generalized Exanthematous Pustulosis (AGEP)) (frequency not known).

These are all very serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

<u>Frequent side effects:</u>

- fever (a temperature above 38 °C), sweating, tiredness, sore throat (a low white blood cell count)
- poor appetite (anorexia)
- sleeplessness
- headache
- cough, runny nose
- feeling sick (nausea), vomiting (being sick), loose stools or constipation

- sores inside your mouth, with a painful, red inner mouth
- liver problems (diagnosed with blood tests)
- skin rash, frequently with itching, or sweating
- hair loss
- back pain, muscle pain
- blood in the urine, protein in the urine.
- flu-like signs, fever, chills
- swelling of ankles, hands, feet and face
- weakness.

Less frequent side effects:

- increased platelet count (seen in blood test)
- sleepiness
- inflammation of blood vessels (you may feel unwell with fever, sweats and tiredness)
- low blood pressure (as shown by blood pressure tests)
- injection site reactions with redness, pain and swelling.
- radiation toxicity (scarring of the air sacs of the lung)
- radiation recall (a skin rash like severe sunburn which may occur on skin that had been exposed to radiotherapy in the past).

Frequency unknown:

- when bacteria and their toxins circulate in the blood and starts to damage the organs (sepsis)
- inflammation of the lining of the large bowel, caused by reduced blood supply (ischaemic colitis)
- a condition where eosinophils, a type of cell ordinarily found in the blood, accumulate in the lungs (pulmonary eosinophilia).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of

GEMCITABINE RTU FRESENIUS.

Patients are asked to report any suspected adverse drug reactions to their healthcare provider or

Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com

and to the relevant medicine's regulatory authority in the country where the product is marketed.

5. How to store GEMCITABINE FRESENIUS RTU

Store all medicine out of reach of children.

Do not use after the expiry date (EXP) which is stated on the carton and vial. The expiry date refers to the last day of that month.

GEMCITABINE FRESENIUS RTU does not require any special storage conditions.

Proposed shelf life of the diluted injection:

Chemical and physical in-use stability after dilution in 0,9 % m/v sodium chloride solution at a concentration of 0,1 mg/ml and 5 mg/ml has been demonstrated for 7 days at 2 °C to 8 °C or at 25 °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. Any unused medicine must be disposed of by the healthcare staff.

Return all unused medicines to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What GEMCITABINE FRESENIUS RTU contains

The active substance is gemcitabine.

Each ml of the concentrate for solution for infusion contains 38 mg gemcitabine (as gemcitabine hydrochloride).

Each vial contains either 200 mg, 1 000 mg or 2 000 mg gemcitabine (as gemcitabine hydrochloride).

The other ingredients are macrogol 400, propylene glycol, sodium hydroxide, hydrochloric acid and water for injection.

What GEMCITABINE FRESENIUS RTU looks like and contents of the pack

GEMCITABINE FRESENIUS RTU is a concentrate for solution for infusion. The concentrate is a clear, colourless to slightly yellow solution. It is filled in clear glass vials sealed with rubber stoppers and aluminium flip-off seals.

Pack sizes:

Each 6 ml vial contains 200 mg gemcitabine.

Each 30 ml vial contains 1000 mg gemcitabine.

Each 100 ml vial contains 2000 mg gemcitabine.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

Fresenius Kabi South Africa (Pty) Limited

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GEMCITABINE 200 mg RTU FRESENIUS: 50/26/0871

GEMCITABINE 1 g RTU FRESENIUS: 50/26/0872

GEMCITABINE 2 g RTU FRESENIUS: 50/26/0874

Access to the corresponding Professional Information