Applicant: Oethmaan Biosims (Pty) Ltd	**SAHPRA approval date:** 9 December 2024
Product: GEMCITABINE 200 mg OETHMAAN GEMCITABINE 1 g OETHMAAN	**Dosage form and strength:** Each vial contains: Gemcitabine hydrochloride equivalent to 200 mg Gemcitabine free base. Each vial contains: Gemcitabine hydrochloride equivalent to 1 g Gemcitabine free base.

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

GEMCITABINE 200 mg OETHMAAN powder for solution for infusion

200 Gemcitabine hydrochloride

Sugar free

GEMCITABINE 1 g OETHMAAN powder for solution for infusion

1 g Gemcitabine hydrochloride

Sugar free

Read all of this leaflet carefully before you are given GEMCITABINE OETHMAAN.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- GEMCITABINE OETHMAAN 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

Initial:	09-12-2024

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1. What GEMCITABINE OETHMAAN is and what it is used for

GEMCITABINE OETHMAAN contains a medicine called gemcitabine hydrochloride, which belongs to a group of medicines called cytotoxics used for chemotherapy. Gemcitabine hydrochloride is used to treat a variety of cancers, either alone or in combination with other medicines, including the following:

GEMCITABINE OETHMAAN is indicated for treatment in patients:

- with non-small cell lung cancer that is either locally advanced or metastatic.
- with locally advanced (non-resectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas.
- with transitional cell bladder cancer.
- with unresectable, locally recurrent or metastatic breast cancer due to relapse following adjuvant/neoadjuvant chemotherapy. Treatment usually in combination with paclitaxel.
- ovarian cancer, together with carboplatin.

Initial:	09-12-2024

2. What you need to know before you are given GEMCITABINE OETHMAAN

You should not be given GEMCITABINE OETHMAAN:

- If you are allergic (hypersensitive) to gemcitabine or any of the other ingredients of GEMCITABINE OETHMAAN.
- If you are pregnant or breastfeeding.
- GEMCITABINE OETHMAAN should not be given to children under 18 years of age due to insufficient data on safety and efficacy.

Warnings and precautions

Take special care with GEMCITABINE OETHMAAN:

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 OETHMAAN. 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).
- you have decreased blood cells and bone marrow function. If you develop a fever, bleeding or think you may be suffering from an infection, please inform your doctor immediately.
- 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.
- you experience symptoms such as headache with confusion, seizures (fits) or changes in vision. This could be a very rare nervous system side effect named posterior reversible encephalopathy syndrome.
- you experience difficulty in 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).
- you have developed a severe skin rash or skin peeling, blistering and/or mouth sores after using GEMCITABINE OETHMAAN. 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.

Men are advised not to father a child during and up to 3 months following treatment with GEMCITABINE OETHMAAN. If you would like to father a child during the treatment or in the 3

months following treatment, seek advice from your doctor or pharmacist. You may want to seek counselling on sperm storage before starting your therapy.

Other medicines and GEMCITABINE OETHMAAN

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

Please 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.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking GEMCITABINE OETHMAAN.

Pregnancy

If you are pregnant, or thinking about becoming pregnant, tell your doctor. The use of GEMCITABINE OETHMAAN should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking GEMCITABINE OETHMAAN during pregnancy.

There is a risk that use of GEMCITABINE OETHMAAN during pregnancy may cause birth defects in your child. If you are sexually active, women are advised to use effective birth control to prevent pregnancy during treatment and for 6 months after treatment discontinuation. Men are advised not to father a child during and up to 3 months following treatment with GEMCITABINE OETHMAAN. If you would like to father a child during the treatment or in the 3 months following

treatment, seek advice from your doctor or pharmacist. You may want to seek counselling on sperm storage before starting your therapy.

Breastfeeding

If you are breastfeeding, tell your doctor. You must discontinue breastfeeding during GEMCITABINE OETHMAAN treatment.

Driving and using machines

It is not always possible to predict to what extent GEMCITABINE OETHMAAN 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 OETHMAAN affects them.

GEMCITABINE OETHMAAN 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 OETHMAAN treatment has not made you feel sleepy.

GEMCITABINE OETHMAAN contains sodium.

After reconstitution, GEMCITABINE 200 mg OETHMAAN and GEMCITABINE 1 g OETHMAAN contains 17,7 mg and 88,5 mg sodium respectively (main component of cooking/table salt) in each. This is equivalent to 0,9 % for GEMCITABINE 200 mg OETHMAAN and 4,43 % for GEMCITABINE 1 g OETHMAAN of the recommended maximum daily dietary intake of sodium for an adult.

3. How GEMCITABINE OETHMAAN is given

The usual dose of GEMCITABINE OETHMAAN 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 OETHMAAN infusion depends on the type of cancer that you are being treated for.

A hospital pharmacist or doctor will have dissolved the GEMCITABINE OETHMAAN powder before it is given to you.

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

If you have further questions on the use of GEMCITABINE OETHMAAN ask your doctor or pharmacist.

If you are given more GEMCITABINE OETHMAAN than you should

In the event of overdosage consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

Since a healthcare professional will administer GEMCITABINE OETHMAAN, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you miss a dose of GEMCITABINE OETHMAAN:

Since a healthcare professional will administer GEMCITABINE OETHMAAN, it is unlikely that the dose will be missed.

4. POSSIBLE SIDE EFFECTS:

GEMCITABINE OETHMAAN can have side effects.

Not all side effects reported for GEMCITABINE OETHMAAN are included in this leaflet. Should your general health worsen while taking GEMCITABINE OETHMAAN, please consult your doctor, pharmacist or other health care professional for advice.

If any of the following happens, stop receiving GEMCITABINE OETHMAAN and tell your doctor immediately or go to the casualty department at your nearest hospital:

- an allergic reaction, symptoms of which includes rash, itching, difficulty in breathing or swelling of the face, lips, throat or tongue

These are very serious side effects. If you have them, you may have had a serious reaction to GEMCITABINE OETHMAAN. You may need urgent medical attention or hospitalisation.

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

- Fever or infection (frequent): if you have a temperature of 38 ºC or greater, sweating or other signs of infection (since you might have less white blood cells than normal which is very frequent).
- Irregular heart rate (arrhythmia) (less frequent)
- Pain, redness, swelling or sores in your mouth (frequent).

- Allergic reactions: if you develop skin rash (very frequent) / itching (frequent), or fever (very frequent).
- Tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have less haemoglobin than normal which is very frequent).
- 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 frequent).
- Difficulty breathing (it is very frequent to have mild breathing difficulty soon after the GEMCITABINE OETHMAAN infusion which soon passes, however less frequently there can be more severe lung problems)
- Headache with changes in vision, confusion, seizures or fits (posterior reversible encephalopathy syndrome)
- Generalised swelling, shortness of breath or weight gain, as you might have fluid leakage from small blood vessels into the tissues (capillary leak 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 (haemolytic uraemic syndrome). It may be fatal (less frequent).
- Severe skin rash with flushing, fever, blisters or ulcers (Stevens - Johnson syndrome) (less frequent)
- Severe rash with reddening, peeling and swelling of the skin that looks like a burn (toxic epidermal necrolysis) (less frequent).

- 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 (AGEPU (frequency not known).

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

Tell your doctor if you notice any of the following:

Side effects with GEMCITABINE OETHMAAN may include:

Frequent 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)

Infections

Fever accompanied by low white blood cell count (febrile neutropenia)

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

Less frequent side effects

Clots forming in small blood vessels (thrombotic microangiopathy).

Interstitial pneumonitis (scarring of the air sacs of the lung)

Spasm of the airways (wheeze)

Abnormal chest X ray/scan (scarring of the lungs)

Irregular heart beat (dysrrhythmia), heart failure

Kidney failure

Serious liver damage, including liver failure

Stroke

Heart attack (myocardial infarction)

Low blood pressure

Inflammation of the blood vessels (peripheral vasculitis).

Skin scaling, ulceration or blister formation

Injection site reactions

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

Gangrene of fingers or toes

Increased platelet count

Anaphylactic reaction (severe hypersensitivity/ allergic reaction)

Sloughing of skin and severe skin blistering, skin redness with swelling (pseudocellulitis)

Ischaemic colitis (inflammation of the lining of the large bowel, caused by reduced blood supply)

Frequency unknown:

Sepsis: when bacteria and their toxins circulate in the blood and start to damage the organs

Lyell's syndrome - rash wher the skin is itchy, red, swollen, blistered or peeling

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

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of GEMCITABINE OETHMAAN.

5. How to store GEMCITABINE OETHMAAN

Before reconstitution: Store below 30 ºC. Protect from moisture, excessive heat and light.

After reconstitution: Store below 30 ºC and should be administered within 24 hours. Discard unused portion. Do not refrigerate as precipitates may occur under these conditions.

KEEP OUT OF REACH OF CHILDREN.

Do not store in bathrooms.

Do not use after the expiry date stated on the label or carton.

Return all unused medicine to your pharmacy. Do not dispose of unused medicine in drains or sewerage systems e.g. toilets.

6. Contents of the pack and other information

What GEMCITABINE OETHMAAN contains

Each GEMCITABINE 200 mg OETHMAAN vial contains: Gemcitabine hydrochloride equivalent to 200 mg Gemcitabine free base as the active substance.

Each GEMCITABINE 1 g OETHMAAN vial contains: Gemcitabine hydrochloride equivalent to 1 g Gemcitabine free base as the active substance.

The other ingredients are:

Sodium acetate,

mannitol,

sodium hydroxide,

hydrochloric acid,

water for injection and

nitrogen.

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What GEMCITABINE OETHMAAN looks like and contents of the pack

GEMCITABINE 200 mg OETHMAAN and GEMCITABINE 1 g OETHMAAN powder for solution for infusion is a white to slightly yellowish powder or cake.

Reconstitution with 0.9 % sodium chloride results in a clear and colourless solution.

GEMCITABINE OETHMAAN are packed in:

GEMCITABINE 200mg OETHMAAN: 10 ml colourless glass vial with a rubber stopper and an aluminium crimp cap with plastic flip off.

GEMCITABINE 1 g OETHMAAN: 50 ml colourless glass vial with a rubber stopper and an aluminium crimp cap with plastic flip off.

Holder of Certificate of Registration

Oethmaan Biosims (Pty) Ltd

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2195

Telephone no. 011 433 0602

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9 December 2024

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Registration number

GEMCITABINE 200 mg OETHMAAN: 41/26/0490

GEMCITABINE 1 g OETHMAAN: 41/26/0489

Access to the corresponding Professional Information

www.oethmaan.co.za

Telephone number: 011 433 0602

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