Applicant : Eurolab (Pty) Ltd
Proprietary name : Cytigem 200 mg & 1 g
Dosage form and strength : Powder for solution for infusion, 200 mg & 1 g
Date of submission : 23 November 2023
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**APPROVED PATIENT INFORMATION LEAFLET FOR CYTIGEM**

**SCHEDULING STATUS:** **S4**

**CYTIGEM 200 mg (Powder for Injection)**

**CYTIGEM 1 g (Powder for Injection)**

**Gemcitabine**

**Contains sugar: Mannitol**

**Read all of this leaflet carefully before you start receiving CYTIGEM**

- 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.

**What is in this leaflet**


1. What CYTIGEM is and what it is used for
2. What you need to know before you are given CYTIGEM
3. How to receive CYTIGEM
4. Possible side effects
5. How to store CYTIGEM

6. Contents of the pack and other information

## 1. What CYTIGEM is and what it is used for

CYTIGEM belongs to a group of medicines called antineoplastic or cytotoxic medicines. You may also hear of these being called chemotherapy medicines.

CYTIGEM works by killing cancer cells and preventing cancer cells from growing and multiplying.

CYTIGEM may be used in combination with other cytotoxic medicines to treat cancer.

CYTIGEM is used to treat patients with:

- Lung cancer.
- Cancer of the pancreas.
- Bladder cancer.
- Breast cancer.
- Ovarian cancer.

## 2. What you need to know before you are given CYTIGEM

**CYTIGEM should not be administered to you:**

- if you are hypersensitive (allergic) to Gemcitabine or any of the other ingredients of CYTIGEM (listed in section 6).
- if you are pregnant or breastfeeding.
- if the packaging is torn or shows signs of tampering.

- if the expiry date printed on the pack has passed.

**Tell your doctor if you have allergies to:**

- any other medicines.
- any other substances such as foods, preservatives or dyes.

**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 CYTIGEM. Before each infusion you will have samples of your blood taken to check if you have enough blood cells to receive CYTIGEM. 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.

Tell your doctor or health care provider before being given CYTIGEM:

- If you have, or have previously had liver disease, heart disease, vascular disease (any abnormal condition of the blood vessels) or problems with your kidneys.
- If you have recently had, or are going to have radiotherapy, as there may be an early or late radiation reaction with CYTIGEM.
- If you have been vaccinated recently, as this can possibly cause bad effects with CYTIGEM.

- If during treatment with CYTIGEM, 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 have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using CYTIGEM. Serious skin reactions including Stevens-Johnson syndrome 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.
- If you develop breathing difficulties or feel very weak and are very pale, 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, as this may be a sign of fluid leaking from your small blood vessels into the tissue.

**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 CYTIGEM**

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

Some medicines may be affected by CYTIGEM or may affect how it works. Your doctor and healthcare professional may have more information on medicines to be careful with or avoid while being given CYTIGEM.

**Pregnancy, breastfeeding and fertility**

Like most medicines used to treat cancer, CYTIGEM is not recommended to be given during pregnancy. If there is a need to consider CYTIGEM during your pregnancy, your doctor will discuss with you the benefits and risks involved.

Tell your doctor if you are breastfeeding or plan to breastfeed.

It is recommended that you do not breastfeed while you are receiving CYTIGEM, as it is not known whether CYTIGEM passes into breast milk.

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 this medicine.

**Driving and using machines**

CYTIGEM may make you feel sleepy. You should not drive or use machinery until you are sure of the effects it has on you.

**CYTIGEM contains sodium**

CYTIGEM contains 3,5 mg (< 1 mmol) of sodium in each 200 mg vial and 17,5 mg (< 1 mmol) sodium in each 1000 mg vial i.e. essentially sodium free.

## 3. How to receive CYTIGEM

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

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

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

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

Your doctor will tell you how long your treatment with CYTIGEM will last. If you have the impression that the effect of CYTIGEM is too strong or too weak, tell your doctor or pharmacist.

**If you receive more CYTIGEM than you should**

Since a healthcare professional will administer CYTIGEM, he/she will control the dosage.

However, in the event of overdosage your doctor will manage the overdosage.

**If you forget to use CYTIGEM**

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

## 4. Possible side effects

CYTIGEM can have side effects.

Not all side effects reported for CYTIGEM are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while receiving CYTIGEM, please consult your health care provider for advice.

CYTIGEM may have unwanted side effects, some of which may be serious. You may need medical treatment if you experience some of the side effects.

If any of the following happens, stop taking / using CYTIGEM and tell your doctor immediately or go to the casualty department at your nearest hospital:

- 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)].
- Bleeding from the gums, nose or mouth or any bleeding that would not stop, reddish or pinkish urine, unexpected bruising.
- Tiredness, feeling faint, becoming easily breathless or if you look pale.
- Mild to moderate skin rash / itching, or fever (allergic reactions).
- Temperature of 38 ºC 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).
- Pain, redness, swelling or sores in your mouth (stomatitis).
- Irregular heart rate (arrhythmia).
- 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.
- Difficulty breathing (it is common to have mild breathing difficulty soon after the CYTIGEM infusion which soon passes, however uncommonly or rarely there can be more severe lung problems).
- Severe chest pain (myocardial infarction).
- 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).

- Generalised swelling, shortness of breath or weight gain, as you might have fluid leakage from small blood vessels into the tissues (capillary leak syndrome).
- Headache with changes in vision, confusion, seizures or fits (posterior reversible encephalopathy syndrome).
- Severe rash with itching, blistering or peeling of the skin (Stevens-Johnson syndrome).

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

Tell your doctor if you notice any of the following:

*Frequent side effects*

- 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).
- Poor appetite (anorexia).
- Headache.
- Insomnia.

- Sleepiness.
- Cough.
- Runny nose.
- Constipation.
- Diarrhoea.
- Itching.
- Sweating.
- Muscle pain.
- Back pain.
- Fever.
- Weakness.
- Chills.

*Less Frequent side effects*

- 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.

*Frequency unknown side effects*

- 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).

Increased platelet count

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.

The benefits and side effects of CYTIGEM may take some time to occur.

Therefore, even after you have finished your CYTIGEM treatment, you should tell your doctor or healthcare professional immediately if you notice any of the side effects listed in this section.

If you are concerned about any side effects, talk to your doctor.

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 or, pharmacist or nurse. 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 CYTIGEM.

## 5. How to store CYTIGEM

**Before reconstitution:** Store at or below 25 °C.

**After reconstitution:** Solutions of CYTIGEM reconstituted with 0,9 % sodium chloride injection without preservatives should be stored below 25 °C and should be administered within 24 hours. Discard unused portion. Do not refrigerate as crystallisation may occur. Reconstituted CYTIGEM should be inspected visually for particulate matter and discolouration, prior to administration. Procedures for proper handling and disposal of anti-cancer drugs should be considered.

**STORE ALL MEDICINES OUT OF REACH OF CHILDREN.**

**Store in original package.**

**Do not use after the expiry date stated on the carton.**

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

## 6. Contents of the pack and other information

### What CYTIGEM contains

CYTIGEM 200 mg (10 mL vial): Each vial contains gemcitabine hydrochloride equivalent to 200 mg gemcitabine free base.

CYTIGEM 1 g (50 mL vial): Each vial contains gemcitabine hydrochloride equivalent to 1 g gemcitabine free base.

Other ingredients: Mannitol, sodium acetate trihydrate, sodium hydroxide, hydrochloric acid 37 %, water for injection.

### What CYTIGEM looks like and contents of the pack

CYTIGEM 200 mg: A white to off white lyophilized powder in a clear glass vial. Reconstitution with 0,9 % sodium chloride injection without preservatives produces a clear, colourless to light straw coloured solution for injection.

CYTIGEM 200 mg: A white to off white lyophilized powder in a clear glass vial. Reconstitution with 0,9 % sodium chloride injection without preservatives produces a clear, colourless to light straw coloured solution for injection.

CYTIGEM 1 g: An outer carton containing one 50 mL USP type 1 clear colourless glass vial with a 20 mm grey bromobutyl rubber stopper and 20 mm aluminium flip off royal blue lavender seal/20 mm plain aluminium flip off lavender seal.

CYTIGEM 200 mg: An outer carton containing one 10 mL USP type 1 clear colourless glass vial with a 20 mm grey bromobutyl rubber stopper and 20 mm aluminium flip off royal blue seal/20 mm plain aluminium flip off Royal blue seal.

**Holder of certificate of registration**

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