Package leaflet: Information for the user

Carmustine 100 mg-Powder and solvent for solution for infusion
carmustine

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, pharmacist or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Carmustine is and what it is used for

Carmustine 100 mg-Powder and solvent for solution for infusion is a medicine which contains carmustine. Carmustine belongs to a group of anticancer substances known as nitrosourea that act by slowing the growth of cancer cells.

Carmustine is used as palliative therapy (relieving and preventing the suffering of patients) as a single agent or in established combination therapy with other approved anticancer substances in certain types of cancers, like:
- Brain tumours- glioblastoma, medulloblastoma, astrocytoma and metastatic brain tumours
- Multiple myeloma (malignant tumour developing from bone marrow)
- Hodgkin's disease (lymphoid tumour)
- Non-Hodgkin's lymphomas (lymphoid tumour)

Carmustine is also used as a conditioning treatment prior to autologous stem cell transplantation (a procedure in which a person receives blood stem cells, which make any type of blood cell) in malignant haematological disease in the lymphatic system such as Hodgkin's lymphoma and non-Hodgkin's lymphoma.

2. What you need to know before you use Carmustine

Do not use Carmustine
- if you are allergic to carmustine, other nitrosourea medicines or any of the other ingredients of this medicine (listed in section 6).

Carmustine should not be used in patients who have reduced number of blood platelets (thrombocytes), white blood cells (leucocytes) or red blood cells (erythrocytes), either as a result of chemotherapy or from other causes.
-if you suffer from higher-grade kidney dysfunction.
-in children and adolescents.

-if you are pregnant or if you are breast-feeding.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Carmustine.

Since the major side effect of this medicine is delayed bone marrow suppression, your doctor will monitor blood counts weekly for at least 6 weeks after a dose. At the recommended dosage, courses of Carmustine would not be given more frequently than every 6 weeks. The dosage will be confirmed with the blood count.

Before treatment, your liver and kidney function will be tested and observed regularly during the treatment.

Since the use of Carmustine can lead to lung damage, an X-ray of the chest region and the lung function tests will be conducted (Please also see the section "Possible side effects").

High–dose treatment with carmustine (up to 600 mg/m^2) is only performed in combination with subsequent stem cell transplantation. Such a higher dose can increase frequency or severity of lung, kidney, liver, heart, and gastrointestinal toxicities as well as infections and disturbances in the electrolyte balance (low blood levels of potassium, magnesium, phosphate).

Abdominal pain (neutropenic enterocolitis) may occur as a therapy-related adverse event during therapy with chemotherapeutic agents.

Patients who suffer from multiple conditions simultaneously and have poorer disease status are at higher risk for adverse events. This is especially important for elderly patients.

Your doctor will talk to you about the possibility of lung damage and allergic reactions and their symptoms. If such symptoms occur, you should contact your doctor immediately (see section 4).

Other medicines and Carmustine

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without prescription, such as:
- Phenytoin, used in epilepsy
- Cimetidine, used for stomach problems like indigestion
- Digoxin, used if you have abnormal heart rhythm
- Melphalan, an anticancer drug

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

<u>Pregnancy and fertility</u>
Carmustine should not be used during pregnancy because it may harm your unborn baby. Therefore this medicine should not normally be administered to pregnant women. If used during pregnancy, the patient must be aware of the potential risk to the unborn baby. Women of childbearing potential are advised to avoid becoming pregnant whilst being treated with this medicine.
Male patients should use adequate contraceptives measures during treatment with Carmustine for at least 6 months to prevent their partners becoming pregnant.

<u>Breast-feeding</u>

You should not breast-feed while taking this medicine.

Driving and using machines

The effect of this medicine on your ability to drive and use machines is not known. You must check with your doctor before driving or operating any tools or machines because the amount of alcohol in this medicine may impair your ability to drive or use machines.

Carmustine contains ethanol (alcohol)
This medicinal product contains 0.57 vol% ethanol (alcohol), which means 7.68 g per dose. This corresponds to 11.32 ml of beer or 4.72 ml wine, per dose. This may be harmful for those suffering from alcoholism, liver disease or epilepsy (fits)

3. How to use Carmustine

Carmustine will always be given to you by a healthcare professional with experience in the use of anticancer agents.
This medication is for intravenous infusion.

Adults

Dosage is based on your medical condition, body size and response to treatment. It is usually given at least every 6 weeks.The recommended dose of Carmustine as a single agent in previously untreated patients is 150 to 200 mg/m^2 intravenously every 6 weeks. This may be given as a single dose or divided into two daily injections such as 75 to 100 mg/m^2 on two successive days. Dosage will also depend on whether Carmustine is given with other anti-cancer drugs.

Doses will be adjusted according to how you respond to the treatment.

The recommended dose of carmustine given in combination with other chemotherapeutic agents before haematopoietic progenitor cell transplantation is 300 – 600 mg/m^2 intravenously.

Your blood count will be monitored frequently to avoid toxicity in your bone marrow and the dose adjusted if necessary.

Route of administration

Carmustine is given into a vein by a drip over a one to two hour period. The time of infusion should not be less than one hour to avoid burning and pain at the injected area. The injected area will be monitored during the administration.

The duration of the treatment is determined by the doctor and may vary for each patient.

Use in elderly
Carmustine can be used with caution in elderly patients. The kidney function will be carefully monitored. In elderly patients, the occurrence of inflammation of mucous membranes of mouth (oral mucositis) is higher when high dose of carmustine is given.

If you use more Carmustine than you should

As a doctor or nurse will be giving you this medicine, it is unlikely that you will receive an incorrect dose. Tell your doctor or nurse if you have any concerns about the amount of medicine that you receive.

If you have any further questions on the use of this product, 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.

Tell your doctor or nurse immediately if you notice any of the following:
Any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body), and feeling you are going to faint. These may be signs of severe allergic reaction.

Carmustine may cause the following side effects:

Very common (may affect more than 1 in 10 people)
- Delayed myelosuppression (decrease in blood cells in bone marrow);
- Ataxia (lack of voluntary coordination of muscle movements);
- Dizziness;
- Headache;
- Transient redness in the eye, blurred vision, retinal bleeding;
- Hypotension (fall in blood pressure) in high-dose therapy;
- Phlebitis (inflammation of the veins);
- Respiratory disorders (lung related disorders) with breathing problems;
- Severe nausea and vomiting; beginning within 2-4 hours of administration and lasting for 4-6 hours;
- When used on the skin, inflammation of the skin (dermatitis)
- Accidental contact with skin may cause transient hyperpigmentation (darkening of an area of skin or nails)

Common (may affect up to 1 in 10 people)
- Acute leukemias and bone marrow dysplasias (abnormal development of the bone marrow) following long term use; The following symptoms may occur: bleeding gums, bone pain, fever, frequent infections, frequent or severe nosebleeds, lumps due to swollen lymph nodes in and around the neck, forearm, abdomen, or groin, pale skin, shortness of breath, weakness, fatigue, or general lack of energy;
- Anaemia (decrease in the amount of red blood cells in the blood);
- Encephalopathy (disorder of brain) in high-dose therapy;
- Loss of appetite (anorexia);
- Constipation;
- Diarrhoea;
- Inflammation of the mouth and lips;
- Reversible liver toxicity in high-dose therapy, delayed up to 60 days after administration. This can result in increased liver enzymes and bilirubin (detected by blood tests);
- Alopecia (loss of hair);
- Flushing of the skin;
- Reactions on the injection site

Rare (may affect up to 1 in 1,000 people)
- Veno-occlusive disease (progressive blockage of the veins) in high-dose therapy; in which very small veins in the liver become blocked. The following symptoms are possible: fluid accumulation in the abdomen, enlargement of the spleen, severe bleeding of the esophagus, yellowing of skin and the

white skin of the eyes;
- Breathing problems due to a type of lung disease in which tissue is scarred (interstitial fibrosis) (with lower doses);
- Kidney problems
- Gynecomastia (breast growth in males)
- Inflammation of the optic nerve and adjacent retina in the eye
- Bleeding in the gastrointestinal tract

Very rare (may affect up to 1 in 10.000 people)
- Inflammation of the vein wall with associated thrombosis (thrombophlebitis)

Not known (frequency cannot be estimated from the available data)
- Allergic reactions
- Muscular pain;
- Secondary tumors (cancers caused by radiation or chemotherapy).
- Seizures (fits) including status epilepticus;
- Tissue damage due to leakage in injection area;
- Infertility;
- Impairment of embryo/fetus development in pregnant women
- Any signs of infection
- Fast heart beat, chest pain
- Disturbances in electrolyte balance (low blood levels of potassium, magnesium, phosphate).
- Abdominal pain (neutropenic enterocolitis).

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Carmustine

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 label and carton after statement "can be used up to'. The expiry date refers to the last day of that month.

This medicine will be stored by your doctor or health care professional.

The unopened vial of the dry drug must be stored in a refrigerator (2°-8°C). After reconstitution as recommended, Carmustine is stable for 24 hours under refrigeration (2°-8°C) in a glass container and must be protected from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist or doctor 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 Carmustine contains
The active substance is carmustine.
A 30 ml vial contains 100 mg carmustine and a 5 ml vial contains 3 ml sterile diluent (dehydrated alcohol).

What Carmustine looks like and contents of the pack

Powder and solvent for solution for infusion.
Yellowish powder for reconstitution.
Appearance of solution: colourless to light yellow

Powder: Type I amber glass vial (30 ml) sealed with a dark grey bromo butyl lyo rubber stopper and aluminium seal having polypropylene cap.

Diluent: Type I glass vial (5 ml) sealed with a grey bromo butyl rubber stopper with an aluminium seal having polypropylene cap.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Tillomed Laboratories Ltd
220 Butterfield
Great Marlings
Luton, LU2 8DL
United Kingdom

Manufacturer[1]

MIAS Pharma Limited
Suite 2, Stafford House, Strand Road
Portmarnock, Co. Dublin
Ireland

Emcure Pharma UK Limited
Basepoint Business Centre,
110 Butterfield,
Great Marlings,
Luton, LU2 8DL
United Kingdom

This leaflet was last revised in 07/2022.

[1] Only actual manufacturer stated on printed leaflet