Package leaflet: Information for the user

/.../ 50 mg powder and solvent for solution for injection/infusion

melphalan

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

What is in this leaflet

1. What /…/ is and what it is used for

/.../ contains a medicine called melphalan. This belongs to a group of medicines called cytotoxics (also called chemotherapy). /.../ is used to treat cancer. It works by reducing the number of abnormal cells your body makes.

/.../ is used for:
- **Multiple myeloma** – a type of cancer that develops from cells in the bone marrow called plasma cells. Plasma cells help to fight infection and disease by producing antibodies
- Advanced **cancer of the ovaries**
- **Childhood neuroblastoma -** cancer of the nervous system
- **Malignant melanoma** – skin cancer
- **Soft tissue sarcoma** – cancer of the muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body

Ask your doctor if you would like more explanation about these diseases.

2. What you need to know before you use /…/

Do not use /…/:
- if you are allergic to melphalan or any of the other ingredients of this medicine (listed in section 6).

Do not have /.../ if the above applies to you. If you are not sure, talk to your doctor or nurse before having /.../.

Warnings and precautions
Talk to your doctor or nurse before using /…/
- if you have had radiotherapy or chemotherapy, now or recently
- if you have a kidney problem.

If you are not sure if any of the above apply to you, talk to your doctor or nurse before having /.../.

Other medicines and /…/
Tell your doctor if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor or nurse if you are taking any of the following:
- other cytotoxic drugs (chemotherapy)
- nalidixic acid (an antibiotic used to treat urinary tract infections)
- ciclosporin (used to prevent rejection of organs or tissues following a transplant or to treat certain skin conditions like psoriasis and eczema or to treat rheumatoid arthritis).

Having vaccines while you are taking /.../
If you are going to have a vaccination speak to your doctor or nurse before you have it. This is because some vaccines (like polio, measles, mumps and rubella) may give you an infection if you have them whilst you are being treated with /.../.

Pregnancy and breast-feeding
Do not have /.../ if you are planning to have a baby. This applies to both men and women. /.../ may harm your sperm or eggs. Reliable contraceptive precautions must be taken to avoid pregnancy whilst you or your partner are having this injection. Ask your doctor for advice.

If you are already pregnant, it is important to talk to your doctor before having /.../.

Do not breast-feed while having /.../. Ask your doctor or midwife for advice.

/…/ contains ethanol (alcohol), sodium and propylene glycol
This medicinal product contains 5.1 vol % ethanol (alcohol), i.e. up to 2894 mg per dose, equivalent to 73.4 ml beer or 30.6 ml wine.
Harmful for those suffering from alcoholism.
To be taken into account in pregnant or breast-feeding women, in children and high-risk groups such as patients with liver disease, or epilepsy.

This medicinal product contains 53.5 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.7% of the recommended daily dietary intake of sodium for an adult.

Propylene glycol in this medicine can have the same effects as drinking alcohol and increase the likelihood of side effects. Your doctor may carry extra checks while you are taking this medicine. Do not use this medicine in children less than 5 years old.

3. How to use /…/

/.../ should only be prescribed for you by a specialist doctor who is experienced in treating blood problems or cancer.

/.../ can be given:
- as an infusion into your vein
- as a perfusion to a particular part of your body through an artery.

Your doctor will decide how much /.../ you will have. The amount of /.../ depends on:
- your body weight or body surface area (a specific measurement taking into account your weight and your size)
- other drugs you are having
- your disease
- your age
- whether or not you have kidney problems.

When you are given /.../, your doctor will take regular blood tests. This is to check the number of cells in your blood. Your doctor may sometimes change your dose as a result of these tests.

If you use more /…/ than you should
Your doctor will give you /.../ so it is unlikely that you will receive too much. If you think you have been given too much or have missed a dose, tell your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you get any of the following, talk to your specialist doctor or go to hospital straight away:
- allergic reaction, the signs may include:
  - a rash, lumps or hives on the skin
  - swollen face, eyelids or lips
  - sudden wheeziness and tightness of the chest
  - collapse (due to cardiac arrest)
- any signs of fever or infection (sore throat, sore mouth or urinary problems)
- any **unexpected** bruising or bleeding or feeling extremely tired, dizzy or breathless, as this could mean that too few blood cells of a particular type are being produced
- if you **suddenly** feel unwell (even with a normal temperature)
- if your muscles are achy, stiff or weak **and** your urine is darker than usual or brown or red in colour – when you have /.../ directly into your arm or leg.

Talk to your doctor if you have any of the following side effects which may also happen with this medicine:

Very common (may affect more than 1 in 10 people)
- a drop in the number of blood cells and platelets
- feeling sick (nausea), being sick (vomiting) and diarrhoea
- mouth ulcers - with high doses of /.../
- hair loss - with high doses of /.../
- a tingling or warm feeling where /.../ was injected
- problems with your muscles like wasting and aching – when you have /.../ directly into your arm or leg

Common (may affect up to 1 in 10 people)
- hair loss - with usual doses of /.../
- high levels of a chemical called urea in your blood – in people with kidney problems who are being treated for myeloma
- a muscle problem which can cause pain, tightness, tingling, burning or numbness – called compartment syndrome. This can happen when you have /.../ directly into your arm or leg

Rare (may affect up to 1 in 1,000 people)
- an illness where you have a low number of red blood cells as they are being destroyed prematurely – this can make you feel very tired, breathless and dizzy and can give you headaches or make your skin or eyes yellow
- lung problems which may make you cough or wheeze and make it difficult to breathe
- liver problems which may show up in your blood tests or cause jaundice (yellowing of the whites of eyes and skin)
- mouth ulcers – with normal doses of /.../
- skin rashes or itching skin

The following side effects also happen with /.../:
- leukaemia – cancer of the blood
- in women: your periods stopping

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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 /…/

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 EXP. The expiry date referes to the last day of that month.

This medicine does not require any special storage conditions.

Your /.../ will be prepared for use by a healthcare professional. Once prepared it should be used immediately and must not be stored or refrigerated.

6. Contents of the pack and other information

What /…/ contains

- The active ingredient is melphalan. Each vial contains 50 mg of melphalan (as melphalan hydrochloride).
- The other ingredients are povidone K12 and hydrochloric acid (for pH-adjustment). /.../ is dissolved in a solvent before being injected. The solvent contains sodium citrate, propylene glycol, ethanol anhydrous and water for injections.

What /…/ looks like and contents of the pack
/…/ is presented as powder and solvent for injection/infusion. The powder is white or almost white freeze-dried powder and the solvent is a clear, colourless sterile solution.

The active substance is packed in type I colourless glass vial (15 ml), closed with type I bromobutyl rubber stopper and aluminium metal cap with polypropylene disk. The vial may be or may not be sheathed in a protective sleeve.
The solvent for reconstitution is packed in type I colourless glass vial (10 ml), closed with type I bromobutyl rubber stopper and aluminium metal cap with polypropylene disk.

Pack size: single pack containing 1 vial of powder and 1 vial of solvent.

Marketing Authorisation Holder and Manufacturer

<[To be completed nationally]>

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

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

<{Name of the Member State}> <{Name of the medicinal product}>
<{Name of the Member State}> <{Name of the medicinal product}>

This leaflet was last revised in <{MM/YYYY}> <{month YYYY}>.

<[To be completed nationally]>

<Detailed information on this medicine is available on the website of {name of MS Agency (link)}>

The following information is intended for healthcare professionals only:

Precautions
/.../ IS AN ACTIVE CYTOTOXIC AGENT FOR USE UNDER THE DIRECTION OF PHYSICIANS EXPERIENCED IN THE ADMINISTRATION OF SUCH AGENTS. Caution should be used during handling and preparation. Use of gloves and other protective clothing to prevent skin contact is recommended.

Safe handling of /.../
The handling of /.../ formulations should follow guidelines for the handling of cytotoxic drugs.

Preparation
/…/ solution for injection/infusion should be prepared at room temperature (approximately 25°C), by reconstituting the freeze-dried powder with the solvent provided.
It is important that both the freeze-dried powder and the solvent provided are at room temperature before starting reconstitution. Warming the diluent in the hand may aid reconstitution. 10 ml of this vehicle should be added quickly, as a single quantity into the vial containing the freeze dried powder, and immediately shaken vigorously (for approximately 1 minute) until a clear solution, without visible particles, is obtained. Each vial must be reconstituted individually in this manner. The resulting solution contains the equivalent of 5 mg/ml melphalan.

/.../ is not compatible with infusion solutions containing dextrose, and it is recommended that ONLY Sodium Chloride Intravenous Infusion 0.9% w/v is used.

Chemical and physical in-use stability of /…/ is limited and the solution should be prepared immediately before use. The reconstituted solution (5 mg/ml) should be transferred into the infusion bag in less than 30 minutes and the diluted solution should be completely administrated within 1 hour of reconstitution.

The reconstituted solution is clear, colourless to slightly yellowish solution free of visible particles, with a final pH of approximately 6.5.

Any unused product or waste material should be disposed of in accordance with local requirements.

Administration
Except in cases where regional arterial perfusion is indicated, /.../ is for intravenous use only.

For intravenous administration it is recommended that /.../ solution is injected slowly into a fast-running infusion solution via a swabbed injection port.

If direct injection into a fast-running infusion is not appropriate, /.../ solution may be administered diluted in an infusion bag.

Care should be taken to avoid possible extravasation of /.../ and in cases of poor peripheral venous access, consideration should be given to use of a central venous line. If high dose /.../ is administered with or without autologous bone marrow transplantation, administration via a central venous line is recommended.

For regional arterial perfusion, the literature should be consulted for detailed methodology.

For further information please refer to the Summary of Product Characteristics (SPC).