Package leaflet: Information for the patient

Dacarbazine medac 500 mg powder for solution for infusion
Dacarbazine medac 1000 mg powder for solution for infusion

Dacarbazine

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

What is in this leaflet

1. What Dacarbazine medac is and what it is used for

Dacarbazine belongs to the group of medicines known as cytostatic agents. These agents influence the growth of cancer cells.

Dacarbazine medac has been prescribed by your doctor for the treatment of cancer, such as:
- advanced malignant melanoma (skin cancer),
- Hodgkin's disease (cancer of the lymphatic tissue)
- soft tissue sarcoma (cancer of muscles, fat, fibrous tissue, blood vessels or other supporting tissue of the body).

Dacarbazine medac can be used in combination with other cytostatic agents.

2. What you need to know before you are given Dacarbazine medac

You will not be given Dacarbazine medac
- if you are **allergic** to dacarbazine or any of the other ingredients of this medicine (listed in section 6),
- if the number of white blood cells and/or platelets in your blood is too low **(leukopenia** and/or **thrombocytopenia)**,
- if you have a severe **liver or kidney disease**,
- if you are **pregnant or breastfeeding**.

Warnings and precautions
Talk to your doctor or pharmacist before you are given Dacarbazine medac.

Before each administration you will have blood tests to check that you have enough blood cells to receive this medicine. Your liver and kidney function will also be monitored.

You should not have a live vaccine if you are having Dacarbazine medac. This is because Dacarbazine medac may weaken your immune system and make you more likely to catch a serious infection.

You should not use fotemustine if you are being treated with Dacarbazine medac.

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

It is not advisable to use any medical treatment without telling your doctor as there may be interactions between Dacarbazine medac and other medicines.
In particular, tell your doctor or pharmacist if you are using or are being treated with any of the following:

- Radiation treatment or other medicines to reduce tumour growth (chemotherapy). Using these medicines with Dacarbazine medac can increase the damage to your bone marrow.
- Other medicines that are metabolised by a system of liver enzymes called cytochrome P450.
- Methoxypsoralen (for skin problems such as psoriasis and eczema) – Having Dacarbazine medac with methoxypsoralen can make you more sensitive to sunlight (photosensitisation).
- Phenytoin (used to treat seizures) – Using Dacarbazine medac and phenytoin at the same time may make it more likely for you to have fits (convulsions).
- Cyclosporine or tacrolimus (used to lower your body's immune reactions) – These medicines may weaken your immune system.
- Fotemustine (used for treatment of skin cancer) – Using Dacarbazine medac and fotemustine at the same time may lead to damage to your lungs.
- Medicines that can cause liver damage e.g. diazepam (used to treat anxiety, muscle spasms and convulsions), imipramine (used to treat symptoms of depression), ketoconazole (used to treat fungal infections), carbamazepine (used to prevent fits, modify some types of pain or to control mood disorders) should be avoided during chemotherapy.
- Anticoagulants (medicines used to prevent formation of blood clots) – Your doctor will decide whether these medicines will be given to you and will check the clotting tendency of your blood.

You should not have a live vaccine if you are having Dacarbazine medac and during 3 months following completion of treatment with Dacarbazine medac. This is because Dacarbazine medac may weaken your immune system and make you more likely to catch a serious infection.
You may have a 'killed' or inactivated vaccine if you are having Dacarbazine medac.

Dacarbazine medac with food, drink and alcohol
During chemotherapy you should not drink alcohol.

Pregnancy, breastfeeding and fertility
Dacarbazine medac must not be given if you are pregnant, think you may be pregnant or are planning to have a baby.

Do not breastfeed while you are being treated with Dacarbazine medac.

You must use an effective method of contraception during treatment with Dacarbazine medac. Men should continue to use effective contraception for at least 6 months after treatment with Dacarbazine medac has stopped.

If you are thinking of becoming pregnant or of breastfeeding, discuss it with your doctor first.

Driving and using machines
Your ability to drive or operate machines may be influenced because of central nervous side effects (effects on the brain and nerves) or feeling sick and being sick; but there is no reason why you cannot drive or use machines between courses of therapy with this medicine unless you feel dizzy or unsure of yourself.

3. How to use Dacarbazine medac

This medicine will be given to you under the direction of a doctor specialised in oncology (cancer treatment) or haematology (the study of diseases of the blood). You will be monitored regularly, during and after your treatment, for any signs of side effects.

Dacarbazine is a substance sensitive to light exposure. The doctor or nurse giving you this medicine will make sure that dacarbazine will be protected from exposure to daylight during administration.

How much Dacarbazine medac you will be given
Your doctor will calculate the dose you will be given. This will depend on the type of cancer you have and how advanced it is, your body surface area (m^2), blood counts and other anticancer medicines or treatments you are currently having. The treating physician will also decide individually how long this medicine will be given to you.

Your doctor may change the dose and frequency of dosing depending on your blood test results, your general condition, further therapies and your response to this medicine. If you have any questions about your treatment, ask your doctor, nurse or pharmacist.

Skin cancer (metastatic malignant melanoma)
The usual dose is 200 – 250 mg per m^2 body surface area, once a day. You are given this dose 5 days in a row, every 3 weeks. It will be given as a fast injection into your vein or as a slow infusion into your vein lasting 15 – 30 minutes.
Alternatively, you can be given one larger dose of 850 mg per m^2 body surface area, every 3 weeks. This will be given as a slow infusion into your vein.

Cancer of the lymphatic tissue (Hodgkin's disease)
The usual dose is 375 mg per m^2 body surface area, every 15 days. You will also be given medicines called doxorubicin, bleomycin and vinblastine (this combination is called the ABVD regimen). It will be given as a slow infusion into the vein.

Cancer of muscles, fat, fibrous tissue, blood vessels or other supporting tissue of the body (soft tissue sarcoma)
The usual dose is 250 mg per m^2 body surface area, once a day. You are given this dose 5 days in a row, every 3 weeks. It will be given as a slow infusion into the vein lasting 15 – 30 minutes.
You will also be given a medicine called doxorubicin (this combination is called the ADIC regimen).

Patients with kidney or liver problems
If you have either mild or moderate kidney or liver problems, you do not usually need to have less of this medicine. If you have both kidney and liver problems, your body will take longer to use the medicine and remove it from your system. Your doctor may give you less of this medicine.

Use in children
No special recommendations for the use of this medicine in children can be given to your doctor until further data become available.

If you have been given more Dacarbazine medac than you should
If you have been given too much Dacarbazine medac, this may cause a severe decline in your blood cells. It may lead to a complete loss of function of your bone marrow. Possible symptoms include signs of infections, bruising due to an increased bleeding tendency or fatigue. This can be delayed by up to 2 weeks.
If you think you have been given too much Dacarbazine medac, tell your doctor or nurse straight away. The number of blood cells will be checked and supportive measures such as transfusions may be required.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Your doctor will discuss these with you and will explain the risks and benefits of your treatment.

Tell your doctor immediately, if you notice anything of the following:
- Signs of infection, such as sore throat and high temperature
- Abnormal bruising or bleeding
- Extreme tiredness
- Persistent or severe vomiting or diarrhoea
- Severe allergic reaction – you may experience a sudden itchy rash, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel like you are going to faint
- Yellowing of the skin and eyes because of liver problems
- Signs of brain-related or nerve-related problems, such as headaches, impaired vision, fits, confusion, lethargy or numbness and tingling of your face
- Severe problems with the liver due to obstruction of the liver blood vessels (veno-occlusive disease [VOD] or Budd-Chiari syndrome) with destruction of liver cells which can be life-threatening. If these complications are suspected, your doctor will decide the right treatment for you.

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

The following other side effects may occur:

Common (may affect up to 1 in 10 people)
- Decreased number of red blood cells (anaemia)
- Decreased number of white blood cells (leukopenia)
- Decreased number of platelets in the blood (thrombocytopenia)

The changes in blood counts are dose-dependent and delayed, with the lowest values often only occurring after 3 to 4 weeks.
- Loss of appetite (anorexia), feeling sick and being sick (all of which may be severe)

Uncommon (may affect up to 1 in 100 people)
- Hair loss (alopecia)
- Increased skin colouring (hyperpigmentation)
- Sensitivity to light (photosensitivity) of the skin
- Flu-like symptoms with exhaustion, chills, fever and muscular pain. These symptoms might happen during administration of the medicine, or a few days after you have been given it. They might also come back the next time you are given dacarbazine.
- Infections

Rare (may affect up to 1 in 1000 people)
- Decreased number of all cells in the blood (pancytopenia)
- Severely decreased number of granulocytes, a special type of white blood cells (agranulocytosis)
- Severe allergic (anaphylactic) reaction resulting in e.g. drop in blood pressure, swelling of the hands, feet, ankles, face, lips, mouth and throat which may cause difficulty in swallowing or breathing, rapid pulse, hives and generalised itching or skin redness
- Headaches
- Impaired vision
- Confusion
- Lethargy
- Fits (convulsions)

- Abnormal sensations of the face (facial paraesthesia), numbness and flushing of the face shortly after injection
- Diarrhoea
- Elevation of liver enzymes
- Impaired kidney function
- Red skin (erythema)
- Skin eruptions (maculopapular exanthema)
- Hives (urticaria)
- Application site irritation

If the medicine is accidentally injected into the tissue around your vein, it may be painful and might lead to tissue damage.

You may experience one or several of these symptoms. If you get any side effects, talk to your doctor or pharmacist.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Dacarbazine medac

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 refers to the last day of that month.

Do not store above 25 °C. Keep the vial in the outer carton in order to protect from light.
The shelf-life under these conditions is 3 years.

Freshly prepared (reconstituted) and further diluted solutions of Dacarbazine medac should also be protected from light and must be used immediately.

Dacarbazine medac is for single use only.
Any portion of the contents remaining after use should be discarded by your doctor as well as solutions where the visual appearance of the product has changed. The diluted solution for infusion should be visually inspected by your doctor and only clear solutions practically free from particles should be used.

6. Contents of the pack and other information

What Dacarbazine medac contains
- The active substance is dacarbazine (as dacarbazine citrate).
- The other ingredients are citric acid, anhydrous, and mannitol.

What Dacarbazine medac looks like and contents of the pack
Dacarbazine medac is a white or pale-yellow powder which is supplied in amber glass vials (Type I, Ph.Eur.).

Each single-dose vial of Dacarbazine medac 500 mg contains 500 mg dacarbazine, as dacarbazine citrate.

After reconstitution and final dilution Dacarbazine medac 500 mg contains 1.4 – 2.0 mg/ml dacarbazine.

Each single-dose vial of Dacarbazine medac 1000 mg contains 1000 mg dacarbazine, as dacarbazine citrate.
After reconstitution and final dilution Dacarbazine medac 1000 mg contains 2.8 – 4.0 mg/ml dacarbazine.

Vials of Dacarbazine medac are packed in boxes each containing 1 vial.

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

Austria	Dacarbazine medac 500 mg/1000 mg, Pulver zur Herstellung einer Infusionslösung
Belgium	DACARBAZINE MEDAC 500 mg/1000 mg, poeder voor oplossing voor infusie DACARBAZINE MEDAC 500 mg/1000 mg, poudre pour solution pour perfusion DACARBAZINE MEDAC 500 mg/1000 mg, Pulver zur Herstellung einer Infusionslösung
Denmark	Dacarbazine medac 500 mg/1000 mg, pulver til infusionsvæske, opløsning
Germany	Detimedac 500 mg/1000 mg, Pulver zur Herstellung einer Infusionslösung
Ireland	Dacarbazine medac 500 mg/1000 mg, powder for solution for infusion
Italy	Dacarbazina medac 500 mg/1000 mg, polvere per soluzione per infusione
Netherlands	Dacarbazine medac 500 mg/1000 mg, poeder voor oplossing voor infusie
Portugal	Dacarbazina medac 500 mg/1000 mg, pó para solução para perfusão
Spain	Dacarbazina medac 500 mg/1000 mg, polvo para solución para perfusión
Sweden	Dacarbazine medac 500 mg/1000 mg, Pulver till infusionsvätska, lösning
United Kingdom	Dacarbazine medac 500 mg/1000 mg, powder for solution for infusion

This leaflet was last revised in 01/2017.

The following information is intended for medical or healthcare professionals only:

Recommendations for safe handling
Dacarbazine is an anti-neoplastic agent and should be handled according to standard procedures for cytostatics that have mutagenic, carcinogenic and teratogenic effects. Before commencing, local cytotoxic guidelines should be referred to.

Dacarbazine should only be opened by trained staff and as with all cytotoxic agents precautions should be taken to avoid exposing staff. Handling of cytotoxic medicinal products should be generally avoided during pregnancy. Preparation of solution for administration should be carried out in a

designated handling area and working over a washable tray or disposable plastic-backed absorbent paper.
Suitable eye protection, disposable gloves, face mask and disposable apron should be worn. Syringes and infusion sets should be assembled carefully to avoid leakage (use of Luer lock fittings is recommended).

On completion, any exposed surface should be thoroughly cleaned and hands and face washed.

In the event of spillage, operators should put on gloves, face masks, eye-protection and disposable apron and mop up the spilled material with an absorbent material tapped in the area for that purpose. The area should then be cleaned and all contaminated material transferred to a cytotoxic spillage bag or bin or sealed for incineration.

Preparation for intravenous administration
Dacarbazine solutions are prepared immediately before use.

Dacarbazine is sensitive to light exposure. During administration, the infusion container and administration set should be protected from exposure to daylight, e.g. by using light-resistant PVC-infusion sets. Normal infusion sets should be wrapped up in e.g. UV-resistant foils.

a) Preparation of Dacarbazine medac 500 mg:
Aseptically transfer 50 ml water for injections into the vial and shake until a solution is obtained. The resulting solution, containing 10 mg/ml of dacarbazine (density of solution: ρ = 1.007 g/ml) has to be further diluted with 200 – 300 ml 0.9 % sodium chloride or 5 % glucose infusion solution. The obtained infusion solution, containing 1.4 – 2.0 mg/ml of dacarbazine, is ready for i. v. infusion and should be given within 20 – 30 minutes.

b) Preparation of Dacarbazine medac 1000 mg:
Aseptically transfer 50 ml water for injections into the vial and shake until a solution is obtained. The resulting solution, containing 20 mg/ml of dacarbazine (density of solution: ρ = 1.015 g/ml) has to be further diluted with 200 – 300 ml 0.9 % sodium chloride or 5 % glucose infusion solution. The obtained infusion solution, containing 2.8 – 4.0 mg/ml of dacarbazine, is ready for i. v. infusion and should be given within 20 – 30 minutes.

Dacarbazine medac 500 mg (1000 mg) is for single use only.
The diluted solution for infusion should be visually inspected and only clear solutions practically free from particles should be used. Do not use the solution if particles are present.
Any portion of the contents remaining after use should be discarded, as well as solutions where the visual appearance of the product has changed.

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