PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Dacarbazine Lipomed 200 mg powder for solution for injection or infusion
Dacarbazine

Read all of this leaflet carefully before you start having this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist.

In this leaflet:

1. WHAT DACARBAZINE LIPOMED IS AND WHAT IT IS USED FOR

What Dacarbazine is
The full name of your medicine is Dacarbazine Lipomed. In this leaflet the shorter name Dacarbazine is used. This belongs to a group of medicines called 'cytotoxic drugs', often called chemotherapy. Treatment with Dacarbazine should only be carried out by doctors who specialise in the treatment of cancer (oncologists) or blood problems (haematologists).

What Dacarbazine is used for
Dacarbazine is used to treat a type of skin cancer called 'metastatic malignant melanoma'. This is a type of skin cancer which has spread to another part of your body.

Dacarbazine is also used together with other medicines for:
- Advanced cancer of a part of your immune system called the 'lymphatic system'. This type of cancer is often called 'Hodgkin's disease'.
- Advanced soft tissue sarcoma in adults (exceptions: mesothelioma, Kaposi sarcoma). Soft tissue sarcomas are malignant tumours which arise from the soft tissues of the body. Tumours may be found in many places such as around your nerves, muscles or blood vessels.

How Dacarbazine works
Dacarbazine helps to stop your cancer cells growing and multiplying.

2. BEFORE YOU HAVE DACARBAZINE LIPOMED

Do not have Dacarbazine if:
- You are allergic (hypersensitive) to dacarbazine or any of the other ingredients of this medicine (listed in Section 6)
- You are pregnant or are breastfeeding your child
- You have a low number of white blood cells (leukopenia) or a low number of platelets (thrombocytopenia)
- You have severe liver or kidney problems

- In combination with yellow fever vaccine

Do not have Dacarbazine if any of the above apply to you. If you are not sure, talk to your doctor, nurse or pharmacist before using Dacarbazine.

Take special care with Dacarbazine

Your doctor will need to ensure appropriate administration of dacarbazine in order to prevent tissue damage and pain. Extravasation (injection of the solution into the tissue around the vein) can lead to tissue damage and severe pain.

Tests:
During your treatment the following things will be checked:
- Liver size and how well your liver is working (through blood tests). This is to check that the veins in your liver are not being blocked. If your liver is affected, treatment will be stopped.
- Amount of red, white and platelet blood cells in your blood (through blood tests). This is to check that your bone marrow is working properly to help create blood cells. If your bone marrow is affected, treatment may be stopped for a while or stopped completely.

Men who are being treated with dacarbazine are advised to take contraceptive measures during therapy and for 6 months after the end of therapy.

Using other medicines
Please tell your doctor or nurse if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription, including herbal medicines. This is because Dacarbazine can affect the way some other medicines work. Also some other medicines can affect the way Dacarbazine works.

In particular, do not have this medicine and tell your doctor, nurse or pharmacist if you are using any of the following:
- Phenytoin – for fits (seizures)
- Other medicines which might damage your liver.

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

Tell your doctor, nurse or pharmacist if you are using any of the following:
- Radiation treatment or other medicines to reduce tumour growth (chemotherapy). Using these medicines with Dacarbazine can increase the damage to your bone marrow.
- Other medicines that are metabolized by a system of liver enzymes called cytochrome P450.
- Methoxypsoralen – for skin problems such as psoriasis and eczema. Having Dacarbazine with Methoxypsoralen can make you more sensitive to sunlight (photosensitisation).
- Fotemustine - You should not use dacarbazine earlier than one week after fotemustine administration to avoid damage to your lungs.
- Cyclosporin or tacrolimus: these medicines may reduce the function of your immune system.

If any of the above apply to you (or you are not sure), please tell your doctor, nurse or pharmacist before having Dacarbazine.

Your doctor will decide whether use of medicines to improve the blood flow should be given to you and will check your clotting tendency of the blood.

Using vaccines
There is different advice for different types of vaccines:
- Yellow-fever - You must not have a yellow-fever vaccine if you are having Dacarbazine.

- Live vaccines – You should not have a 'live' vaccine if you are having Dacarbazine. This is because Dacarbazine may weaken your immune system and make you more likely to catch a serious infection.
- Killed vaccines – You may have a 'killed' or inactivated vaccine if you are having Dacarbazine.

Having Dacarbazine with food and drink
- Do not eat just before having Dacarbazine. This could make you feel less sick or be less sick.
- Do not drink alcohol during your treatment.

Pregnancy and breast-feeding
- Do not have Dacarbazine if you are pregnant or planning to become pregnant. This is because the medicine can damage your unborn child.
- During treatment men and women need to use a reliable method of contraception. If you become pregnant, tell your doctor straight away.
- Men who are being treated with Dacarbazine also need to use a reliable method of contraception for 6 months after the end of therapy.
- Do not breast-feed during your treatment with Dacarbazine.

Driving and using machines
You may feel sleepy, confused or having impaired vision while having Dacarbazine. You may also feel or be sick. If any of these happen, do not drive or use any tools or machines.

3. HOW YOU HAVE DACARBAZINE LIPOMED

Your doctor will decide how long your treatment should last. This will depend upon:
- The type of cancer you have and how advanced it is
- Which treatment you are being given and how well you are responding to it
- Whether you are having any side effects

How much you will be given
The amount you are given is worked out depending on your size (m^2 body surface area).

Skin cancer that has spread (metastatic malignant melanoma)
- The usual dose is 200-250 mg per m^2 body surface area, once a day.
- You are given this 5 days in a row, every 3 weeks. You then have a break.
- It will be given as a fast injection into your vein or as a slow infusion into your vein lasting 15 to 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 your lymphatic system (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 vinblastin (this combination is called the ABVD regimen).
- You will usually do this 6 times.
- It will be given as a slow infusion into the vein.

Cancer of the tissues that join your body togeher (soft tissue sarcoma)
- The usual dose is 250 mg per m^2 body surface area, once a day.
- You will also be given a medicine called doxorubicin (this combination is called the ADIC regimen).
- You are given this 5 days in a row, every 3 weeks. You then have a break.

- It will be given as a slow infusion into the vein lasting 15-30 minutes.

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.

Elderly people
There are no special instructions for the use of Dacarbazine in elderly people.

Children
Until further data become available, no special recommendations for the use of Dacarbazine in children can be given.

If you have more Dacarbazine than you should
If you think that you have been given too much Dacarbazine, tell your doctor or nurse straight away.
- If an overdose is suspected, the numbers of your blood cells will be checked and supportive measures such as transfusions may be required.
- An overdose would cause severe damage to your bone marrow (bone marrow toxicity). This can lead to a complete loss of function of your bone marrow (bone marrow aplasia). This can be delayed by up to 2 weeks.

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

4. POSSIBLE SIDE EFFECTS

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

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist.

Common (affects 1 to 10 users in 100)
- Loss of appetite (anorexia), feeling sick or being sick. If anyone helps to clean up your sick, they must wear gloves. This is because some of the medicine may pass into their skin.
- Blood problems. These are dependent on how strong your dose is and are most likely after 3 to 4 weeks. You may feel tired, look pale, bruise more easily than usual or get more infections than usual. They are shown by blood tests:
  - anaemia (decreased red blood cells)
  - leukopenia (decreased white blood cells)
  - thrombocytopenia (decreased platelets)
  - bone marrow suppression (decreased formation of all blood cells in the bone marrow)

Uncommon (affects 1 to 10 users in 1,000)
- Flu-like symptoms such as tiredness, chills, fever or muscle pain. These are more likely in the first few days of each treatment cycle
- Abnormal kidney function or increased liver enzymes (shown in tests)
- Liver damage (hepatotoxicity)
- Blockage of a vein in your liver (also called Budd-Chiari syndrome)
- Liver tissue damage (necrosis) due to blockage of a vein in your liver. The signs include fever, stomach pain, yellow eyes and skin (jaundice). Your doctor would also be able to see that your liver was larger and you would have changes in the numbers of your blood cells. This is most likely in your second cycle.
- Dark patches on your skin (hyperpigmentation)
- Increased sensitivity of your skin to sunlight (photosensitivity)

- Hair loss (alopecia)
- Feeling confused
- Flushed face
- Transient rash
- Blurred vision

Rare (affects 1 to 10 users in 10,000)
- Injection site reactions such as vein irritation
- Red skin (erythema), a rash with spots and blisters (maculopapular exanthema) or a nettle rash (urticaria)
- Skin reactions where the medicine is injected
- Swelling of the face, lips, mouth and throat with difficulty breathing (anaphylactic reaction)
- Feeling sleepy, having impaired vision
- Headache
- Fits (seizures)
- Pins and needles sensation in the face
- Diarrhoea. If anyone helps to clean up your diarrhoea, they must wear gloves. This is because some of the medicine may pass into their skin.
- Blood problems. These are dependent on how strong your dose is and are most likely after 3 to 4 weeks. You may feel tired, look pale, bruise more easily than usual or get more infections than usual. They are shown by blood tests
    - pancytopenia (all blood cells decreased)
    - agranulocytosis (marked decrease in one type of white blood cell called a “granulocyte”)

If the medicine is accidentally injected into the tissue around your vein, it will be painful and there will be tissue damage.

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 national reporting system:
IMB Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.imb.ie
e-mail: imbpharmacovigilance@imb.ie
By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE DACARBAZINE LIPOMED

Keep out of the reach and sight of children.

Do not use Dacarbazine after the expiry date which is stated on the carton and bottle after EXP. The expiry date refers to the last day of that month.

Do not use Dacarbazine if the solution is cloudy or has bits floating in it.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Do not store above 25°C.
Store in the original package in order to protect from light.

Shelf life of the reconstituted solution
Chemical and physical in-use stability has been demonstrated for 8 hours at room temperature and protected from light and for 5 days at 2 to 8°C and protected from light. From a microbiological point of view, the reconstituted solution should be used immediately.
If the reconstituted solution is not used immediately, the duration and conditions of storage are the responsibility of the user. The reconstituted solution should not be stored for longer than 24 hours in a refrigerator (2 to 8°C) and protected from light, unless the reconstitution has taken place under controlled and validated aseptic conditions.

Shelf life of diluted solution for infusion
Chemical and physical in-use stability has been demonstrated for 8 hours at room temperature and protected from light and for 5 days at 2 to 8°C and protected from light. From a microbiological point of view, the diluted solution for infusion should be used immediately.
If the diluted solution for infusion is not used immediately, the duration and conditions of storage are the responsibility of the user. The diluted solution for infusion should not be stored for longer than 24 hours in a refrigerator (2 to 8°C) and protected from light, unless the reconstitution and dilution have taken place under controlled and validated aseptic conditions.

From a microbiological point of view, it is recommended not to exceed a total storage time of 24 hours after opening of the product.

6. FURTHER INFORMATION

What Dacarbazine contains
- The active substance is dacarbazine. Each vial contains 200 mg dacarbazine. After reconstitution, the solution contains 10 mg/ml dacarbazine.
- The other ingredients are citric acid monohydrate and mannitol (E 421).

What Dacarbazine looks like and contents of the pack
Dacarbazine is a powder for solution for injection or infusion. It is a white powder that is made up into a clear liquid for injection or infusion. It is packed in cartons each containing 10 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Lipomed GmbH
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D-79576 Weil am Rhein
Germany
Telephone number: +49-7621-1693-472
Fax number: +49-7621-1693-474
E-mail: lipomed@lipomed.com

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

Austria: Dacarbazin Lipomed 200 mg Pulver zur Herstellung einer Injektions- oder Infusionslösung
Germany: Dacarbazin Lipomed 200 mg Pulver zur Herstellung einer Injektions- bzw. Infusionslösung
France: Dacarbazine Lipomed 200 mg poudre pour solution injectable ou perfusion
Italy: Dacarbazina Lipomed 200 mg polvere per soluzione iniettabile o per soluzione per infusione
Cyprus: Dacarbazine Lipomed 200 mg κόνις για ενέσιμο διάλυμα ή διάλυμα προς έγχυση

Denmark: Dacarbazine Lipomed 200 mg pulver til injektions- og infusionsvæske, opløsning
Finland: Dacarbazine Lipomed 200 mg injektio-/infuusiokuiva-aine liuosta varten
Norway: Dacarbazine Lipomed 200 mg pulver til injeksjons-/infusjonsvæske, oppløsning
Ireland: Dacarbazine Lipomed 200 mg powder for solution for injection or infusion
Romania: Dacarbazină Lipomed 200 mg pulbere pentru soluţie injectabilă sau perfuzabilă

This leaflet was last approved in March 2019.

The following information is intended only for doctors and/or medical personnel

It is recommended that the patency of the vein is tested with 5 to 10 ml of isotonic sodium chloride solution or glucose 5%. The same solution will be used to rinse the remaining medicine out of the infusion tube.

Administration of the injection/infusion
After reconstitution (preparation of the solution) with water for injections and without further dilution with isotonic sodium chloride solution or glucose 5%, Dacarbazine Lipomed preparations are hypo-osmolar (ca. 100 mOsmol/kg) which means that the solutions contain a lower concentration of dissolved substances than blood; it should therefore be given by slow intravenous injection, e.g., over 1 minute and not as an i.v. bolus injection (fast injection) over a few seconds.

Dacarbazine is sensitive to light. Reconstituted solutions must therefore be protected from light, including during the infusion (light-resistant infusion set).

The solution must be administered carefully to avoid extravasation (injection of the solution into the tissue around the vein), as this can cause local pain and tissue damage.

If extravasation occurs the injection must be immediately interrupted and the remaining dose administered in a different vein.

Notes on safe handling
Dacarbazine is an antineoplastic agent (it reduces the growth of cancer cells). Before preparing a solution, local cytotoxic (cell damaging) guidelines should be referred to regarding handling of cytotoxic agents. Dacarbazine should only be opened by trained staff. As with all cytotoxic agents, precautions should be taken to avoid exposing staff. Handling of cytotoxic drugs should be generally avoided during pregnancy. Preparation of the solution for administration should be carried out in a designated handling area and working over a washable tray or disposable plastic-backed absorbent paper. It is recommended that suitable eye protection, disposable gloves, face mask and a disposable apron are worn. Syringes and infusion sets should be assembled carefully to avoid leaks (use of Luer lock fittings is recommended). Once completed, any exposed surface should be thoroughly cleaned and the hands and face washed. In the event of spillage, operators should put on gloves, face masks, eye-protection and a disposable apron and mop up the spilled material with an absorbent material laid out 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 of the solution for intravenous dosing (administration into a vein)
Dacarbazine Lipomed solutions should be prepared immediately before use. Dacarbazine is sensitive to light. During the treatment the infusion container and infusion set has to be protected from light, for example by using a light-resistant PVC infusion set. Other infusion sets should, for example, be wrapped in light resistant aluminium foil.

Preparation and administration of the solution for injection/infusion
Dacarbazine Lipomed 200 mg powder for solution for injection or infusion will be reconstituted with 19.7 ml of water for injections, that means the powder will be completely dissolved. The resulting

solution contains 10 mg/ml dacarbazine. The solution will be given as a slow injection – it will be injected slowly into a vein. At higher doses, the reconstituted solution will be diluted with 200 ml glucose 5% or sodium chloride solution 0.9% and infused intravenously over 15 to 30 minutes (given slowly into a vein).

Dacarbazine Lipomed is for single use only.

Dacarbazine solution is chemically incompatible with the medicinal products heparin, hydrocortisone, L-cysteine and sodium hydrogen carbonate; this means that dacarbazine solution should not be mixed with medicines that contain these substances. This medicinal product must not be mixed with other medicinal products except those mentioned above.

Shelf life of the reconstituted solution
Chemical and physical in-use stability has been demonstrated for 8 hours at room temperature and protected from light and for 5 days at 2 to 8°C and protected from light. From a microbiological point of view, the reconstituted solution should be used immediately.
If the reconstituted solution is not used immediately, the duration and conditions of storage are the responsibility of the user. The reconstituted solution should not be stored for longer than 24 hours in a refrigerator (2 to 8°C) and protected from light, unless the reconstitution has taken place under controlled and validated aseptic conditions.

Shelf life of diluted solution for infusion
Chemical and physical in-use stability has been demonstrated for 8 hours at room temperature and protected from light and for 5 days at 2 to 8°C and protected from light. From a microbiological point of view, the diluted solution for infusion should be used immediately.
If the diluted solution for infusion is not used immediately, the duration and conditions of storage are the responsibility of the user. The diluted solution for infusion should not be stored for longer than 24 hours in a refrigerator (2 to 8°C) and protected from light, unless the reconstitution and dilution have taken place under controlled and validated aseptic conditions.

From a microbiological point of view, it is recommended not to exceed a total storage time of 24 hours after opening of the product.