

DACARBAZINE NEAPOLIS[®]

Powder for solution for injection/infusion

DACARBAZINE 100 mg & 200 mg

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Read all of this leaflet carefully before you start taking this medicine

- Keep this leaflet. You may need to read it again.
- If you have any further questions, if in doubt, ask your doctor or pharmacist for more information.
- This medicine has been prescribed for you only. Do not pass it on to others, even if their signs of illness are the same as yours, it may harm 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 or pharmacist.

In this leaflet :
 1. WHAT IS DACARBAZINE NEAPOLIS, powder for solution for injection/infusion AND IN WHICH CASE IS IT USED ?
 2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE DACARBAZINE NEAPOLIS, powder for solution for injection/infusion ?
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1. WHAT IS DACARBAZINE NEAPOLIS, powder for solution for injection/infusion AND IN WHICH CASE IS IT USED ?

Pharmacotherapeutic class
What is dacarbazine ?
 It belongs to a family of medicines called "cytotoxic medicines", often referred to as chemotherapy. Dacarbazine treatment should only be given by specialized doctors in the treatment of cancer (oncologists) or blood problems (hematologists).
Therapeutic indications
When is dacarbazine used ?
 Dacarbazine is used to treat a type of skin cancer called "metastatic malignant melanoma". This is a type of skin cancer that has spread to another part of your body.
 Dacarbazine is also used 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 (except mesothelioma, Kaposi's sarcoma). Soft tissue sarcomas are malignant tumors that start in the soft tissues of the body. Tumors can be present in various places, such as around nerves, muscles or blood vessels.

How does dacarbazine work ?
 Dacarbazine helps prevent your cancer cells from growing and multiplying.
2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE DACARBAZINE NEAPOLIS, powder for solution for injection/infusion ?

List of information needed before taking the medicine
 Not applicable.
Contraindications
Never take dacarbazine if :
 • you are allergic (hypersensitive) to dacarbazine or any of the other components of this medicine (listed in section 6) ;
 • you are pregnant or breastfeeding your child ;
 • you have a low white blood cell count (leukopenia) or a low platelet count (thrombocytopenia) ;
 • you have severe liver or kidney disease ;
 • you receive in combination a vaccine against yellow fever.
 You should not receive dacarbazine if any of the above apply to you. If you are not sure, talk to your doctor, nurse or pharmacist before you are given dacarbazine.

Precautions for use ; special warnings
Be careful with dacarbazine :
 Your doctor will need to ensure that dacarbazine is given correctly to avoid tissue damage and pain. medicine extravasation (injection of the solution into the tissues surrounding the vein) could cause tissue damage and severe pain.
 Examinations:
 During your treatment, the following points will be checked:
 • The size of your liver and how well it is working (through blood tests). This is to check that the veins in your liver are not blocked. If your liver is affected, treatment will be stopped.
 • The number of red blood cells, white blood cells and platelets in your blood (through blood tests). This is to check that your bone marrow is working properly and playing its part in the creation of blood cells. If your bone marrow is affected, treatment may be stopped temporarily or permanently.
 Men being treated with dacarbazine will be advised to take contraceptive measures during treatment and for up to 6 months after treatment has ended.

Interactions with other medicines
Use of other medications
 If you are taking or have recently taken any other medicines, tell your doctor or nurse. This includes medicines obtained without a prescription, including herbal medicines. This is necessary because dacarbazine may affect the way other medicines work. Some medicines can also affect how dacarbazine works.
 In particular, you must not be given this medicine and you should tell your doctor, nurse or pharmacist if you are using any of the following:
 • phenytoin, used to treat seizures,
 • other medicines that could damage your liver.
 You should not be given dacarbazine if any of the above applies to you. If you are not sure, talk to your doctor, nurse or pharmacist before you are given dacarbazine. Tell your doctor, nurse or pharmacist if you are using any of the following treatments:
 • Radiation therapy or medicines to reduce the growth of a tumor (chemotherapy). Using these treatments along with dacarbazine may amplify the damage to your bone marrow.
 • Other medicines metabolized by an enzyme system in the liver called cytochrome P450.
 • Methoxy psoralen, used for skin problems like psoriasis and eczema. If you receive dacarbazine and methoxy psoralen simultaneously, you may be more sensitive to sunlight (photosensitization).
 • fotemustine; you must not be given dacarbazine within one week of receiving fotemustine as it may harm

your lungs.
 • Ciclosporin or tacrolimus : these medicines could weaken your immune system.
 If any of the above apply to you (or if you are not sure), talk to your doctor, nurse or pharmacist before you are given dacarbazine.
 Your doctor will decide if you should receive medicines to improve blood flow and control your blood clotting.
Vaccinations
 Recommendations vary depending on the type of vaccine :
 • Yellow fever: you should not take a yellow fever vaccine when you receive dacarbazine.
 • Live virus vaccines : you should not receive a so-called "live" vaccine when you receive dacarbazine because dacarbazine can weaken your immune system and you may catch serious infections more easily.
 • Inactivated virus vaccines : You may receive an inactivated vaccine ("inactivated" virus) when you receive dacarbazine.

Interactions with food and drinks
Food and drinks
 • Do not eat just before taking dacarbazine as you may experience more nausea or vomiting.
 • Do not drink alcohol during your treatment.
Interactions with phytotherapy products or alternative therapies
 Not applicable.
Use During Pregnancy and Breastfeeding
Pregnancy and Breastfeeding
 • You must not be given dacarbazine if you are pregnant or plan to be pregnant as the medicine may harm your unborn child.
 • During treatment, both men and women should use a reliable method of contraception. If you become pregnant, tell your doctor immediately.
 • Men taking dacarbazine should also use reliable contraception during treatment and for up to 6 months after treatment ends.
 • Do not breastfeed while taking dacarbazine.

Sports
 Not applicable.
Effects on the ability to drive or using machines
Driving and using machines
 You may feel drowsy, confused or have blurred vision when you receive dacarbazine.
 You may also have nausea or vomit. If you experience any of these effects, do not drive or use any tools or machines.
List of excipients with known effect
 Not applicable.
3. HOW TO USE DACARBAZINE NEAPOLIS powder for solution for injection / infusion ?
Instructions for proper use
 Your doctor will decide the duration of your treatment. This will depend on :
 • the type of cancer you have and its stage ;
 • the treatment you receive and how you respond to it ;
 • the appearance or not of side effects.

Dosage, Mode and/or route(s) of administration, Frequency of administration and Duration of treatment
How much will you receive?
 The amount of medicine you will receive is based on your height (your body surface area in m²).
Skin cancer that has spread (metastatic malignant melanoma)
 • The usual dose is 200-250 mg per m² body surface area, once daily.
 • You will receive this dose 5 days in a row, every 3 weeks. You will then take a break.
 • The medicine will be given as a rapid injection into a vein or as a slow infusion into a vein over 15 to 30 minutes.
 • You may also receive a higher dose of 850 mg per m² body surface area every 3 weeks. It will then be given to you as a slow infusion into a vein.

Cancer of the lymphatic system (Hodgkin's disease)
 • The usual dose is 375 mg per m² of body surface, every 15 days.
 • You will also receive medicines called doxorubicin, bleomycin and vinblastine (this combination is called ABVD treatment).
 • This treatment is usually administered 6 times.
 • It will be given to you as a slow infusion into a vein.
Soft tissue sarcoma (cancer of the tissues supporting the structures and organs of the body)
 • The usual dose is 250 mg per m² body surface area, once daily.
 • You will also be given a medicine called doxorubicin (this combination is called ADIC treatment).
 • You will receive this treatment 5 days in a row, every 3 weeks. You will then take a break.
 It will be given to you by slow infusion into a vein over 15-30 minutes.

Patients with kidney or liver problems
 If your kidney or liver problems are mild or moderate, it is usually not necessary to lower your dose of medicine. If you have both kidney and liver problems, it will take longer for your body to use the medicine and eliminate it from your body. Your doctor may decide to lower your dose of medicine.

Elderly
 There are no special instructions for the use of dacarbazine in the elderly.
Children
 Until we have additional information, no particular recommendation can be given regarding the use of dacarbazine in children.
Symptoms and instructions in case of overdose
If you have taken more DACARBAZINE NEAPOLIS than you should :
 If you think you have been taking too much dacarbazine tell your doctor or nurse immediately.
 • If an overdose is suspected, your blood cell counts will be checked and symptomatic treatment, such as transfusions, may be required.

An overdose will cause severe damage to your bone marrow (bone marrow toxicity). Your bone marrow may stop working completely (aplastic anemia). These effects may appear up to 2 weeks later.
Instructions in case of omission of one or more doses
 Not applicable.
Risk of withdrawal syndrome

Not applicable.
 If you have any further questions on the use of this medicine, ask your doctor, nurse or pharmacist.
4. Possible side effects
Description of side effects
 Like all medicines, DACARBAZINE NEAPOLIS can cause side effects, although not everybody gets them.
If you notice any of the side effects listed as serious, or if you notice any side effects not listed in this leaflet, please inform your doctor, nurse or pharmacist.
Common (occurs in 1 to 10 users in 100)
 • Loss of appetite (anorexia), nausea or vomiting. If someone is helping you clean up your vomit, they should wear gloves because some of the medicine could get through their skin.
 • Blood problems. These depend on the dose you receive and most often appear after 3 to 4 weeks. You may feel tired, look pale, bruise more easily than usual, or get more infections than usual. Blood tests can show them:
 - anemia (decrease in red blood cells),
 - leukopenia (decrease in white blood cells),
 - thrombocytopenia (decrease in platelets),
 - myelosuppression (decreased formation of all blood cells in the bone marrow).
Uncommon (occurs in 1 to 10 users in 1,000)
 • Flu-like symptoms such as fatigue, chills, fever or muscle aches. These are more common during the first few days of each treatment cycle.
 • Abnormal kidney function or increased liver enzymes (shown by blood tests).
 • Liver damage (hepatotoxicity).
 • Blockage of a vein in the liver (also called Budd-Chiari syndrome).
 • Damage to liver tissue (necrosis) due to blockage of a vein in your liver. Fever, upset stomach, yellowing of the eyes and skin (jaundice) may be signs. Your doctor might also detect an increase in the size of your liver and a change in your blood cell count. This occurs most often during the second cycle of treatment.
 • Dark spots on the skin (hyperpigmentation).
 • Increased sensitivity of the skin to light (photosensitivity).
 • Hair loss or body hair (alopecia).
 • Feeling of confusion.
 • Hot flushes in the face.
 • Transient rash.
 • Blurred vision.

Rare (occurs in 1 to 10 users in 10,000)
 • Injection site reactions such as vein irritation.
 • Redness on the skin (erythema), rash with pimples and blisters (maculopapular exanthema) or hives.
 • Skin reactions where the medicine is injected.
 • Swelling of the face, lips, mouth and throat with difficulty in breathing (anaphylactic reaction).
 • Drowsiness, blurred vision.
 • Headache.
 • Seizures (convulsions).
 • Tingling sensation in the face.
 • Diarrhea. If someone is helping you clean up your diarrhea, they should wear gloves because some of the medicine could get through their skin.
 • Blood problems. These depend on the dose you receive and most often appear after 3 to 4 weeks. You may feel tired, look pale, bruise more easily than usual, or get more infections than usual. Blood tests can show them.
 - pancytopenia (decrease in all blood cells).
 - agranulocytosis (marked reduction in a type of white blood cell called a granulocyte).
 If the medicine is accidentally injected into the tissue around the vein, you will feel pain and the tissue will be damaged.
 If you notice any side effects not listed in this leaflet, or if any side effects get serious, please tell your doctor or pharmacist.

5. HOW TO STORE DACARBAZINE NEAPOLIS, powder for solution for injection / infusion ?
 Keep out of the reach and sight of children.
Expiration date
 Do not receive DACARBAZINE NEAPOLIS after the expiry date which is stated on the box and the vial after EXP. The expiry date refers to the last day of the month.
Storage conditions
 Store at lower temperature between 2°C and 8°C, away from light.
 Store in the original outer packaging, away from light.
If necessary, warnings against certain visible signs of deterioration
 You should not be given DACARBAZINE NEAPOLIS if the solution is cloudy or contains visible particles. Medications should not be disposed of via sewage system or household waste. Ask your pharmacist what to do with unused medicine. These measures will help protect the environment.

6. ADDITIONAL INFORMATION
Complete list of active substances and excipients
What does DACARBAZINE NEAPOLIS contain ?
The active substance is: dacarbazine.
 Each vial contains 100 mg of dacarbazine.
 Each vial contains 200 mg of dacarbazine.
The other components are : citric acid anhydrous, mannitol.
Pharmaceutical form and content
What DACARBAZINE NEAPOLIS looks like and content of the outer packaging ?
 This medicine is in the form of a powder for solution for injection / infusion in boxes of 1 or 10 vials.
Marketing authorisation holder and Manufacturer
 Les Laboratoires Neapolis Pharma
 Road of Tunis Km 7 - PB 206 Nabeul 8000 - Tunisia.
 Tel: +216.31 338 420
 Fax: +216.31338 421
 E-mail : neapolispharma@neapolispharma.com
Supply conditions : Table A/Liste 1

M.A. N :
 DACARBAZINE NEAPOLIS 100mg, box of 1 vial: 9393221H
 DACARBAZINE NEAPOLIS 100mg, box of 10 vials : 9393222H
 DACARBAZINE NEAPOLIS 200mg, box of 1 vial : 9393223H
 DACARBAZINE NEAPOLIS 200mg, box of 10 vials : 9393224H
This leaflet was last reviewed : 11/2022
Information for health professionals only
The following information is intended for healthcare professionals only:
 It is recommended to first test the patency of the vein using 5 to 10 ml of isotonic solution of sodium chloride or 5% glucose. The same solution will be used to flush medical product residues in the infusion set.

Administration of the injection/infusion
 After reconstitution (preparation of the solution) with water for injections and without any further dilution with isotonic sodium chloride or 5% glucose solution, DACARBAZINE NEAPOLIS preparations are hypo osmolar (approx. 100 mOsmol/kg), which means that the solution contains a lower concentration of dissolved substances than blood; it must therefore be administered by slow intravenous injection, e.g. over 1 minute, not by bolus IV injection (rapid injection) over a few seconds.
 Dacarbazine is sensitive to light. The reconstituted solutions must therefore be kept away from light, including during the infusion (opaque infusion set).
 The solution should be administered with care to avoid extravasation (injection of the solution into the tissue surrounding the vein), as this may cause localized pain and tissue damage.
 In case of extravasation, the injection should be stopped immediately and the rest of the dose should be administered into another vein.
Advice on safe handling
 Dacarbazine is an anti-neoplastic agent (it reduces the development of cancer cells). Prior to preparing the solution, local guidelines should be consulted regarding the handling of cytotoxic agents (which damage cells). DACARBAZINE NEAPOLIS must only be opened by trained staff. As with any cytotoxic agent, precautions should be taken to prevent personnel from being exposed to it. In general, handling cytotoxic medicines should be avoided during pregnancy. The solution to be administered must be prepared in a space dedicated to this handling, by operating over a washable surface or disposable absorbent paper with a laminated front face. It is recommended to wear suitable protective eyeglasses, disposable gloves, mask and disposable apron. Syringes and infusion sets should be assembled carefully to avoid leaks (use of LuerLok fittings is recommended). Upon completion of manipulations, all exposed surfaces should be thoroughly cleaned and users should wash their hands and face. In case of a splash, operators must put on gloves, a mask, protective goggles and a disposable apron and wipe up the spilled substance using an absorbent material placed in the work area for this purpose. The workspace should then be cleaned and all contaminated materials should be transferred to a cytotoxic waste bag or receptacle or other airtight container for incineration.

Preparation of the solution for intravenous administration (into a vein)
 The DACARBAZINE NEAPOLIS solution must be prepared immediately before use. Dacarbazine is light sensitive. During treatment, the solution bag/vial and infusion set should be away from light, for example by using an opaque PVC infusion set. The other infusers can, for example, be wrapped in aluminum foil to be away from light.
Preparation and administration of DACARBAZINE NEAPOLIS 100 mg, solution for injection/infusion
 DACARBAZINE NEAPOLIS 100 mg powder for solution for injection or infusion must be reconstituted with 9.9 ml of water for injections, which means that the powder will be completely dissolved. The solution thus obtained contains 10 mg/ml of dacarbazine. The solution will be given as a slow injection (gently injected into a vein). At a higher dose, the reconstituted solution will be diluted in 200 ml of 5% glucose solution or 0.9% sodium chloride solution and injected by intravenous infusion over 15 to 30 minutes (introduced slowly into a vein).
Preparation and administration of DACARBAZINE NEAPOLIS 200 mg, solution for injection/infusion
 DACARBAZINE NEAPOLIS 200 mg powder for solution for injection or infusion must be reconstituted with 19.7ml of water for injections, which means that the powder will be completely dissolved. The solution thus obtained contains 10 mg/ml of dacarbazine. The solution will be given as a slow injection (gently injected into a vein).
 At a higher dose, the reconstituted solution will be diluted in 200 ml of 5% glucose solution or 0.9% sodium chloride solution and injected by intravenous infusion over 15 to 30 minutes (introduced slowly into a vein).
 DACARBAZINE NEAPOLIS is strictly for single use
 DACARBAZINE NEAPOLIS solution is chemically incompatible with heparin, hydrocortisone, L cysteine and sodium bicarbonate ; this means that DACARBAZINE NEAPOLIS solution must not be mixed with medicines containing these substances. This medicinal product must not be mixed with other medicinal products except those mentioned above.

Other
 Not applicable.

THIS IS A MEDICINE

- A medicine is not like other consumer goods.
- A medicine is a product that affects your health and its consumption without compliance to the prescription exposes you to danger.
- You should strictly follow your doctor's prescription and directions for use, as well as the advice of your pharmacist.
- Your doctor and your pharmacist are familiar with the medicine, its indications and contraindications.
- Do not stop treatment on your own during the prescribed period.
- Do not resume, do not increase doses without consulting your doctor

KEEP THE MEDICINES OUT OF THE REACH OF CHILDREN



