Package leaflet: Information for the user

Bleomedac 15000 IU (Ph. Eur.) = 15 U (USP)/vial, powder for solution for injection

bleomycin sulphate

Read all of this leaflet carefully before you are given 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Bleomedac is and what it is used for

This medicine contains bleomycin sulphate. This substance is from a group called cytostatic medicines. These medicines are anti-cancer medicines sometimes referred to as chemotherapy. They attack cancer cells and prevent them from dividing.

Bleomedac is usually used with other anti-cancer medicines or radiotherapy. It is used to treat:

- Cancers of the head and neck, cervix and external genitalia
- Hodgkin's disease and non-Hodgkin's lymphomas (cancers of the lymph glands)
- Cancer of the testicles
- Accumulation of fluid in the lungs as a result of cancer

2. What you need to know before you are given Bleomedac

Bleomedac will not be given
- if you are allergic to bleomycin or any of the other ingredients of this medicine (listed in section 6). An allergic reaction may include rash, itching, difficulty in breathing or swelling of the face, lips, throat or tongue.
- if you have a lung infection or other problems with your lungs.
- if you have had certain side effects of the lungs, which (possibly) are caused by bleomycin.
- if you have ataxia telangiectasia (a very rare inherited disease causing movement problems and risk of infections).
- if you are breast-feeding.

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

Special care should be taken if you have any of the following conditions:
- A kidney or liver disorder.
- A lung disorder.
- You have had radiation therapy for your lungs or if you are having radiation therapy during the treatment with bleomycin.
- You use oxygen.

- You are older than 60 years of age.

If you belong to the groups mentioned above, you may be more sensitive to the damaging effects of bleomycin on the lungs.

The doctor will probably examine you more often and/or take X-rays of your lungs.If you are being treated with bleomycin, a lung function test should be carried out regularly to monitor potential harmful effects of bleomycin on your lungs.
Tell your doctor straightaway if you cough and/or you suffer from shortness of breath, as this can be a sign of damaging effects of bleomycin to the lungs.

Like other cytotoxic active substances, bleomycin can trigger tumour lysis syndrome in patients with rapidly growing tumours. Appropriate supportive treatment and pharmacological measures might prevent or alleviate such complications.

Cases of cancer in the blood (acute myeloid leukaemia) and a syndrome where the bone marrow does not make enough healthy blood cells or platelets (myelodysplastic syndrome) have been reported in patients treated concomitantly with bleomycin and other cytostatics (substances which inhibit cell growth/cell division).

Other medicines and Bleomedac
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.
This refers especially to any of the following medicines as they may interact with Bleomedac:
- carmustin, mitomycin-C, cyclophosphamide and methotrexate (a medicinal product that is used for certain forms of cancer, rheumatism and severe skin diseases). There is an increased possibility of damage to the lungs.
- vinca alkaloids (vincristin, vinblastin; a group of medicinal products which are used for certain forms of cancer); a restriction of the blood supply to the fingers, toes and nose can occur. In very severe cases, tissue death in these body parts can occur.
- cisplatin (an anti-cancer medicine) and other kidney-damaging medicines; there is an increased possibility of side effects with bleomycin.
- digoxin (for heart disorders): there is a risk of reduced effect of digoxin.
- phenytoin (used for epilepsy).
- live vaccines; severe and fatal infections can occur.

You may know the above mentioned medicines under different names, often their brand names. Please always read carefully the outer packaging or the package leaflet of the medicine to find out what active substance it contains. Please note that the above mentioned products can also refer to medicines taken recently or to medicines you will use in the future.

Also tell your doctor if:
- you have had or are going to have radiotherapy to your chest; the risk of side effects on the lungs and/or skin is increased
- you are going to be administered oxygen; there is a greater risk of lung toxicity when you receive oxygen during narcosis

It may still be alright for you to be given Bleomedac. Your doctor will be able to decide what is suitable for you.

Pregnancy, breast-feeding and fertility

Pregnancy
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.
There is not enough clinical data on Bleomedac to judge the possible harmfulness during pregnancy.
In animal tests, however, bleomycin was found to be harmful to foetuses.

The use of bleomycin should be avoided during pregnancy, especially during the first 3 months.If you become pregnant during treatment with Bleomedac, you should speak to your doctor about the risks for the unborn child, and should be monitored carefully.
If you are considering getting pregnant after the therapy, you should have genetic counseling first.
You should use effective contraception to avoid pregnancy during treatment and for at least 6 months after treatment with this medicine.

Breast-feeding
It is not known whether this medicine passes into your milk, but since there is a possibility that bleomycin is harmful to your child, you should not breast-feed during treatment with Bleomedac. It may cause damage to your child.

Fertility
If you are a man, you should seek advice about conserving your sperm, because there is a possibility of your sperm becoming irreversibly infertile by the treatment.

Driving and using machines
Do not drive or operate machinery. This medicine may cause nausea (feeling sick) and vomiting, which may affect your ability to drive.

3. How Bleomedac will be given to you

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

If you notice that the effect of Bleomedac is too strong or too weak, consult your doctor, pharmacist or nurse.

Dose
The recommended dose is dependent on the indication, age, kidney function and combination with other anti-cancer medicines. This may result in e.g. one or two injections per week. Your doctor will decide on the dose of bleomycin, the length of the treatment and the number of treatments. They may vary per patient.

There is a risk of serious hypersensitivity reactions especially in lymphoma patients, which may occur directly or some time after receiving the medicine. Therefore, your doctor will give you a test dose and will observe you for 4 hours before starting bleomycin therapy for the first time.

Method of administration
Your doctor will give bleomycin as an infusion (drip) or injection into the veins or arteries, underneath the skin, into the space surrounding the lungs (intrapleural), into the abdominal cavity (intraperitoneal), into the muscles or directly into the tumour.

If you have been given more Bleomedac than you should
Symptoms that can occur if you have received too much Bleomedac are: a drop in blood pressure, fever, faster heart rate and shock. If you suspect an overdose, you should tell your doctor immediately, and treatment has to be stopped immediately.

If you have not received Bleomedac when you should
If you have missed an injection, please contact your doctor to discuss if and how to make up for the forgotten injection.

If you stop using Bleomedac
If you suddenly stop using Bleomedac without talking to your doctor, the symptoms that existed before the start of the treatment can develop again.

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

4. Possible side effects

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

Serious side effects
If you develop any of the following side effects, tell your doctor immediately:
- Coughing
- Breathlessness
- Cracking or popping sound when breathing

You may need to have your treatment stopped.

The following side effects have also been reported:

Very common (may affect more than 1 in 10 people)
- Pneumonia (inflammation of the lungs). This can cause permanent damage to the lungs and can be fatal. Tell your doctor immediately if you suffer from coughing and/or shortness of breath (see section 2 “Warnings and precautions”).
- Inflammation of the mucous membrane of the mouth (stomatitis). Inflammation or ulceration of the mucous membranes can be worsened in combination with radiation or other medicines that are harmful to the mucous membranes. Inflammation of the mucous membrane of the mouth is rarely severe and usually disappears after the completion of the therapy.
- Feeling sick, vomiting, loss of appetite, weight loss.
- Rash, itching, and thickening of the skin. Sensitivity and swelling of the finger tips, stretch marks (striae), hyperpigmentation (increased pigment formation), blisters, changing of the nails, swelling of the skin at pressure sensitive points such as the elbows, hair loss, red scaly skin together with fever; skin problems on the hands and feet such as redness and skin rash are rarely severe and usually disappear after the completion of the therapy.

Common (may affect up to 1 in 10 people)
- Severe hypersensitivity reactions. These reactions may occur immediately, or after a delayed period of a few hours after the first or second dose**. Tell your doctor straight away if you experience any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).**
- Allergic reactions.
- Acute respiratory insufficiency (acute respiratory distress syndrome - ARDS).
- Pulmonary embolism
- Fever (2 to 6 hours after the first injection), pain in the area of the tumour, and headache.

Uncommon (may affect up to 1 in 100 people)
- Changes in the blood can be noticed by unexpected bleeding and/or bruising. This disappears after the treatment is finished.
- Changes in the numbers of white blood cells (this can be detected by a test carried out by a doctor) called leukopaenia (reduction in white blood cell count) and neutropaenia (reduction in neutrophil granulocytes in the blood).
- Haemorrhage (bleeding).
- Diarrhoea.

Rare (may affect up to 1 in 1,000 people)
- Neutropaenic fever (fever caused by a decrease in white blood cells).
- Heart attack, disorders of the blood vessels in the heart.
- Insufficient peripheral blood circulation (shock), elevated temperature and death related to the administration of bleomycin within the space surrounding the lungs (intrapleural administration) has been reported.

- With doses that are higher than is recommended, acute reactions with elevated temperatures and serious side effects with respect to the heart and respiration have been reported.
- Damage to the blood vessels (e.g. blood flow disorders in the brain, inflammation of the blood vessels in the brain and a severe disorder of the kidneys and the blood (so-called haemolytic uraemic syndrome), arterial thrombosis.
- Hepatic impairment.

Very rare (may affect up to 1 in 10,000 people)
- Tumour lysis syndrome (condition following rapid breakdown of tumours).

Not known (frequency cannot be estimated from the available data)
- Infections including overwhelming infection (sepsis).
- Severe reduction in blood cells (pancytopenia).
- Reduction in red blood cells (anaemia).
- Pain in the muscles and limbs
- During and just after chemotherapy with bleomycin abnormal sperm cells (aneuploid spermatozoa) can occur.
- Hardening of the skin.
- Low blood pressure.
- Closing of a blood vessel.
- Reduced blood supply to the fingers, toes, tip of the nose (Raynaud's Phenomenon).
- Ticklishness, itching or tingling without cause (paraesthesia).
- Abnormal increase in sensitivity to stimuli of the sense (hyperaesthesia).
- Pain at the site of the injection.
- Inflammation of the blood vessels (thrombophlebitis).

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 listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Bleomedac

Keep this medicine out of the sight and reach of children. Your doctor and/or hospital pharmacist are responsible for the correct storage, use and disposal of Bleomedac. It should be stored in its original packaging in a refrigerator at 2 °C–8 °C.

After reconstitution
After reconstitution in the vial, chemical and physical stability has been demonstrated for 24 hours at 2 °C to 8 °C and for 72 hours at 25 °C.

After dilution
After dilution, chemical and physical stability has been demonstrated for 72 hours at 25 °C in glass bottles and polypropylene syringes.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

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 date of that month.

Do not use this medicine if you notice any visible signs of deterioration of the product or the vial such as deviated colour of the cake, damages to the vial, the stopper or the cover.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist 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 Bleomedac contains
The active substance is bleomycin sulphate. This medicine contains no other ingredients.

One vial of 10 ml contains 15000 IU (Ph. Eur.) of bleomycin sulphate.
1 mg of dry weight of the powder is equivalent to at least 1500 IU (Ph. Eur.).

What Bleomedac looks like and contents of the pack
Bleomedac is a white to yellowish white powder.

Bleomedac is available as a box of 1 or 10 vials (type I glass).

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
medac
Gesellschaft für klinische Spezialpräparate mbH
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This medicine is authorised in the Member States of the EEA under the following names:

Bulgaria	Блеомицин медак 15 000 IU (Ph. Eur.), прах за инжекционен разтвор
Czech Republic	Bleomedac
Estonia	Bleomycin medac 15000 RÜ süstelahuse pulber
Lithuania	Bleomycin medac 15000 TV milteliai injekciniam tirpalui
Latvia	Bleomycin medac 15000 SV pulveris injekciju šķīduma pagatavošanai
Netherlands	Bleomedac, poeder voor oplossing voor injectie 15000 IU (Ph. Eur.)
Poland	Bleomedac
Slovenia	Bleomicin medac 15000 i.e. (Ph. Eur.), prašek za raztopino za injiciranje
Slovak Republic	Bleomedac 15000 IU

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The following information is intended for healthcare professsionals only:

Special precautions for disposal and other handling

Method of administration

Intramuscular and subcutaneous injection: dissolve the required dose in a maximum of 5 ml of a suitable diluent, such as sodium chloride 9 mg/ml (0.9%) solution. If pain occurs at the site of the injection a local anaesthetic (1% lidocaine solution) can be added to the solution suitable for injection.

Intravenous administration: dissolve the required dose in 5–1000 ml sodium chloride 9 mg/ml (0.9%) solution and slowly inject or add to a running infusion.

Intraarterial administration: a slow infusion with a sodium chloride 9 mg/ml (0.9%) solution is used.

Intrapleural injection: dissolve 60 x 10^3 IU in 100 ml sodium chloride 9 mg/ml (0.9%) solution.

Local/intratumoural injections: bleomycin is dissolved in sodium chloride 9 mg/ml (0.9%) solution to concentrations of 1 – 3 x 10^3 IU/ml solution.

The usual caution for the preparation and administration of cytostatic medicines is required. For safety information and disposal processing, the guideline with respect to safe handling of antineoplastic medicinal products must be followed.
Specially trained personnel must take care of the preparation. Pregnant women must be warned to avoid handling of cytotoxic agents. The preparation must be done under aseptic circumstances. This should be performed in a designated area.
It is forbidden to smoke, eat, or drink in this area. Protective measures consist of the use of gloves, mask, safety goggles, and protective clothing. Use of a laminar airflow (LAF) cabinet is recommended. During the administration, gloves should be worn. Disposal processing procedures must take into account the cytotoxic nature of this substance. Direct contact with the skin, eyes, and mucous membranes must be prevented. In case of direct contact, immediately wash thoroughly with water. For the cleaning of the skin, soap can be used.
Excreta and vomit must be handled with care.

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