CURRENT APPROVED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

BUSILVEX (Solution for injection)

COMPOSITION OF THE MEDICINE, THAT IS, WHAT THIS MEDICINE CONTAINS:

Each 10 ml ampoule contains 60 mg busulfan (1 ml of concentrate contains 6 mg busulfan) After dilution: 1 ml of solution contains 0,5 mg busulfan.
The product also contains the following inactive ingredients: Polyethylene glycol 400 and dimethylacetamide.

APPROVED INDICATION AND USE, THAT IS, WHAT THIS MEDICINE IS USED FOR:

BUSILVEX is used in adults as a treatment prior to transplantation in combination with cyclophosphamide. You will receive this preparative medicine before receiving a transplant of either bone marrow or haematopoietic progenitor cell.

INSTRUCTION BEFORE TAKING THE MEDICINE:

Do not use BUSILVEX:

- if you are hypersensitive to busulfan or any of the other
- ingredients if you are pregnant or think you are pregnant
- if you suffer from hepatic insufficiency
- there is no experience of use of Bulsufex in children

Take special care with BUSILVEX:

BUSILVEX is a potent cytotoxic drug that results in profound decrease of blood cells. At the recommended dose, this is the desired effect. Therefore, careful monitoring will be performed. It is possible that the use of BUSILVEX may increase the risk of suffering another malignancy in the future.

You should tell your doctor if:

- You have a liver, kidney, heart or lung problem
- You have a history of seizures
- You are currently taking other medicines

If you are taking medicines on a regular basis, concomitant use of medicine may cause undesirable interactions. Please consult your doctor, pharmacist or other health care professional for advice.
Particular caution should be taken if you use itraconazole (used for certain types of infections) or ketobemidone (used to treat pain) because this may increase the side-effects.

Paracetamol should be used with caution during the 72 hours prior to or with BUSILVEX administration.

If you are pregnant or breast feeding your baby while taking this medicine please consult your doctor, pharmacist or other health care professional for advice.

INSTRUCTIONS ON HOW TO TAKE MEDICINE:

The dose will be calculated according to your body weight. The recommended dose is 0,8 mg/kg of body weight in adult patients. In combination with cyclophosphamide.

BUSILVEX is administered by a qualified health care professional as a central intravenous infusion, after dilution of the individual ampoule. Each infusion will last 2 hours. BUSILVEX will be administered every 6 hours during 4 consecutive days prior to transplant.

Before receiving BUSILVEX you will be medicated with:
- anticonvulsive agents to prevent seizures
- antiemetic agents to prevent vomiting

Do not share medicines prescribed for you with others.

In the event of overdosage consult your doctor or pharmacist. If neither is available, rush the patient to the nearest hospital or poison control centre.

SIDE-EFFECTS:

Serious side-effects:

The most serious side-effects of BUSILVEX therapy or the transplant procedure may include decrease in circulating blood cell counts (intended effect of the drug to prepare you for your transplant infusion).

Infection, liver disorders including blocking of a liver vein, graft versus host disease (the graft attacks your body) and lung complications. Your doctor will monitor your blood counts and liver enzymes regularly to detect and manage these events.

Very common side-effects (reported in more than 1 patient our of 10):
Blood: decrease of blood circulating cells (red and white) and platelets.
Nervous system: insomnia, anxiety, dizziness and depression.
Nutrition: decrease in magnesium, calcium, potassium phosphate in blood and increase in blood sugar.
Cardiac: increase in heart rate., increase or decrease of blood pressure, vasodilation and blood clots.
Respiratory: shortness of breath, nasal secretion, sore throat, cough, hiccup, nosebleeds, abnormal breath sounds.
Gastro-intestinal: Nausea, inflammation of the mucosa of the mouth, vomiting, loss of appetite, diarrhoea, constipation, heart burn, anus discomfort.
Hepatic: jaundice, elevate liver enzymes.
Skin: rash, itching, loss of hairs.
Muscle and bone: back, muscle and joint pain.
Renal: increase in creatinine elimination, discomfort in urination and decrease in urine output. **General:** weight increase, fever, headache, abdominal pain, weakness, chills, pain, allergic reaction, oedema, general pain and inflammation at the injection site, chest pain.

Common side-effects (reported in 1 to 10 patients out of 100):
Nervous system: confusion
Nutrition: low blood sodium
Cardiac: changes and abnormalities in heart rhythm, fluid retention or inflammation around the heart, decreased heart output.
Respiratory: increase in breath rhythm, respiratory failure, alveolar bleeding, asthma, collapse of small portions the lung, fluid around the lung.
Gastro-intestinal: inflammation of the mucosa of oesophagus, paralysis of the gut, Vomiting blood.
Hepatic: enlarged liver.

Renal: increase in amounts of nitrogen in the blood stream, blood in the urine, moderate renal insufficiency.

Uncommon side-effects (reported in 1 to 10 patients out of 1000):
Nervous system: delirium nervousness, hallucination, agitation, abnormal brain function, cerebral haemorrhage and seizure.
Cardiac: clotting of femoral artery, thrombosis, extra heart beats, decrease in heart rate, diffuse leak of fluid from the capillaries (small blood vessels).
Respiratory: decrease in blood oxygen.
Gastro-intestinal: bleeding in the stomach or gut.

Not all side-effects reported for this medicine are included in this leaflet. Should your general health worsen while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

STORAGE AND DISPOSAL INFORMATION:

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN
Store between + 2 °C and + 8 °C (in refrigerator) in the closed original packaging.
Do not freeze

PRESENTATION:
10 ml Type I flint glass trim lip gold band ampoules. 8 Ampoules are packed in a cardboard carton.

IDENTIFICATION:
Clear solution, essentially free of particulate matter.

REGISTRATION NUMBER:
37/26/0668

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
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