PACKAGE LEAFLET: INFORMATION FOR THE USER

NIPENT® 10 mg
Powder for solution for injection, powder for solution for infusion
(Pentostatin)

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. WHAT NIPENT IS AND WHAT IT IS USED FOR

Nipent is an anti-cancer medicine used to treat adults with hairy cell leukaemia, a form of cancer affecting lymphocytes (white blood cells important for fighting invading viruses and bacteria).

2. BEFORE YOU USE NIPENT

Do not use Nipent:
- if you have ever had an allergic reaction to Nipent (pentostatin) or mannitol
- if you have impaired kidney function (creatinine clearance < 60 ml/min)
- if you have an infection (raised temperature or fever, chills or feeling of achiness)

Tell your doctor if the above applies to you before this medicine is used.

Nipent is not recommended for use in children.

Take special care with Nipent:
- if you have liver problems

Tell your doctor if the above applies to you before this medicine is used.

Tests
Before receiving Nipent for the first time, your kidneys will be checked to make sure that they are working normally. A blood test will also be done and repeated regularly during your treatment with Nipent.

Please discuss with your doctor if after you have received Nipent you suffer from for example: confusion, dizziness, sleep disturbance, pins and needles, forgetfulness, staggering walk, twitching, shaking, fainting, headache, fits or other conditions of the nervous system.

Taking other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Nipent should not be used with:
- fludarabine (other anti-cancer medicine)

Tell your doctor if you are taking the following:
- vidarabine (anti-viral drug)
- cyclophosphamide, etoposide, carmustine (other anti-cancer medicines)
- allopurinol (medicine used to treat gout, high levels of uric acid in the body caused by certain cancer medications, and kidney stones)

Pregnancy and breast-feeding
Nipent is not recommended if you are pregnant. Please tell your doctor if you are pregnant, trying to become pregnant or breast-feeding.

If you are **of child bearing age** you must use appropriate contraceptive methods. Should you become pregnant, consult your doctor.

Men should not attempt to father any children during treatment or for 6 months after stopping Nipent therapy.

Driving and operating machinery
You may feel unwell or suffer from dizziness or sight problems after being given this medicine. You should not drive or operate machinery if you suffer from these side effects.

Nipent contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3. HOW TO USE NIPENT

Your medicine will always be given to you under the supervision of a doctor.

Dosage

Your doctor will work out exactly how much you need according to your height, weight and state of health. The normal dose for adults including the elderly is 4 mg/m² given every other week. This medicine is given as a single short injection or a longer 20-30 minute infusion (drip) into your vein.

Before and after being given Nipent you will also receive an infusion into your vein of a solution (dextrose or dextrose saline) to ensure there is plenty of fluid in your body. This will help get the medicine to where it is needed and reduce any side effects.

Treatment Duration

You will be treated with Nipent until the cancer cells have been destroyed. Your doctor will check 6 and 12 months after you started receiving Nipent that you are responding to treatment.

If you receive a higher dose of Nipent

If you receive a higher than recommended dose of Nipent, important organs (brain, liver, kidney, lungs) may be affected which can potentially lead to a serious medical condition. If you experience any of the symptoms listed below, **call your doctor immediately as this may indicate an acute and possibly life-threatening medical emergency**: confusion; drowsiness; seizures; loss of consciousness for a period of time; pain, burning, numbness, or tingling in the hands or feet; weakness in the arms or legs, loss of ability to move your arms or legs, or visual and auditory disturbances (difficulty focusing and tinnitus).

You may also notice: yellowing of the skin and the whites of the eyes (jaundice); itching; pain in the upper right portion of the abdomen; rash, unexplained fatigue and weakness, or loss of appetite. Other symptoms may include: need to urinate frequently, especially at night (nocturia); swelling of the legs and puffiness around the eyes (fluid retention); shortness of breath, dry cough and general discomfort while breathing or worsening of symptoms when lying on your back.

4. POSSIBLE SIDE EFFECTS

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

Nipent works by killing cancer cells, but sometimes it also kills some of your normal blood cells, which can increase the chance of you getting an infection. It can also lower the number of platelets (which are necessary for proper blood clotting). Your doctor will be checking your condition, and will tell you if this occurs. There are certain precautions you can take, to reduce the risk of infection or bleeding. If possible, avoid people with infections.

- **Check with your doctor immediately** if you think you are getting an infection or if you get a fever, sweating or chills, cough or hoarseness, difficulty swallowing, sores in the mouth or on lips, swollen runny nose, painful sinuses, lower back or side pain, pain, inability or difficulty when urinating (passing water), severe headache with confusion (encephalitis).

- **Check with your doctor immediately** if you notice any unusual bleeding, nosebleeds or bruising, black tarry stools, blood in urine or stools, pinpoint red spots on your skin, sore throat, jaundice (yellowing of whites of the eyes and skin, pale stools or dark urine), allergic reactions (e.g. severe rash, difficulty in breathing, runny nose, swelling of the face, painful sores in the mouth), tremor, twitching, severe chest pain which may also affect your arm and neck (heart attack).

Consult with your doctor or nurse as soon as possible if any of the following side effects occur:

Very common (occurs in more than 1 in 10 people)

- stomach pain or feeling of being sick

- loss of appetite
- diarrhoea or blood in the stools
- headache
- cough, runny nose, cold, sore throat or breathing problems
- rash, itchy skin or skin problems
- muscle pain, joint or bone problems
- tiredness, weakness or pain
- fever, sweating or chills
- jaundice

Common (occurs in fewer than 1 in 10 people)

- abdominal pain, indigestion, bloating or gas, constipation, weight change
- inflammation of the gums (gingivitis), mouth or lips or swelling of the throat
- teeth problems, taste changes, dry mouth
- dehydration
- mood swings, aggression, anxiety, nervousness, depression, strange dreams or thoughts, hallucinations, neurosis
- confusion, memory loss
- dizziness, shaking of the body or limbs, twitching, fits, fainting
- trouble sleeping or feeling sleepy
- staggering walk, speech disorder, paralysis, inflammation of the coverings of the brain, nerve damage
- rash, flaking, swelling, redness, infection or itching of the skin
- dry skin, acne, oily skin, discolouration of the skin, skin sensitivity to light
- hair loss
- dry eyes or altered tear production, eye pain, eye infections, eye sensitivity to light, changes in vision and damage to the back of the eye (retina)
- ringing in the ears, pain in the ears, deafness, balance problems, vertigo
- shortness of breath, asthma, blood clot or fluid in the lungs, nose bleeds
- irregular, slow or fast heart beat, changes to the ECG, high or low blood pressure, shock
- chest pain, angina, fluid around the heart, heart failure, heart arrest
- blood clots in or inflammation of the veins, bleeding
- infections such as sinusitis, pneumonia or bronchitis, abscesses, bone, skin, kidney or urinary tract infections, fungal infections (eg mouth thrush), shingles
- skin cancer or other cancers, leukaemia
- problems following a transplant
- enlarged spleen, bruising, enlarged lymph nodes
- gout, changes in the electrolytes in your blood (eg sodium, potassium and calcium)
- arthritis, joint problems
- kidney disorders, difficulty or pain when passing urine, kidney failure, stones in the kidney, inability to empty the bladder
- lack of periods, lumps in breasts, impotence

Uncommon (occurs in fewer than 1 in 100 people)

- gastroenteritis, Clostridium Difficile bowel infection
- infections such as bladder (cystitis), CMV (Cytomegalovirus), fungal lung infection

- tumour lysis syndrome (involves breakdown products of dying cancer cells)
- specific problems with red blood cells (Pure Red Cell Aplasia and certain types of anaemia), red or purple skin marks due to low platelet count
- graft failure
- heart attack, heart muscle problems, low oxygen levels in the blood
- organ failure
- severe breathing problems

Rare (occurs in fewer than 1 in 1000 people)

- Alzheimer's disease (memory loss, problems thinking and speaking)
- epileptic fits
- migraine
- Parkinson's disease (loss of co-ordination, shaking of body and limbs)
- swelling of eyelids
- inflammation of the covering of the heart, reduction in heart function
- fungal infection of the food pipe (oesophagus)

Very rare (occurs in fewer than 1 in 10,000 people)

- severe eye pain with vision loss

This medicine may also cause the following side effects that your doctor will watch for:

Very common (occurs in more than 1 in 10 people)

- blood disorders affecting red blood cells, white blood cells and platelets (clotting factors)
- changed blood results for liver or kidney function

Common (occurs in fewer than 1 in 10 people)

- kidney stones
- swollen glands
- heart and circulation problems
- an enlarged spleen

Sometimes the effects of Nipent may not occur until months or years after the medicine is used and, in some cases, severe side effects have caused fatalities. These delayed effects may commonly include the development of certain types of cancer (e.g. skin and acute leukaemia). Discuss these possible effects with your doctor.

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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Ireland

HPRA Pharmacovigilance. Website: www.hpra.ie.

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

5. HOW TO STORE NIPENT

Keep this medicine out of the sight and reach of children.

Do not use Nipent after the expiry date printed on the vial label and carton (after "EXP"). Where only a month and year is stated, the expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C).

Prepared injections or infusions should be used immediately, however, if this is not possible they may be stored for up to 8 hours below 25ºC.

6. FURTHER INFORMATION

What Nipent contains:

The active substance is pentostatin. Each glass vial contains 10 mg of the active ingredient.
The other ingredients are mannitol**,** sodium hydroxide or hydrochloric acid.

What Nipent looks like and contents of the pack:

Nipent is a white powder which is made into a solution by adding sterile water before it is given as an injection or infusion.

Nipent is supplied in single-dose, 10 mg vials packaged in individual cartons (packs of 1 vial).

The Marketing Authorisation Holder in Ireland is:

Pfizer Healthcare Ireland
9 Riverwalk, National Digital Park
Citywest Business Campus
Dublin 24 Ireland

The Marketing Authorisation Holder in Malta is:

Pfizer Hellas S.A.
243 Messoghion Ave.
Neo Psychiko 15451,
Greece

The Manufacturer is:

Pfizer Service Company BV, Hoge Wei 10, 1930 Zaventem, Belgium.

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NIPENT® 10 mg Powder for solution for injection, powder for solution for infusion

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

To be administered by bolus intravenous injection or intravenous infusion. Do not administer by any other route.

Instructions on preparation and dilution:

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

Prescribers should refer to national or recognised guidelines on handling cytotoxic agents.

Procedures for proper handling and disposal of anticancer drugs should be followed.

1. Reconstitution of Nipent should only be carried out by trained personnel in a cytotoxic-designated area.
2. Adequate protective gloves should be worn.
3. The cytotoxic preparation should not be handled by pregnant staff.
4. Adequate care and precautions should be taken in the disposal of items syringes, needles etc. used to reconstitute cytotoxic drugs.
5. Contaminated surfaces should be washed with copious amounts of water.
6. Any remaining solution should be discarded.

Transfer 5 ml of Sterile Water for Injection to the vial containing Nipent and mix thoroughly to obtain complete dissolution. The solution should be colourless to pale yellow and yield 2 mg/ml pentostatin. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Nipent may be given intravenously by bolus injection or diluted in a larger volume (25 to 50 ml) with 5% Dextrose Injection (5% glucose solution) or 0.9% Sodium Chloride Injection (0.9% saline solution). Dilution of the entire contents of a reconstituted vial with 25 ml or 50 ml provides a pentostatin concentration of 0.33 mg/ml or 0.18 mg/ml, respectively, for the diluted solutions.

Nipent solution when diluted for infusion with 5% Dextrose Injection (5% glucose solution) or 0.9% Sodium Chloride Injection (0.9% saline solution) does not interact with PVC infusion containers or administration sets at concentrations of 0.18 mg/ml to 0.33 mg/ml.

Acidic solutions should be avoided (the pH of the reconstituted powder is 7.0 to 8.2).

Storage and shelf life:

The reconstituted solution for injection or reconstituted and further diluted solution for infusion should be used within 8 hours and should not be stored above 25°C. Immediate administration after reconstitution is recommended.