Package Leaflet: Information for the patient

Vincristine Sulfate 1 mg/ml Solution for Injection or Infusion

vincristine sulfate

Read all of this leaflet carefully before you start using 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 Vincristine Sulfate is and what it is used for

Vincristine Sulfate is an anti-cancer medicine in the form of a solution for injection or infusion. Treatment with an anti-cancer medicine is sometimes called cancer chemotherapy.
Vincristine Sulfate is mainly used in the treatment of cancers of the blood (leukaemia). It may also be given in combination with other anti-cancer medicines to treat other types of cancer, for example cancers of the breast, brain or lung and some cancers in children.

2. What you need to know before you use Vincristine Sulfate

Vincristine Sulfate must never be injected into the spine (intrathecally).

Do not use Vincristine Sulfate

- if you are allergic to Vincristine Sulfate or any of the other ingredients of this medicine (listed in section 6)
- if you have Charcot-Marie-Tooth syndrome (weakness in the leg muscles)
- if you have an infection that is not being treated
- for treatment of diseases that are not cancers, except for using to reduce your immune response

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Vincristine Sulfate

- **to make sure that this medicine is ONLY given to you through a vein either by intravenous infusion (IV) or intravenous injection (IV push) (it should not be given by any other route). If you notice any pain during, or soon after this medicine is given, tell your doctor or nurse immediately**
- if you have a mental or nervous system disorder
- if you have had or are receiving radiotherapy

- if you have an infection
- if you have a low white cell count measured on blood test
- if you have kidney problems
- if you have liver problems (can increase the severity of side effects that you may experience)
- if you are elderly
- if you have breathing problems. Acute shortness of breath and severe bronchospasm have been reported following the administration of vinca alkaloids. Vincristine Sulfate is an example of a vinca alkaloid
- to avoid any contact of Vincristine Sulfate with your eyes. If Vincristine Sulfate is accidently spilt into your eye tell your doctor or nurse immediately.

Other medicines and Vincristine Sulfate
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.
Use of the following medicines may make the side effects of Vincristine Sulfate worse:

- allopurinol (medicine used to treat gout)
- pyridoxine (vitamin B_6)
- isoniazid (medicine used to treat tuberculosis)
- itraconazole, fluconazole or voriconazole (medicines used to treat fungal infections)
- phenytoin (a medicine used to treat epilepsy). Vincristine Sulfate may alter the effect of phenytoin therefore blood levels of phenytoin will need to be monitored.
- L-asparaginase, methotrexate, mitomycin-C, dactinomycin (medicines used to treat some kinds of cancers)
- platinum containing cancer medicines and other medicines that may cause hearing or balance problems

Vincristine Sulfate used with methotrexate in the treatment of cancer may alter its effect.

St John's Wort (Hypericum perforatum) may decrease the effect of vincristine sulfate and should be used with caution.

Pregnancy, breast-feeding and fertility
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.

Women of childbearing potential should use appropriate contraception methods during treatment and for at least 7 months following the last dose of Vincristine Sulfate.

Men are advised to use appropriate contraception methods during treatment and for at least 4 months following the last dose of vincristine sulfate.

Because of the possibility of serious reactions to the nursing child, mothers are advised not to breast-feed during treatment and for 1 month following last dose of vincristine sulfate.

Treatment with vincristine sulfate can affect your fertility. Men and women who may want to have children after treatment with vincristine sulfate are recommended to discuss with their doctor options for fertility preservation.

Talk to your doctor about birth control methods that are right for you and your partner.

Driving and using machines
Do not drive or use machines if you experience any side effect which may lessen your ability to do so.

3. How to use Vincristine Sulfate

The dose of medicine given to you will depend on your medical condition, your body surface area, and how well your liver is working. The dosage will be adjusted and will vary between patients according to individual responses. The usual dose is 1.4 to 1.5 mg/m^2 in adults and 1.4 to 2.0 mg/m^2 with a maximum dose of 2 mg weekly in children. For children weighing 10 kg or less, the starting dose should be 0.05 mg/kg administered once a week. A reduction in the dose of vincristine sulfate is recommended for patients with liver impairment.

This medicine must ONLY be given through a vein either by intravenous infusion (IV) or intravenous injection (IV push). Vincristine Sulfate is usually given at weekly intervals.

If you are given too little or too much Vincristine Sulfate
As this medicine will be given to you whilst you are in hospital it is unlikely that you will be given too little or too much, however, tell your doctor or nurse if you have any concerns. In children under the age 13, a dosage 10 times higher than the recommended dosage has been fatal. In adults a dosage higher than 3 mg/m^2 can cause the individual to experience increased side effects as can dosage of 3-4 mg/m^2 in children under 13 years of age.

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

4. Possible side effects

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

If any of the following happen, tell your doctor immediately:

- severe allergic reaction – you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint
- pain or swelling at the administration site during or immediately after the administration
- severe chest pains possibly radiating to the jaw or arm, sweating, breathlessness and nausea
- severe breathing problems or shortness of breath

These are very serious side effects. You may need urgent medical attention.

If you experience any of the following tell your doctor as soon as possible:

Very common side effects: may affect more than 1 in 10 people

- reduction in blood platelets, which increases risk of bleeding
- reduction in red blood cells which can make the skin pale and cause tiredness
- reduced blood levels of sodium
- loss of appetite

- effects on the nerves, especially nerves of the leg, causing nerve pain, numbness and pins and needles. This can cause the foot to drop and can cause problems with walking
- losing your sense of touch
- constipation
- stomach cramps
- being sick or feeling sick
- hair loss
- muscle weakness or wasting
- pain in bones
- weight loss

Common side effects: may affect up to 1 in 10 people

- pain in jaw and throat
- diarrhoea
- difficulty passing urine

Uncommon side effects: may affect up to 1 in 100 people

- coma

Not Known: frequency cannot be estimated from the available data

- infections
- fever, sore throat, skin rashes, or sores on your body (which may indicate a reduction in the number of white blood cells)
- dehydration
- elevated blood uric acid levels
- paralysis
- convulsions (fits)
- paralysis of your face or throat which may cause difficulty in talking
- dizziness or difficulty with balance
- loss of reflexes
- headache
- disorders of brain function
- problems with eyesight or eyeball movement
- hearing difficulty
- build up of plaque in arteries
- high or low blood pressure
- shortness of breath or wheezing
- mouth ulcers
- liver problems
- back pain
- bladder problems, excessive urine production, or difficulty urinating
- severe pain and ulceration might occur around the site of administration
- being less fertile or missing your menstrual period

Vincristine Sulfate may lead to changes in your blood cells, including a type of anaemia in which red blood cells are destroyed (haemolytic anaemia). Your doctor may take blood samples to monitor for these and also to check how well your liver is working.

Vincristine Sulfate may lead to an altered brain structure and/or function.

There have been reports of other malignancies (cancers) occurring at a later date after Vincristine Sulfate has been used in combination with other anti-cancer drugs. This happens rarely.

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
www.medicinesauthority.gov.mt/adrportal

Cyprus
Pharmaceutical Services
Ministry of Health
CY-1475 Nicosia
Tel.: +357 22608607
Fax: + 357 22608669
Website: www.moh.gov.cy/phs

5. How to store Vincristine Sulfate

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

Do not use this medicine after the expiry date which is stated on the 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 (2ºC – 8ºC). Keep vial in the outer carton in order to protect from light.

Do not use this medicine if you notice evidence of precipitation or any other particulate matter.

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 to protect the environment.

6. Contents of the pack and other information

What Vincristine Sulfate contains
The active substance is vincristine sulfate. Each millilitre (ml) of solution contains 1 milligram (mg) of vincristine sulfate. Each 2 ml vial contains 2 mg of vincristine sulfate.

The other ingredients are mannitol and water for injections.

What Vincristine Sulfate looks like and contents of the pack
Vincristine Sulfate is a colourless solution which comes in glass containers called vials. It is available in packs containing 5 x 2 ml vials.

Marketing Authorisation Holder

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

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

Cyprus:
Pfizer Hellas A.E.
243 Messoghion Ave.
154 51 N. Psychiko
Greece

Local Representative for Cyprus:
Pfizer Hellas A.E. (Cyprus Branch)
Tel.: +357 22817690

Manufacturer

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

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

You should be experienced in the handling and use of cytotoxic agents and familiar with the Summary of Product Characteristics (SmPC) for this product. Reference should also be made to local policy guidelines on the safe handling of cytotoxic agents.

Further to the information included in section 3 of the patient information leaflet, practical information on the preparation/handling of the medicinal product is provided here.

INCOMPATIBILITIES

It is not recommended that Vincristine Sulfate should be mixed with any other drug and should not be diluted in solutions that raise or lower the pH outside the range 3.5 to 5.5. It should not be mixed with anything other than normal saline (50 ml sodium chloride 9 mg/ml (0.9%)) or 5% Dextrose.

Frusemide both in syringe and injected sequentially into Y-site with no flush between, results in immediate precipitation.

SHELF LIFE

Unopened: 2 years
Once opened: use immediately.

Chemical and physical in-use stability has been demonstrated for up to 24 hours at 2 - 8°C and at 25°C when Vincristine Sulfate injection is diluted with 0.9% Sodium Chloride or 5% Dextrose in infusion bags and protected from light. If stored under normal light at 25°C, when diluted with 0.9% Sodium Chloride or 5% Dextrose, the diluted product is stable for 8 hours or 4 hours respectively.

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 - 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

INSTRUCTIONS FOR USE, HANDLING AND DISPOSAL

Instructions for Use
This preparation is for intravenous use only. It should only be administered by individuals experienced in vincristine administration.

FOR INTRAVENOUS USE ONLY.
FATAL IF GIVEN BY OTHER ROUTES

Should be administered only by or under the direct supervision of a qualified physician who is experienced in the use of cancer chemotherapeutic agents.

Great care should be exercised in calculating the dose as overdosage may be extremely serious or even fatal. The dose should not be increased beyond the level, which produces therapeutic benefit. In general, individual doses should not exceed 2 mg; and white cell counts should be carried out before and after giving each dose.

The calculated dose of vincristine sulphate solution should be administered ONLY through a vein either by intravenous infusion (IV) or intravenous injection (IV push) according to the treatment protocol and under constant supervision for signs of extravasation.

Intravenous infusion
The diluted vincristine sulphate injection may be infused via a flexible plastic container (e.g.: infusion bag) either directly into an intravenous catheter/needle or into a running intravenous infusion of normal saline (50 ml sodium chloride 9 mg/ml (0.9%)) or 5% Dextrose. It is recommended to administer the

solution over 5 to 10 minutes after dilution in a 50 ml infusion bag (50 ml sodium chloride 9 mg/ml (0.9%) Solution for Injection or 5% Dextrose). After administration the vein must be flushed through thoroughly. Care should be taken to avoid extravasation as this may cause local ulceration.

TO REDUCE THE POTENTIAL FOR FATAL MEDICATION ERRORS DUE TO INCORRECT ROUTE OF ADMINISTRATION, VINCRISTINE SULPHATE IS RECOMMENDED TO BE DILUTED IN A FLEXIBLE PLASTIC CONTAINER AND PROMINENTLY LABELLED AS INDICATED FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES.

Alternatively, Vincristine Sulfate may be injected directly into a vein over about a minute.

For single use only, discard any unused contents.

Instructions for Handling
Local guidelines on safe preparation and handling should be consulted.

1. Chemotherapeutic agents should be prepared for administration only by professionals who have been trained in the safe use of preparation.

2. Operations such as reconstitution of powder and transfer to syringes should be carried out only in the designated area. The work surface should be covered with disposable plastic-backed absorbent paper.

3. The personnel carrying out these procedures should be adequately protected with clothing, masks, gloves and eye shield.

4. Pregnant personnel are advised not to handle chemotherapeutic agents.

5. Use Luer-lock fittings on all syringes and sets. Large bore needles are recommended to minimise the pressure and the possible formation of aerosols. The latter may be reduced by the use of a venting needle.

6. Do not add extra fluid to the vial prior to removal of the dose. Withdraw the solution of vincristine sulfate into an accurate syringe, measuring the dose carefully. Do not add extra fluid to the vial in an attempt to empty it completely.

7. Adequate care and precaution should be taken in the disposal of items (syringes, needles, etc.) used to reconstitute cytotoxic drugs.

8. Whenever solution and container permit, parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Instructions for Contamination
(a) In the event of contact with the skin or eyes, the affected area should be washed with copious amounts of water or normal saline. A bland cream may be used to treat the transient stinging of skin. Medical advice should be sought if the eyes are affected.

(b) In the event of spillage, operators should put on gloves and mop up the spilled material with a sponge kept in the area for that purpose. Rinse the area twice with water. Put all solutions and sponges into a plastic bag and then seal it.

Instructions for Disposal
Syringes, containers, absorbent materials, solution and any other contaminated material should be placed in a thick plastic bag or other impervious container and incinerated.

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