Package leaflet: Information for the user

Etoposide 20mg/ml Concentrate for Solution for Infusion

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 Etoposide is and what it is used for
2 What you need to know before you use Etoposide
3 How to use Etoposide
4 Possible side effects
5 How to store Etoposide
6 Contents of the pack and other information

1 What Etoposide is and what it is used for

The name of this medicine is Etoposide 20mg/ml Concentrate for Solution for Infusion. It contains the active ingredient etoposide. Etoposide belongs to a group of medicines called cytostatics which are used in the treatment of cancer.

Etoposide is used in the treatment of certain types of cancers in adults:
- testicular cancer
- small cell lung cancer
- cancer of the blood (acute myeloid leukaemia)
- tumour in the lymphatic system (Hodgkin's lymphoma, non-Hodgkin's lymphoma)
- reproductive system cancers (gestational trophoblastic neoplasia and ovarian cancer)

Etoposide is used in the treatment of certain types of cancers in children:
- cancer of the blood (acute myeloid leukaemia)
- tumour in the lymphatic system (Hodgkin's lymphoma, non-Hodgkin's lymphoma)

The exact reason why you have been prescribed Etoposide is best discussed with your doctor.

2 What you need to know before you use Etoposide

Do not use Etoposide:
- if you are **allergic** to etoposide, or any of the other ingredients of this medicine (listed in section 6)
- if you have recently been given a **live vaccine**, including 'Yellow fever' vaccine.
- if you are **breast-feeding** or planning to breast-feed.

If any of the above affects you, or if you are unsure if they do, tell your doctor who will be able to advise you.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before received Etoposide:
- if you have any **infections**
- if you have had **radiotherapy or chemotherapy** recently.
- if you have low levels of a protein called **albumin** in your blood.
- if you have **liver** or **kidney** problems.

Effective anti-cancer treatment can destroy cancer cells rapidly in large numbers. On very rare occasions this may cause harmful amounts of substances from these cancer cells to be released into the blood. If this happens it can cause problems with the liver, kidney, heart or blood, which may result in death if not treated.

In order to prevent this, your doctor will need to do regular blood tests to monitor the level of these substances during treatment with this medicine.

This medicine can cause a reduction in the level of some blood cells, which could cause you to suffer from infections, or may mean that your blood doesn't clot as well as it should if you cut yourself. Blood tests will be taken at the start of your treatment, and before each dose you take, to make sure that this isn't happening.

If you have reduced liver or kidney function, your doctor may also want you to take regular blood tests to monitor these levels.

Other medicines and Etoposide
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is especially important
- if you are taking a medicine called ciclosporin (a drug used to reduce the activity of the immune system).
- if you are being treated with cisplatin (a medicine used to treat cancer).
- if you are taking phenytoin or any other medicines used to treat epilepsy.
- if you are taking warfarin (a medicine used to prevent blood clots from forming).
- if you have recently been given any live vaccines.
- if you are taking phenylbutazone, sodium salicylate, or aspirin.
- if you are taking any anthracyclines (a group of medicines used to treat cancer).
- if you are taking any drugs with a similar mechanism of action as Etoposide.

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 using this medicine.

Etoposide must not be used during pregnancy unless clearly indicated by your doctor.

You must not breastfeed while you are receiving Etoposide.

Both male patients and female patients of child-bearing age should use an effective contraceptive method (*e.g.*, the barrier method or condoms) during treatment and for at least 6 months after the end of treatment with Etoposide.

Male patients treated with etoposide are advised not to father a child during treatment and for up to 6 months after treatment. In addition, men are advised to seek counselling on sperm preservation before starting treatment.

Both male and female patients who are considering having a child after having treatment with Etoposide should discuss this with their doctor or nurse.

Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed. However, if you feel tired, sick to your stomach, dizzy or light-headed you should not do so until you have discussed it with your doctor.

Etoposide contains ethanol
19.5% ethanol (alcohol) i.e. up to 0.79g per vial. This may be dangerous for patients suffering from alcoholism and for patients in high-risk groups such as those with liver problems, epilepsy (fits), brain injury or disease and children and pregnant women. The amount of alcohol in this product may alter the effects of other medicines.

3 How to use Etoposide

Etoposide concentrate for solution for infusion will be given to you by a doctor or nurse. It will be given as a slow infusion into a vein. This may take between 30 to 60 minutes.

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Etoposide 20mg/ml Concentrate for Solution for Infusion

The following information is intended for healthcare professionals only:

Preparation of Intravenous Solution
Procedures for proper handling and disposal of anti-cancer drugs should be followed.

Etoposide solutions must be prepared under aseptic conditions.

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 seal it.

Pregnant women must avoid contact with cytostatic drugs.

Bodily waste matter and vomit should be disposed with care.

A damaged bottle must be regarded and treated with the same precautions as contaminated waste. Contaminated waste must be stored in waste containers specifically marked for this. See section "Disposal".

Etoposide 20 mg/ml Concentrate for Solution for Infusion should not be used without diluting.

Etoposide 20 mg/ml Concentrate for Solution for Infusion must be diluted immediately prior to use with either 5% glucose or 0.9 % sodium chloride solution to give a final concentration of 0.2 to 0.4 mg/ ml, usually not more than 0.25 mg/ml. At higher concentrations precipitation of etoposide may occur.

Etoposide needs to be diluted with volumes ranging from 250–1,000 ml, based on the individual dosage. Care should be taken not to exceed the final concentration of 0.4 mg/ml.

Examples of approximate volumes of diluent needed for different dose ranges:

Amount of etoposide (mg)	Amount of solution needed to prepare the dilution (ml)
≤100 mg	250 ml
101 mg to 200 mg	500 ml
>200 mg	750 - 1000 ml

Only use clear solutions. Cloudy or discoloured solutions must be discarded.

Solutions showing any signs of precipitation should not be used.

Etoposide is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Etoposide should not be physically mixed with any other medicinal product.

The intravenous solution is suitable for infusion only in glass and PVC containers.

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The dose you receive will be specific to you, which the doctor will calculate. The usual dose, is 50 to 100 mg/m^2 body surface area, daily for 5 days in a row or 100 to 120 mg/m^2 body surface area on days 1, 3 and 5. This course of treatment may then be repeated, depending on the results of blood tests, but this will not be for at least 21 days after the first course of treatment.

For children being treated for cancer of the blood or lymphatic system the dose used is 75 to 150 mg/m^2 body surface area daily for 2 to 5 days.

The doctor may sometimes prescribe a different dose particularly if you are receiving, or have received, other treatments for your cancer or if you have kidney problems.

If you are given more Etoposide than you should

As Etoposide is given to you by a doctor or nurse, overdose is unlikely. However, if this does occur your doctor will treat any symptoms that follow.

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.

Tell your doctor or nurse immediately if you get any of the following symptoms: swelling of your tongue or throat, breathing difficulties, fast heartbeat, flushing of the skin or a rash. These may be signs of a severe allergic reaction.

Severe **liver, kidney or heart damage** from a condition called tumour lysis syndrome, caused by harmful amounts of substances from the cancer cells getting into the blood stream, has been seen sometimes when Etoposide is taken along with other drugs used to treat cancer.

Possible side effects experienced with Etoposide that are:

Very common side effects (may affect more than 1 in 10 people)
- blood disorders (this is why you will be having blood tests between courses of treatment)
- temporary hair loss
- nausea and vomiting
- abdominal pain
- loss of appetite
- changes in skin colour (pigmentation)
- constipation
- feeling weak (asthenia)
- generally feeling unwell (malaise)
- damage to the liver (hepatotoxicity)
- increased liver enzymes
- jaundice (increased bilirubin)

Common side effects (may affect up to 1 in 10 people)
- acute leukaemia
- irregular heart beat (arrhythmia), or a heart attack (myocardial infarction)
- dizziness
- diarrhoea
- reactions at the site of infusion
- severe allergic reactions
- high blood pressure
- low blood pressure
- sore lips, mouth or throat ulcers
- skin problems such as itching or rash
- inflammation of a vein
- infection

Uncommon side effects (may affect up to 1 in 100 people)
- tingling or numbness in hands and feet
- bleeding

Rare side effects (may affect up to 1 in 1,000 people)
- acid reflux
- flushing
- difficulty swallowing
- a change in the way things taste
- severe allergic reactions
- convulsions (seizure)
- fever
- sleepiness or tiredness
- breathing problems
- temporary blindness
- serious reactions of the skin and/or mucous membranes which may include painful blisters and fever, including extensive detachment of the skin (Steven-Johnson syndrome and toxic epidermal necrolysis)
- a sunburn-like rash that may occur on skin that has previously been exposed to radiotherapy and can be severe (radiation recall dermatitis)

Not known (frequency cannot be estimated from the available data)
- tumour lysis syndrome (complications of substances released from treated cancer cells entering the blood)
- face and tongue swelling
- infertility
- difficulty breathing

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 Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard

5 How to store Etoposide

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 carton and the vial after 'EXP'. The expiry date refers to the last day of that month.

Do not store above 25°C. Do not refrigerate or freeze.

Keep the vial in the outer carton in order to protect from light.

If the solution is cloudy or a deposit that does not dissolve is noticed, the bottle should be discarded.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

After dilution:
Chemical and physical in-use stability has been demonstrated the diluted solution 0.2 mg etoposide/ml for 96 hours and for the diluted solution 0.4 mg etoposide/ml for 24 hours at 25°C, without any special protection from light. From a microbiological point of view, the product should be used immediately.

6 Contents of the pack and other information

What Etoposide contains
- The active substance is etoposide. 1 ml of concentrate for solution for infusion contains 20 mg of etoposide. One vial of 5 ml concentrate for solution for infusion contains 100 mg etoposide.
- The other ingredients are macrogol 400, polysorbate 80, ethanol anhydrous and citric acid, anhydrous (for pH adjustment).

What Etoposide looks like and contents of the pack

Etoposide is a clear, pale yellow concentrate for solution for infusion, slightly viscous, free from visible particles in glass injection vials. Etoposide is contained in 8 ml Type I colourless glass vial with bromobutyl rubber stop and sealed with aluminium metallic cap with flip off. One vial of 5 ml of concentrate for solution for infusion contains 100 mg etoposide.

Pack sizes: 1 or 10 vials per carton
Vial is packed with a protective plastic overwrap.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Actavis Group PTC ehf.
Reykjavíkurvegi 76-78
220 Hafnarfjörður
Iceland

Manufacturer
S.C. Sindan- Pharma S.R.L
11 Ion Mihalache Blvd
011171 Bucharest
Romania

This leaflet was last revised in January 2018.

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Administration and dosage

Etoposide is administered by slow intravenous infusion (usually over a 30 to 60 minute period) since hypotension has been reported as a possible side effect of rapid intravenous injection. Etoposide SHOULD NOT BE GIVEN BY RAPID INTRAVENOUS INJECTION.

The recommended dose of etoposide is 50 to 100 mg/m2/day on days 1 to 5 or 100 to 120 mg/m2 on days 1, 3, and 5 every 3 to 4 weeks in combination with other drugs indicated in the disease to be treated. Dosage should be modified to take into account the myelosuppressive effects of other drugs in the combination or the effects of prior radiation therapy or chemotherapy which may have compromised bone marrow reserve.

Administration Precautions: As with other potentially toxic compounds, caution should be exercised in handling and preparing the solution of etoposide. Skin reactions associated with accidental exposure to etoposide may occur. The use of gloves is recommended. If etoposide solution contacts the skin or mucosa, immediately wash the skin with soap and water and flush the mucosa with water.

Care should be taken to avoid extravasation.

Elderly

No dosage adjustment is necessary in elderly patients (age > 65 years old), other than based on renal function.

Paediatric use

Etoposide in paediatric patients has been used in the range of 75 to 150 mg/m2/day for 2 to 5 days in combination with other antineoplastic agents. The treatment regimen should be chosen according to the local standard of care.

Renal impairment

In patients with impaired renal function, the following initial dose modification should be considered based on measured creatinine clearance.

Measured creatinine clearance	Dose of etoposide
>50 ml/min	100% of dose
15-50 ml/min	75% of dose

Subsequent dosing should be based on patient tolerance and clinical effect. In patients with creatinine clearance less than 15 ml/min and on dialysis further dose reductions should be considered.

Disposal

All materials that have been used for the preparation and administration, or which have been in contact with etoposide in any way, must be disposed of according to local cytotoxic guidelines.
Remnants of the medicinal products as well as all materials that have been used for dilution and administration must be destroyed according to hospital standard procedures applicable to cytotoxic agents and in accordance with local requirements related to the disposal of hazardous waste.

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