Package leaflet: Information for the user
Etoposide 20 mg/ml concentrate for solution for infusion
Etoposide

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 or nurse.
- If you get any side effects, talk to your doctor 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

The name of this medicine is 'Etoposide 20 mg/ml concentrate for solution for infusion' but in the rest of the leaflet it will be called 'etoposide'. It contains the active ingredient etoposide. Etoposide belongs to the 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 are given etoposide

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

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 you receive etoposide:
- if you have low levels of a protein called **albumin** in your blood.
- if you have had **radiotherapy** or **chemotherapy** recently
- if you have any **infections**
- 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 if you are taking, have recently taken or might take any other medicines.
This is especially important
- if you are taking warfarin (a medicine used to prevent blood clots from forming).
- if you are taking a medicine called cyclosporin (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 phenylbutazone, sodium salicylate, or aspirin
- if you have recently been given any live vaccines.
- 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.

The amount of alcohol in this medicine may alter the effects of other medicines. Talk to your doctor or pharmacist if you are taking other medicines.

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 for advice before taking this medicine.

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

Breast-feeding
You must not breast-feed while you are receiving etoposide.

Fertility
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, benzyl alcohol and polysorbate 80

Ethanol
This medicine contains 241.4 mg of alcohol (ethanol) in 1 ml which is equivalent to 24.14 % w/v. The amount in 10.38 ml of dose is equivalent to 62.64 ml of beer or 25.06 ml of wine.

The alcohol in this preparation is likely to affect children. These effects may include feeling sleepy and changes in behaviour. It may also affect their ability to concentrate and take part in physical activities.

The amount of alcohol in this medicine can affect your ability to drive or use machines. This is because it may affect your judgement and how fast you react.

If you have epilepsy or liver problems, talk to your doctor or pharmacist before taking this medicine.

If you are pregnant or breast-feeding, talk to your doctor or pharmacist before taking this medicine.

If you are addicted to alcohol, talk to your doctor or pharmacist before taking this medicine.

Because this medicine is usually given slowly over 1 hour, the effects of alcohol may be reduced.

Benzyl alcohol

This medicine contains 30 mg benzyl alcohol per ml.

Benzyl alcohol may cause allergic reactions.

Ask your doctor for advice if you have liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called “metabolic acidosis”).

Do not use for more than a week in young children (less than 3 years old), unless advised by your doctor or pharmacist.

Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called “gasping syndrome”) in young children. Do not give to your newborn baby (up to 4 weeks old), unless recommended by your doctor.

P**olysorbate 80**
Etoposide contains polysorbate 80. A life threatening syndrome, with liver and kidney failure, decline in respiratory function, fall in platelet count and swelled abdomen has been reported in premature infants when administered polysorbate 80 containing vitamin E injection.

3. How you will be given etoposide

Etoposide 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.

The dose you receive will be specific to you, which the doctor will calculate. The usual dose, based on etoposide, is 50 to100 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 a doctor or nurse will be giving you your medicine, 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 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: 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: 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 (including infections seen in patients with a weakened immune system, e.g. a lung infection called pneumocystis jirovecii pneumonia)

Uncommon: may affect up to 1 in 100 people

- tingling or numbness in hands and feet
- bleeding

Rare: may affect up to 1 in 1,000 people

- acid reflux
- flushing
- difficulty swallowing
- serious reactions of the skin and/or mucous membranes which may include painful blisters and fever, including

- a change in the way things taste
- severe allergic reactions
- convulsions (seizure)
- fever
- sleepiness or tiredness
- breathing problems
- temporary blindness
- extensive detachment of the skin (Stevens-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

For UK: Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

For Ireland: HPRA Pharmacovigilance
Website: www.hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

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

This medicinal product does not require any special temperature storage conditions. Do not freeze. Store in the original package, in order to protect from light.

Do not store the diluted product in a refrigerator (2°C to 8°C) as this might cause precipitation. Solutions showing any sign of precipitation should not be used.

After dilution
Chemical and physical in-use stability of the solution diluted to a concentration of 0.2 mg/ml or 0.4 mg/ml has been demonstrated up to 24 hours at 15°C to 25°C.

From a microbiological point of view, the diluted 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 12 hours at 15°C to 25°C, unless dilution has taken place in controlled and validated aseptic conditions.

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 etoposide contains

- The active substance is Etoposide. Each 1 ml concentrate for solution for infusion contains 20 mg of etoposide.
  Each 5 ml vial contains 100 mg of etoposide.
  Each 10 ml vial contains 200 mg of etoposide.
  Each 25 ml vial contains 500 mg of etoposide.
  Each 50 ml vial contains 1000 mg of etoposide.

- The other ingredients are: macrogol 300, polysorbate 80 (E433), benzyl alcohol (E1519), ethanol and anhydrous citric acid (E 330)

What etoposide looks like and contents of the pack

Etoposide is a clear, light yellow to pale yellow solution packaged in type-I, clear, moulded glass vials of 5 ml, 10 ml, 30 ml and 50 ml, closed with 20 mm bromobutyl rubber closure and sealed with 20 mm flip-off Aluminium overseals (Green, Blue, Red and Yellow respectively).

Pack sizes: Etoposide is available in packs containing 1 vial of 5 ml, 10 ml, 25 ml and 50 ml.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
For UK:
Fresenius Kabi Limited
Cestrian Court
Eastgate Way, Manor Park
Runcorn, Cheshire, WA7 1NT
United Kingdom

For IE:
Fresenius Kabi Deutschland GmbH
Else-Kröner-Straße 1,
61352 Bad Homburg v.d.Höhe
Germany

Manufacturer
Fresenius Kabi Deutschland GmbH
Pfingstweide 53
61169 Friedberg
Germany

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Austria	Etoposid Kabi 20 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Belgium	Etoposide Fresenius Kabi 20 mg/ml concentraat voor oplossing voor infusie
Denmark	Etoposid Fresenius Kabi
Estonia	Etoposide Kabi 20 mg/ml
Finland	Etoposid Fresenius Kabi 20 mg/ml infuusiokonsentraatti, liuosta varten
Hungary	Etoposide Kabi 20 mg/ml koncentrátum oldatos infúzióhoz
Ireland	Etoposide 20 mg/ml concentrate for solution for infusion

Latvia	Etoposide Kabi 20 mg/ml koncentrāts infūziju šķīduma pagatavošanai
Lithuania	Etoposide Kabi 20 mg/ml koncentratas infuziniam tirpalui
Malta	Etoposide 20 mg/ml concentrate for solution for infusion
The Netherlands	Etoposide Fresenius Kabi 20 mg/ml concentraat voor oplossing voor infusie
Norway	Etoposid Fresenius Kabi
Portugal	Etoposido Kabi
Romania	Etopozida Kabi 20 mg/ml concentrat pentru soluţie perfuzabilă
Sweden	Etoposid Fresenius Kabi 20 mg/ ml koncentrat till infusionsvätska, lösning
Slovenia	Etopozid Kabi 20 mg/ml koncentrat za raztopino za infundiranje
United Kingdom (Northern Ireland)	Etoposide 20 mg/ml concentrate for solution for infusion

This leaflet was last revised in December 2023.

The following information is intended for healthcare professionals only:

Cytotoxic agent

Instructions on how to dilute, store and dispose of etoposide

Dilution

Etoposide 20 mg/ml concentrate for solution for infusion must be diluted immediately prior to use with either 50 mg/ ml (5%) dextrose in water, or 9 mg/ ml (0.9%) sodium chloride solution to give a final concentration of 0.2 mg/ml to 0.4 mg/ml. At higher concentrations precipitation of etoposide may occur.

Etoposide is administered by slow intravenous infusion (usually over a 30 to 60 minute period). Etoposide SHOULD NOT BE GIVEN BY RAPID INTRAVENOUS INJECTION.

Storage of the prepared solution

After dilution
Chemical and physical in-use stability of the solution diluted to a concentration of 0.2 mg/ml or 0.4 mg/ml has been demonstrated up to 24 hours at 15°C to 25°C.

From a microbiological point of view, the diluted 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 12 hours at 15°C to 25°C, unless dilution has taken place in controlled and validated aseptic conditions.

Handling and disposal
The normal procedures for proper handling and disposal of anti-cancer medicinal products should be adopted:

- Staff should be trained to reconstitute the medicinal product.
- Pregnant staff should be excluded from working with this medicinal product.
- Staff handling this medicinal product during dilution should wear protective clothing including mask, goggles and gloves.
- All items for administration or cleaning, including gloves, should be placed in high-risk, waste disposal bags for high-temperature incineration.
- Accidental contact with the skin or eyes should be treated immediately with copious amounts of water.

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