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 taking 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 pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Etoposide Injection is and what it is used for.
2. What you need to know before you are given Etoposide Injection.
3. How you will be given Etoposide Injection.
4. Possible side effects.
5. How to store Etoposide Injection.
6. Contents of the pack and other information.

1. What Etoposide Injection is and what it is used for

This medicine contains the active substance etoposide. This medicine belongs to the group of medicines called cytostatics which are used in the treatment of cancer.

Etoposide Injection 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 Injection 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 Injection is best discussed with your doctor.

2. What you need to know before you are given Etoposide Injection

Do not take Etoposide Injection
- if you are allergic to etoposide or any 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 or pharmacist or nurse before receiving Etoposide Injection:
- if you have low levels of a protein called **albumin** in your blood.
- if you have had **chemotherapy** or radiotherapy 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 Injection
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 any drugs with a similar mechanism of action as Etoposide Injection.
- if you have recently been given any live vaccines.
- if you are taking phenylbutazone, sodium salicylate ,or aspirin.
- if you are taking warfarin (a medicine used to prevent blood clots from forming).
- if you are taking phenytoin or any other medicines used to treat epilepsy.
- if you are taking any anthracyclines (a group of medicines used to treat cancer).
- if you are being treated with cisplatin (a medicine used to treat cancer).
- if you are taking a medicine called ciclosporin (a drug used to reduce the activity of the immune system).

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 Injection must not be used during pregnancy unless clearly indicated by your doctor. You must not breastfeed while you are receiving Etoposide Injection.

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 Injection. Male patients treated with Etoposide Injection 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 Injection 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 Injection contains alcohol
This medicine contains 30.5% alcohol (ethanol) which corresponds to 240.64 mg of ethanol per ml of concentrate i.e up to 1.2 gm of ethanol per 5 ml vial, equivalent to 30 ml of beer or 12.55 ml of wine and up to 3 gm of ethanol per 12.5 ml vial, equivalent to 75 ml of beer or 31.4 ml of wine. This is harmful for patient suffering from alcoholism, brain damage, pregnant women, breastfeeding women, children and high-risk groups such as patients with liver disease, or epilepsy. The effect of other medicines may be reduced or increased.

Etoposide Injection contains benzyl alcohol
Etoposide Injection contains 30 mg/ml of benzyl alcohol.
Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called "gasping syndrome") in young children. It should not be given to newborn babies (up to 4 weeks old) or used for more than a week in young children (less than 3 years old), unless recommended by your doctor.

Ask your doctor or pharmacist for advice if you are pregnant or breast-feeding or if you have a 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").

Benzyl alcohol may cause allergic reactions.

Etoposide Injection contains Polysorbate 80
Etoposide Injection contains 80 mg/ml of polysorbate 80.

In newborn infants a life threatening liver and kidney failure syndrome, decrease in respiratory function, decreased platelet count and swelling of the abdomen has been associated with an injectable vitamin E product containing polysorbate 80.

3. How you will be given Etoposide Injection

Etoposide Injection will always be given to you by healthcare professionals only. 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, is 50 to 100 mg/m2 body surface area, daily for 5 days in a row or 100 to 120 mg/ m2 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 Injection than you should
As this medicine is given to you by healthcare professional, 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 notice 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 Injection is taken along with other drugs used to treat cancer.

Possible side effects experienced with Etoposide Injection 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)
- nausea and vomiting
- loss of appetite
- abdominal pain
- constipation
- temporary hair loss
- damage to the liver (hepatotoxicity)
- increased liver enzymes
- changes in skin colour (pigmentation)

- jaundice (increased bilirubin)
- feeling weak (asthenia)
- generally feeling unwell (malaise)

Common (may affect up to 1 in 10 people)
- acute leukaemia (severe blood cancer)
- irregular heart rhythm (arrhythmia) or a heart attack (myocardial infarction),
- dizziness
- high blood pressure
- low blood pressure
- sore lips, mouth or throat ulcers
- redness of skin
- infection (including infections seen in patients with a weakened immune system, e.g. a lung infection called *pneumocystis jirovecii* pneumonia)
- diarrhoea
- skin problems such as itching or rash
- inflammation of vein
- severe allergic reactions
- reactions at the site of infusion

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

Rare (may affect up to 1 in 1000 people)
- convulsions (seizure)
- sleepiness or tiredness
- a change in the way things taste
- swallowing difficulties
- serious reactions of the skin and/or mucous membranes which may include painful blisters and fever, including 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)
- fever
- temporary blindness
- breathing problems
- acid reflux
- flushing

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
- acute renal failure

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

You can also report side effects directly via
HPRA Pharmacovigilance
Website: www.hpra.ie.

5. How to store Etoposide Injection

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

Keep the vial in the outer carton in order to protect from light.
Do not refrigerate or freeze.
Chemical and physical in-use stability of the solution diluted to a concentration of 0.2 mg/ml and 0.4 mg/ml has been demonstrated in sodium chloride injection (0.9 % w/v) and glucose injection (5% w/v) for up to 96 hours and 48 hours at temperature 20°- 25° C 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. Do not store the diluted product in a refrigerator (2-8 °C) as this might cause precipitation.

Do not use Etoposide Injection if you notice sign of precipitation or contains visible particles.
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.

6. Contents of the pack and other information

What Etoposide Injection contains:
Etoposide Injection contains the active ingredient etoposide.
1 ml contains 20 mg Etoposide.

Each 5 ml vial contains 100 mg of etoposide.
Each 10 ml vial contains 200 mg of etoposide.
Each 12.5 ml vial contains 250 mg of etoposide.
Each 20 ml vial contains 400 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 citric acid anhydrous, benzyl alcohol, polysorbate 80, Macrogol 300 and ethanol anhydrous.

What Etoposide Injection looks like and contents of the pack:
Etoposide Injection is a clear, colourless to pale yellow solution for infusion.
Pack sizes:
1 × 5 ml vial
1 × 10 ml vial
1 × 12.5ml vial
1 × 20 ml vial
1 × 25 ml vial
1 × 50 ml vial

Not all pack sizes may be marketed.

Marketing Authorisation Holder:

Accord Healthcare Ireland Ltd,
Euro House,
Euro Business Park,
Little Island,
Cork T45 K857,
Ireland

Manufacturer:
Accord Healthcare Polska Sp.z o.o.,
ul. Lutomierska 50,95-200 Pabianice, Poland

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

Name of the Member State	Name of the medicine
Austria	Etoposide Accord 20 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Belgium	Etoposide Accord Healthcare 20 mg/ml, Concentraat voor oplossing voor infusie
Bulgaria	Etoposide Accord 20 mg/ml Concentrate for Solution for Infusion
Cyprus	Etoposide Accord 20 mg/ml Concentrate for Solution for Infusion
Czech Republic	Etoposide Accord 20 mg/ml koncentrát pro infuzní roztok
Denmark	Etoposid Accord
Germany	Etoposide Accord 20 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Estonia	Etoposide Accord 20 mg/ml
Finland	Etoposide Accord 20 mg/ml Infuusiokonsentraatti, liuosta varten
Hungary	ETOPOSIDE Accord 20 mg/ml Koncentrátum oldatos infúzióhoz
Ireland	Etoposide 20 mg/ml Concentrate for Solution for Infusion
Iceland	Etópósíð Accord 20 mg / ml innrennslisþykkni, lausn til innrennslis
Italy	Etoposide Accord
Latvia	Etoposide Accord 20 mg/ml koncentrāts infūziju šķīduma pagatavošanai
Lithuanian	Etoposide Accord 20 mg/ml koncentratas infuziniam tirpalui
Malta	Etoposide 20 mg/ml Concentrate for Solution for Infusion
The Netherlands	Etoposide Accord 20 mg/ml, concentraat voor oplossing voor infusie
Norway	Etoposide Accord
Portugal	Etoposido Accord
Poland	Etopozyd Accord
Romania	Etoposid Accord 20 mg/ml Concentrat pentru soluţie perfuzabilă
Slovenia	Etoposide Accord 20 mg/ml koncentrat za raztopino za infundiranje
Sweden	Etoposide Accord 20 mg/ml Concentrate for Solution for Infusion
Slovak Republic	Etoposide Accord 20 mg/ml Concentrate for Solution for Infusion
Spain	Etopósido Accord 20 mg/ml concentrado para solución para perfusión
United Kingdom (Northern Ireland)	Etoposide 20 mg/ml Concentrate for Solution for Infusion

The leaflet was last revised in 12/2023.

The following information is intended for medical or healthcare professionals only

Administration and Dosage
Etoposide Injection 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 Injection SHOULD NOT BE GIVEN BY RAPID INTRAVENOUS INJECTION.

The recommended dose of etoposide is 50-100 mg/m^2/ day on days 1 to 5 or 100 to 120 mg/m^2 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.

The necessary dose of etoposide must be diluted either with a 5% w/v glucose solution or a 0.9% w/v sodium chloride solution, in order to achieve a final concentration of 0.2 – 0.4 mg/ml of etoposide (i.e 1 ml or 2 ml concentrate in 100 ml of diluent to achieve concentration of 0.2 mg/ml and 0.4 mg/ml respectively). The concentration of diluted product should not exceed 0.4 mg/ml because of risk of precipitation. During preparation and reconstitution a strictly aseptic technique should be used.

Etoposide must not be mixed with other drugs when administered. It must not be mixed with other product except than those listed above.

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 have 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

In patients with creatinine clearance less than 15 mL/min and on dialysis further dose reduction is likely to be required as etoposide clearance is further reduced in these patients .Subsequent dosing in moderate and severe renal impairment should be based on patient tolerance and clinical effect.
Since etoposide and its metabolites are not dialyzable, it can be administered pre- and post-haemodialysis.

Instruction for Use/Handling
Procedures for proper handling and disposal of anti-cancer drugs should be followed.

Care must be taken whenever handling cytostatic products. Always take steps to prevent exposure. As with other potentially toxic compounds, caution should be exercised in handling and preparing etoposide solutions. Skin reactions associated with accidental exposure to etoposide may occur. The use of gloves is recommended. If etoposide should contact 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.

If solution showing sign of precipitation or contains visible particles, it should be discarded.

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

Shelf life after dilution:
Chemical and physical in-use stability of the solution diluted to a concentration of 0.2 mg/ml and 0.4 mg/ml has been demonstrated in sodium chloride injection (0.9 % w/v) and glucose injection (5% w/v) for up to 96 hours and 48 hours at temperature 20°- 25° C 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. Do not store the diluted product in a refrigerator (2-8 °C) as this might cause precipitation.

Storage

Keep the vial in the outer carton in order to protect from light.
Do not refrigerate or freeze.