PACKAGE LEAFLET: INFORMATION FOR THE USER

ETOPOSIDE-TEVA 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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- 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-Teva is and what it is used for

The name of this medicine is Etoposide-Teva. Etoposide belongs to the group of medicines called cytostatics which are used in the treatment of cancer.

Etoposide-Teva 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-Teva 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-Teva is best discussed with your doctor.

2. What you need to know before you are given Etoposide-Teva

Do not take Etoposide-Teva
- 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 receiving Etoposide-Teva

- 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-Teva
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 taking this medicine.

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

You must not breastfeed while you are receiving Etoposide-Teva.

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 6 months after the end of treatment for females and 3 months after the end of treatment for males.

Male patients treated with Etoposide-Teva are advised not to father a child during treatment and for up to 3 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-Teva 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-Teva contains ethanol (alcohol)
A vial with Etoposide contains 30 vol % alcohol (ethanol).
This medicine contains 1.2 g of alcohol (ethanol) in each 5 ml vial, 2.4 g of alcohol (ethanol) in each 10 ml vial, 4.8 g of alcohol (ethanol) in each 20 ml vial, 6 g of alcohol (ethanol) in each 25 ml vial and 12 g of alcohol (ethanol) in each 50 ml vial, which is equivalent to 241 mg/ml concentrate. The amount in one ml of this medicine is equivalent to 6 ml beer or 2 ml wine.

Adults
The amount of alcohol in this medicine is not likely to have an effect in adults.
The alcohol in this medicine may alter the effects of other medicines. Talk to your doctor or pharmacist if you are taking other medicines.
If you are pregnant, talk to your doctor or pharmacist before using this medicine.
If you are addicted to alcohol, talk to your doctor or pharmacist before using this medicine.

Children and adolescents
The alcohol in this medicine may alter the effects of other medicines. Talk to your doctor or pharmacist if you are taking other medicines.
The alcohol in this preparation is likely to affect children weighing 17 kg (or less). These effects may include feeling sleepy and changes in behaviour. It may also affect their ability to concentrate and take part in physical activities. If the child has epilepsy or liver problems, talk to your doctor or pharmacist before using this medicine.

Because this medicine is usually given slowly over 30-60 minutes, the effects of alcohol may be reduced.

Etoposide-Teva contains polysorbate 80
Polysorbate 80 may cause serious conditions in premature children such as liver and kidney failure, lung deterioration, reduction in platelets which increases risk of bruising or bleeding and a build-up of fluid of around the stomach.

3. How you will be given Etoposide-Teva

Etoposide-Teva 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 of etoposide 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-Teva than you should
As Etoposide-Teva 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-Teva are:

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

Common side effects (affecting between 1 in 10 and 1 in 100 people)
- infection **(including infections seen in patients with a weakened immune system, e.g. a lung infection called pneumocystis jirovecii pneumonia)**
- acute leukaemia
- severe allergic reactions
- dizziness
- irregular heart beat (arrhythmia), or a heart attack (myocardial infarction)
- high blood pressure
- low blood pressure
- diarrhoea
- sore lips, mouth or throat ulcers
- skin problems such as itching or rash
- reactions at the site of infusion
- inflammation of a vein.

Uncommon side effects (affecting between 1 in 100 and 1 in 1,000 people)
- tingling or numbness in hands and feet
- bleeding.

Rare side effects (affecting between 1 in 1,000 and 1 in 10,000 people)
- temporary blindness
- sleepiness or tiredness
- convulsions (seizure)

- breathing problems
- difficulty swallowing
- a change in the way things taste
- acid reflux
- a sunburn-like rash that may occur on skin that has previously been exposed to radiotherapy and can be severe (radiation recall dermatitis)
- 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)
- severe allergic reactions
- flushing
- fever.

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

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 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-Teva

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises.

Do not store above 25°C. Store in the original container in order to protect from light.

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 outer packaging. The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What Etoposide-Teva contains
- The active substance is etoposide. Each ml of concentrate for solution for infusion contains etoposide 20 mg.
  - Each 5 ml vial contains 100 mg etoposide.
  - Each 10 ml vial contains 200 mg etoposide.
- The other ingredients are citric acid, polysorbate 80, absolute ethanol, macrogol 300.

What Etoposide-Teva looks like and contents of the pack
- Etoposide-Teva Concentrate for Solution for Infusion is a clear, yellowish, slightly viscous solution in clear, colourless glass vials.
- Etoposide-Teva contains etoposide 20 mg/ml and is available as a sterile concentrate for solution for infusion, in 5 ml and 10 ml sterile multiple dose vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
Teva Pharma B.V.
Swensweg 5
2031GA Haarlem
Netherlands

Manufacturer:
Pharmachemie B.V.
Swensweg 5
2003 RN Haarlem
The Netherlands

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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-Teva 20 mg/ml must be prepared under aseptic conditions.

Etoposide-Teva 20 mg/ml must be diluted with either 5% dextrose injection, or sodium chloride 9 mg/ml (0.9%) solution for injection, to give a final concentration of 0.2 mg/ml.

Solutions showing any signs of precipitation should not be used.

Etoposide-Teva should not be physically mixed with any other drug.

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

Storage

Unopened container:
Do not store above 25°C. Store in the original container in order to protect from light.

Storage instructions following dilution:
On dilution with sodium chloride 9 mg/ml (0.9%) solution for injection or 5% dextrose, Etoposide-Teva 20 mg/ml is physically and chemically stable for 96 hours, however from a microbiological point of view, the solution for infusion can only be used within 8 hours of preparation, when stored below 25°C.

Etoposide-Teva 20 mg/ml can be stored for 48 hours below 25°C following piercing of the rubber stopper. The vial should be pierced no more than 3 times during the 48 hour in-use storage period. Any remaining product after this time must be discarded appropriately.

Administration and Dosage

Etoposide-Teva 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-Teva SHOULD NOT BE GIVEN BY RAPID INTRAVENOUS INJECTION.

The recommended dose of etoposide is 50 to 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.

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-Teva 20 mg/ml 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/m^2/day (etoposide equivalent) 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 reduction should be considered.