EN

Etoposide Viatris 20 mg/mL 100 mg/5 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.
- 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 Viatris 20 mg/mL, concentrate for solution for infusion is and what it is used for

Pharmacotherapeutic group: anticancer and immunosuppressive agents, ATC code: L01CB01.

Etoposide belongs to the group of medicines called cytostatics which are used in the treatment of cancer.

Etoposide Viatris 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 Viatris and associated names 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 Viatris is best discussed with your doctor.

It is usually used in combination with other drugs.

2. What you need to know before you use Etoposide Viatris 20 mg/mL, concentrate for solution for infusion

Do not use Etoposide Viatris 20 mg/mL, concentrate for solution for infusion:
- 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.
- in premature or full-term babies, due to the presence of benzyl alcohol.

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 Viatris 20 mg/mL, concentrate for solution for infusion.
- 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.

This proprietary medicinal product is for hospital use only.

Treatment with Etoposide Viatris 20 mg/mL, concentrate for solution for infusion must be conducted under the supervision of a qualified doctor experienced in the use of cancer chemotherapy agents; you must strictly follow the instructions for your treatment. The doctor will verify your blood regularly.

If you experience any pain or sensation of burning at the injection site during administration, this could be indicative of extravasation, i.e. the etoposide leaks outside the blood vessel. Inform your doctor.

Action to be taken in case of extravasation during intravenous infusion:
- stop the infusion at the first signs of burning,
- inject a corticosteroid (100 to 300 mg of hydrocortisone or 4 to 12 mg of dexamethasone) subcutaneously around the lesion,
- apply 1 % hydrocortisone ointment around the infiltrated area until the erythema disappears,
- apply dry dressings on the infiltrated area for 24 h.

Etoposide may cause severe myelodepression (bone marrow disorder): the number of white blood cells will decrease, which will make you more sensitive to infections (leukopenia). Bleeding may occur more easily (thrombocytopenia).

Etoposide must not be administered to patient with a number of neutrophils below 1500/mm^3 or a number of platelets below 100000/mm^3, unless the values are caused by the cancer.

If you are or have already been treated with other cancer products or if you have been irradiated, you must discuss it with your doctor because this element is taken into consideration, especially to determine the total dose of etoposide you will receive.

Acute leukaemia associated or non-associated with a myelodysplastic syndrome (blood cancer) have been reported in patients treated with cancer products including with etoposide.

An abnormality of the chromosome 11q23 band (abnormal chromosomes) have been observed in some cases of secondary leukaemia in patients who had received epipodophyllotoxins (medicinal product class that includes etoposide).

If you present signs of anaphylactic reaction (serious allergic reaction which could be fatal) such as shivering, fever, acceleration of heart beats, bronchospasm (bronchial spasm), dyspnoea (difficulty breathing) and/or drop in blood pressure, you must inform your doctor immediately.

Etoposide must only be administered by strict infusion intravenous route in slow infusion (generally within 30 to 60 minutes). Etoposide may cause hypotension in case of excessively fast intravenous administration.

Each time the use of etoposide is envisaged, your doctor must evaluate the interest of administering you this medicine. The doctor will measure the benefit expected from this treatment relative to the potential risks.

Most of the adverse events are reversible when detected early. In case of occurrence of a serious adverse drug reaction, the dose will be reduced or the medicine will be discontinued and appropriate corrective actions will be taken by your doctor. The resumption of the treatment must be done cautiously, your doctor will re-evaluate the need for the medicine and will monitor closely for any possible reappearance of the undesirable effects.

The toxicity of etoposide may increase in patients with low concentrations of albumin in blood.

If you have a liver or kidney disease, your liver and kidney functions will be regularly verified, due to a risk of an increase in side effects.

If you have an infection, even very mild, before receiving etoposide, it is also important to report it to your doctor.

If you desire to have children: men and women must use effective contraceptive measures (pill, condoms) during the treatment and for the following seven months for the women and four months for the men. Men who wish to father children in the future should seek information on the conservation of sperm prior to starting etoposide treatment, as there is a risk of reduced fertility after treatment (see Pregnancy and Breast-feeding section).

This medicinal product contains polysorbate 80. In premature babies, a syndrome that could be fatal, characterised by hepatic and renal impairment (liver and kidney disease), pulmonary deterioration, thrombocytopenia (insufficient amount of cells present in the blood required for blood coagulation) and ascites (abnormal presence of liquid in the abdomen), have been associated with a vitamin E for injection formulation containing polysorbate.

This medicine contains 1.24 g of alcohol (ethanol) per vial of 5 mL and 2.48 g of alcohol (ethanol) per vial of 10 mL. The amount in each 5 mL vial of this medicine is equivalent to 31 mL beer or 13 mL wine and in each 10 mL vial is equivalent to 62 mL beer or 25 mL wine.

The amount of alcohol in this medicine is not likely to have an effect in adults and adolescents, and its effects in children are not likely to be noticeable. It may have some effects in younger children, for example feeling sleepy.

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

This medicine contains 150 mg benzyl alcohol in each 5 mL vial and 300 mg benzyl alcohol in each 10 mL vial.

Benzyl alcohol may cause allergic reactions.

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.

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

Ask your doctor or pharmacist for advice if you are pregnant or breast-feeding. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

Ask your doctor or pharmacist for advice 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").

IN CASE OF DOUBT, DO NOT HESITATE TO ASK YOUR DOCTOR OR PHARMACIST FOR ADVICE.

Other medicines and Etoposide Viatris 20 mg/mL, concentrate for solution for infusion

Tell your doctor or pharmacist if you are using, have recently used or might use 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 Viatris 20 mg/mL, concentrate for solution for infusion.

Pregnancy and breast-feeding

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 Viatris 20 mg/mL, concentrate for solution for infusion must not be used during pregnancy unless clearly indicated by your doctor.

You must not breastfeed while you are receiving Etoposide Viatris 20 mg/mL, concentrate for solution for infusion.

Both male patients and female patients of childbearing age should use an effective contraceptive method (e.g., the barrier method or condoms) during treatment and for at least 7months for the women after the end of treatment with Etoposide Viatris 20 mg/mL, concentrate for solution for infusion.

Male patients treated with Etoposide Viatris 20 mg/mL, concentrate for solution for infusion are advised not to father a child during treatment and for up to 4 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 Viatris 20 mg/mL, concentrate for solution for infusion 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.

3. How to use Etoposide Viatris 20 mg/mL, concentrate for solution for infusion

Etoposide Viatris 20 mg/mL, 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.

Posology

The dose you receive will be specific to you, which the doctor will calculate. The usual dose, based on 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.

In dose intensification protocols (acute leukemia, malignant lymphoma) :
- 40 to 60 mg/kg as a single dose, when etoposide is given with fractionated whole body irradiation,

or
- 40 mg/kg as a single dose or 300 to 400 mg/m^2 for 3 consecutive days, when etoposide is given in combination with other chemotherapeutic drugs, 3 to 8 days before transplantation, by a 4-hour infusion.

Dose adjustment

The etoposide dose will be adjusted by your doctor depending on any combination with other cancer drugs or the effects of a previous cancer treatment or irradiation which may have modified your bone marrow.

Patients must not start a new etoposide treatment cycle if the number of neutrophils (some white blood cells) is below 1500/mm^3 or the number of platelets (blood cells required for coagulation) is below 100000/mm^3, unless these values are caused by the cancer.

After the initial dose, the following doses must be adjusted if the number of neutrophils (some white blood cells) is below 500/mm^3 for more than 5 days or associated with a fever or infection, if the number of platelets (blood cells required for coagulation) is below 25000/mm^3, if any other severe toxicity occurs or if the renal clearance drops below 50 mL/min.

Method and route of administration

Intravenous infusion only.

Like all other nonaqueous solutions for injection, etoposide should be removed from the vial with a glass or polypropylene syringe.

Etoposide can be diluted in 0.9 % sodium chloride or 5 % glucose injection.

A diluted solution which is not clear should not be used.

Precautions for use

Hypotension has sometimes been observed following a fast intravenous administration. It is recommended to administer the etoposide solution over 30 to 60 minutes.

Like for all other potentially toxic products, the preparation and handling of this product must be carried out with caution. Skin reactions related to accidental etoposide exposure may occur. The use of gloves is recommended. In case of contact of the skin or mucous membranes with the etoposide solution, wash the skin or mucous membrane immediately with copious amounts of soap and water.

Etoposide is administered by slow intravenous infusion. ETOPOSIDE MUST NOT BE ADMINISTERED BY FAST INTRAVENOUS INJECTION.

In patients with impaired renal function, the dosage must be adjusted as a function of creatinine clearance, which reflects the degree of renal impairment.

Creatinine clearance	Etoposide dose
>50 mL/min	100% of dose
15-50 mL/min	75% of dose
<15 mL/min	No data available for these patients. An additional dose reduction is recommended (as a function of the tolerance and clinical effect of the medicine).

If you are given more Etoposide Viatris 20 mg/mL, concentrate for solution for infusion than you should

As Etoposide Viatris 20 mg/mL, concentrate for solution for infusion 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 Viatris 20 mg/mL, concentrate for solution for infusion is taken along with other drugs used to treat cancer.

Possible side effects experienced with Etoposide Viatris 20 mg/mL, concentrate for solution for infusion that are:

Very common side effects (affect more than 1 in 10 patients):
- 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)

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 Viatris 20 mg/mL, concentrate for solution for infusion solutions must be prepared under aseptic conditions.

Etoposide Viatris 20 mg/mL, concentrate for solution for infusion can be administered without further dilution or it can be further diluted with 5% glucose solution or 0.9% sodium chloride solution.

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

Etoposide Viatris 20 mg/mL, concentrate for solution for infusion is for single use only.

Etoposide Viatris 20 mg/mL, concentrate for solution for infusion 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.

Administration and Dosage

Etoposide Viatris 20 mg/mL, concentrate for solution for infusion is administered by slow intravenous infusion (usually over a 30 to 60 minute period) (see section 4.4).

Etoposide Viatris 20 mg/mL, concentrate for solution for infusion SHOULD NOT BE GIVEN BY RAPID INTRAVENOUS INJECTION.

The recommended dose of Etoposide Viatris 20 mg/mL, concentrate for solution for infusion is 50 to 100 mg/m^2/day (etoposide equivalent) 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 Viatris 20 mg/mL, concentrate for solution for infusion. Skin reactions associated with accidental exposure to Etoposide Viatris 20 mg/mL, concentrate for solution for infusion may occur. The use of gloves

Common side effects (affecting between 1 in 10 and 1 in 100 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 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)
- acid reflux
- flushing
- difficulty swallowing
- a change in the way things taste
- severe allergic reactions
- convulsions (seizure)
- temporary blindness
- 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)
- fever
- sleepiness or tiredness
- breathing problems
- 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
- acute renal failure

Blood toxicity
Myelodepression (bone marrow disorder) with fatal outcome has been reported after the administration of etoposide. Myelodepression usually results in the limitation of the dose. The bone marrow usually recovers within 20 days. No cumulative toxicity has been reported.
The lowest blood level (nadir) of granulocytes (some white cells) and platelets (blood cells required for coagulation) tend to be attained 10 to 14 days after the administration of etoposide and earlier with intravenous administration than with oral administration.
Leukopenia and thrombocytopenia, which could be severe, may occur.
Fever and infections can also occur in case of neutropenia (drop in certain white blood cells).

Gastrointestinal toxicity
The most intense gastrointestinal reactions are nausea and vomiting, which are generally relieved by an antiemetic treatment.
Anorexia and inflammation of the oral mucous membrane in case of intravenous administration, as well as diarrhoea, may also occur.

Hair loss
A progressive hair loss, sometimes evolving to total baldness, may occur very frequently.

Blood pressure fluctuation
Hypotension (decrease in blood pressure):
Transient hypotension has been reported following a fast intravenous administration. The occurrence of hypotension has not been associated with cardiac toxicity or modifications in the electrocardiogram recording (recording of the electric trace of the heart).
If hypotension occurs, it generally responds to a suspension of the treatment and/or a support treatment. On resumption of infusion, a slower infusion time must be chosen. No delayed hypotension has been observed.

Hypertension (increase in blood pressure):
Cases of hypertension have been reported in clinical studies. If hypertension occurs, an appropriate support treatment must be started.

Allergic reaction
Anaphylactic reactions (serious allergic reactions) have been reported during or immediately after the intravenous administration of etoposide. Most of the time the blood pressure becomes normal within hours after stopping the infusion.
Fatal acute reactions, associated with a bronchospasm (bronchial spasm) have been reported with etoposide.

Metabolic complications
If the severity of your disease is very high, it is possible that your body will be unable to eliminate all the waste derived from the destruction of cells by etoposide (tumour lysis syndrome). This could result in renal impairment, hyperkalaemia (excessive amounts of potassium in the blood), metabolic acidosis (excessive amounts of acid in the blood), haematuria (blood in the urine), uratic crystals in the urine (crystals in the urine), hyperuricaemia (excessive amounts of uric acid in the blood), hyperphosphataemia (excessive amounts of phosphorous in the blood), hypocalcaemia (excessive amounts of calcium in the blood) and cardiac problems which could be life-threatening.

5. How to store Etoposide Viatris 20 mg/mL, concentrate for solution for infusion

Keep this medicine out of the sight and reach of children.
Do not use Etoposide Viatris 20 mg/mL, concentrate for solution for infusion after the expiry date which is stated on the label.
The expiry date refers to the last day of that month.
This medicinal product should be stored at a temperature below 25°C.
Do not refrigerate.
After dilution, the solution may be stored for a maximum of 6 hours at a temperature below 25°C.
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 Viatris 20 mg/mL, concentrate for solution for infusion contains
- The active substance is:
  Etoposide . . . . . 20 mg
  For 1 mL of concentrate for solution for infusion
- The other components are:
  Anhydrous citric acid, benzyl alcohol, polysorbate 80, macrogol 300, ethanol.

What Etoposide Viatris 20 mg/mL, concentrate for solution for infusion looks like and contents of the pack
This medicine is a concentrate for solution for infusion.
Box of 1 vial of 5 mL.

Marketing Authorisation Holder
Benta S.A.L. - Lebanon

Under license from
Viatris Sante - 1 Rue de Turin
69007 Lyon - France

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The following information is intended for healthcare professionals only:

is recommended. If Etoposide Viatris 20 mg/mL, concentrate for solution for infusion 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 Viatris 20 mg/mL, concentrate for solution for infusion 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.