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 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 your medicine is 'Etoposide 20 mg/ml concentrate for solution for infusion' but in the rest of the leaflet it will be called 'etoposide'. This medicine contains the active substance etoposide. Etoposide belongs to a type of drugs known as podophyllotoxin derivatives. Etoposide works by interfering with the production of new DNA, which is needed to make more cells. Therefore, when etoposide is taken up by the cancer cells, it stops the growth of new cancer cells.

This medicine is used in adults to treat variety of cancers. It can be used alone or in combination with other anti-cancer medicines to treat:
- small-cell lung cancer.
- acute monoblastic & acute myelomonoblastic leukaemia (cancer of the blood-forming tissues of bone marrow).
- Resistant non-seminomatous testicular tumours (cancer of testis).

2. What you need to know before you use etoposide

Do not use Etoposide
- If you are allergic to etoposide, podophyllotoxines or podophyllotoxine-derivatives or any other ingredients of this medicine (listed in section 6)
- If your liver is not working properly
- If your bone marrow does not produce enough blood cells
- If you are breast-feeding
- If you have a weak immune system and you are being vaccinated against yellow fever at the same time.

Warnings and precautions

Talk to your doctor or nurse before using Etoposide:
- if you have received other anticancer treatment or radiotherapy, your doctor should check the number of blood cell in your blood before treatment starts.
- if you have a bacterial infection, it should be treated before etoposide is given.
- your doctor will consider the function of your liver, kidney and peripheral nervous system for the decision of treatment with etoposide.
- if your bone marrow is in low state (myelosuppression)

Tell your doctor about any other treatment you receive for your illness.

Children

Safety and effectiveness in children have not been established.

Other medicines and etoposide

Tell your doctor , if you are using, have recently used or might use any other medicines, such as:
- anti-coagulants such as warfarin which are used to thin the blood.
- phenylbutazone, sodium salicylate, acetylsalicylic acid (medicines used to treat inflammation, mild to moderate pain, and fever).
- the immunosuppressant cyclosporine (often given after an organ transplant).
- other drugs used to treat other forms of cancers such as cisplatin.
- Concurrent use of other myelosuppressive (inhibiting bone marrow activity) medicines may increase the effect.
- You should not be vaccinated with live vaccines (e.g. yellow fever) during treatment.
- phenytoin (medicine used in the treatment of epilepsy) may reduce the effects of etoposide.
- the effect of anthracyclines may be reduced due to cross resistance between anthracyclines and etoposide.

Etoposide can also have effects on other medicines used to treat cancer. Your doctor will take these effects into account when deciding on your treatment.

Etoposide with food and drink

Etoposide is not affected by food or drink.

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

Pregnancy

Etoposide can cause malformation of embryo or fetus. Therefore etoposide should not normally be administered to pregnant women. If used during pregnancy, the patient must be aware of the potential risk to the foetus.

Women of childbearing potential must avoid pregnancy and take effective contraceptive measures during treatment with etoposide and until at the earliest 6 months after the therapy with etoposide.

Breast-feeding

Etoposide is excreted into human breast milk. Women must not breast-feed during the treatment etoposide.

Fertility

Men treated with etoposide are advised not to father a child during, and up to 6 months after treatment. Advice on conservation of sperm should be sought prior to treatment because of the possibility of irreversible infertility.

Driving and using machines

Do not drive or use any tools or machines shortly after treatment with etoposide as it may make you feel very sleepy or you might not be able to see for a short time.

Etoposide concentrate for solution for infusion contains ethanol (alcohol) and benzyl alcohol

Ethanol (alcohol)

This medicinal product contains approximately 30% ethanol (**alcohol**), i.e. up to 1.5 g per dose. This is equivalent to 30 ml of beer or 12.5 ml of wine per dose. This is harmful for patients suffering from alcoholism, brain damage, pregnant women, breast-feeding women, children and high-risk groups such as patients with liver problems or epilepsy (fits).

Benzyl alcohol

This medicine contains 30 mg/ml of benzyl alcohol. **Must not** be given to premature babies or neonates. May cause toxic and allergic reactions in **infants and children** up to 3 years old.

3. How to use etoposide

Etoposide concentrate for solution for infusion will always be given to you by a healthcare professional with experience in the use of chemotherapeutic agent. This medicine will be diluted with 0.9 % sodium chloride solution. or 5 % dextrose and will be given to you as an infusion (a "drip") into a vein.

The dose of etoposide will be individually determined by your doctor. The dose you are given depends on your size: it varies with your surface area. Technically, this is measured in square meters, and is worked out from your height and weight.

Adults

The recommended dose of etoposide is 60-120 mg/m^2 daily for 5 days.

You will receive a treatment cycle consisting of one dose a day during 3 - 5 days, followed by a 10 - 20 days rest.

For non-haematological indications courses may not be repeated more frequently than at 21 day intervals.

The administration will take at least 30 to 60 minutes.

The duration of the treatment and the number of treatments is determined by the doctor and may vary for each patient.

Etoposide may be given alone or in combination with other medicines.

Elderly patients

The dosage does not need to be adjusted.

Your condition will be closely monitored during treatment. This routinely involves blood tests and controls of your liver function.

Patients with impaired kidney function

Your dose may be changed depending on your kidney function.

XXXXX ← **Cipla Inventory Code**

The following information is intended for medical or healthcare professionals only:

Cytotoxic agent

Posology and method of administration

By intravenous infusion.

<u>*Adults*</u>

The recommended dose of etoposide is 60-120 mg/m^2 i. v. per day for 5 subsequent days. As etoposide causes myelosuppression, the course of treatment must not be repeated more often than in intervals of 10 to 20 days. For non-haematological indications courses may not be repeated more frequently than at 21 days intervals. Repeated courses of treatment with etoposide infusion must not be given before the blood picture has been controlled for signs of myelosuppression and found satisfactory.

Overall, a dosage schedule of 100 mg/m^2 for 5 days or 120 mg/m^2 every other day on days 1, 3, and 5 is used frequently.

<u>Elderly patients</u>

The dosage does not need to be adjusted.

<u>Renal impairment</u>

The dosage needs to be adjusted according to creatinine clearance.

<u>Method of administration</u>

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

Etoposide 20 mg/ml concentrate for solution for infusion PHARMACODE AREA XXXXX

XXXXX PHARMACODE AREA **Etoposide 20 mg/ml concentrate for solution for infusion**

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Use in children and adolescents:
Safety and effectiveness in children have not been established.

If you use more Etoposide than you should
As a doctor or nurse will be giving you your medicine, it is unlikely that you will receive an incorrect dose. Tell your doctor or nurse if you have any concerns about the amount of medicine that you receive.
If you have any further questions on the use of this product, 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 notice any of the following:
- Any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body), and feeling you are going to faint (these may be signs of severe allergic reactions or an anaphylactic shock)

Very Common (may affects more than 1 in 10 people)
- myelosuppression (decreased production of blood cells and platelets),
- leucopenia (few blood cell),
- thrombocytopenia (decreased platelet count),
- neutropenia (low number of white blood cell),
- reduction of haemoglobin (anaemia)
- nausea (feeling sick)
- vomiting,
- loss of appetite, abdominal pain and constipation,
- hair loss resulting in total baldness (alopecia, grows back after end of therapy),
- liver damage (problem with your liver including increase in liver blood test values (bilirubin, SGOT and alkaline phosphatase),
- pigmentation (discoloration of the skin and mucous membrane),
- weakness and feeling discomfort.

Common (may affect up to 1 in 10 people)
- acute leukaemia (cancer of blood),
- redness of the skin,
- high blood pressure,
- dizziness
- diarrhoea,
- arrhythmias (irregular heart rhythm) and myocardial infarction,
- mucositis (inflammation of mucosal membrane), stomatitis, oesophagitis (heart burn),
- skin irritation,
- leakage of the infusion solution into the surrounding tissue with swelling, pain phlebitis.
- serious allergic reaction which causes difficulty in breathing or dizziness
- fatigue and drowsiness
- low blood pressure (hypotension) may occur if the infusion is administered too rapidly.

Uncommon (may affect up to 1 in 100 people)
- Damage to nerves of the hand and feet (loss of sensation).

Rare (may affect up to 1 in 1000 people)
- transitory loss of vision (cortical blindness transient),
- inflammation of optic (vision) nerve (Optic neuritis),
- seizures,
- tiredness, somnolence,
- interstitial pneumonitis (lung inflammation),
- formation of scar tissue in the lungs,
- taste impairment,
- swallowing difficulties,
- Severe skin reaction due to an allergic reaction (Stevens–Johnson syndrome; toxic epidermal necrolysis), symptoms include fever, general ill feeling, itching of the skin, joint aches, multiple skin lesions or blisters, which may involve the face or lips.
- radiation recall dermatitis (i.e skin redness, swelling and/or blistering of skin).

Tumour lysis syndrome (sometimes fatal) has been reported when etoposide was used with other anticancer drugs.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly, in UK via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard and in Ireland via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

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.

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

Do not freeze.

Do not store the diluted product in a refrigerator (2 – 8 °C) as this might cause precipitation.

Left-overs of used solutions should be discarded. Solutions showing any signs of precipitation should not be used.

Avoid unnecessary contact with the fluid. Rinse skin immediately after contact with the solution. Be sure your doctor or nurse removes any syringes or vials for disposal.

Do not throw away any medicine via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the enviroment.

6. Contents of the pack and other information

What Etoposide contains
- The active substance is etoposide. 1 ml concentrate for solution for infusion contains 20mg etoposide
  One 5 ml vial contains 100 mg of etoposide.
- The other ingredients are benzyl alcohol, citric acid, ethanol, polysorbate 80 and macrogol 300.

What Etoposide looks like and contents of the pack
Etoposide concentrate for solution for infusion is a clear to pale yellow sterile non-aqueous solution pH : 3.00-4.00

The concentrate is filled in 5 ml Type I moulded transparent flint glass vials with a rubber stopper and sealed with an aluminium flip-off tear-off seal.

Pack sizes: 1 vial or 10 vials

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Cipla (EU) Limited, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW, United Kingdom.

Manufacturer:
Cipla (EU) Limited, 4th Floor, 1 Kingdom Street, London, W2 6BY, United Kingdom

This medicinal product is authorised in the Member States of the EEA under the following names:

Croatia	Etopozid Cipla 20 mg/ml koncentrat za otopinu za infuziju
France	Etoposide 20 mg/ml solution à diluer pour perfusion
Germany	Etoposide 20 mg/ml concentrate for solution for infusion
Ireland	Etoposide 20 mg/ml concentrate for solution for infusion
United Kingdom	Etoposide 20 mg/ml concentrate for solution for infusion

This leaflet was last revised in MM/YYYY

Cipla

XXXXX ← Cipla Inventory Code

Instruction for Use/Handling
Etoposide should be handled in accordance with instruction for cytotoxic agents.

Etoposide should not be used without diluting. Dilute with 0.9% sodium chloride or 5% dextrose. Solutions showing any signs of precipitation should not be used.

For waste-disposal and safety information, guidelines on safe-handling of antineoplastic drugs should be followed.

Any contact with the fluid should be avoided. During preparation and reconstitution a strictly aseptic working technique should be used; protective measures should include the use of gloves, mask, safety goggles and protective clothing. Use of a vertical laminar airflow (LAF) hood is recommended.

Gloves should be worn during administration. Waste-disposal procedures should take into account the cytotoxic nature of this substance.

If etoposide contacts skin, mucosae or eyes, immediately wash thoroughly with water. Soap may be used for skin cleansing.

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

Storage of the prepared solution
“Chemical and physical In-use stability has been demonstrated for 24 hours at temperatures 25°C ±2 oC in 0.9% sodium chloride injection and 5% glucose. 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”.

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

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Body text : 9pt Sub Heading : 10pt Main Heading : 12pt leading between two lines : 3pt

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PACKAGING DEVELOPMENT

Product Name : Etoposide 20 mg	**Item Code : XXXXX**	**Item : PIL**	**Date : 08-06-15**
Coordinator : Prashant J.	**Artist : Atul**	**Software : Illustrator CS5**	
Fonts : Convert to curve			
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Spectro-Densitometer Delta-E reading (△E) for colour: NOT MORE THAN dE2.5	**Glossmeter reading (for white surface): NOT LESS THAN 80 %**		
Supersedes / Reference :	**Screen : # 150**	**Unwinding Direction :**	
Tuck flap:	**Side / Collar flap overlap:**	**Caliper (Thickness) for Board:**	
Links :			
2Dcode :		**Design : Folded**	
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Actual Size : 200 x 607mm		**Size after Folding : 34 x 47mm**	
Print repeat length :			
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NOTE TO THE PRINTER :

- **Return approved artwork alongwith the proof.**
- **The proof must be verified against the approved hardcopy, should be certified and signed by an authorised QA person. The unsigned proof will not be accepted.**
- **Colour scheme must be as approved by packaging development co-ordinator.**
- **Any deviation must be brought to the notice of packaging development co-ordinator immediately.**
- **For any clarification, please contact packaging development co-ordinator immediately.**