Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

VEPESID 50 mg capsule, soft

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 50 mg etoposide

Excipients with known effect:

Each 50 mg capsule, soft contains:

- - 0.93 mg of sodium ethyl parahydroxybenzoate (E215) and
- - 0.47 mg of sodium propyl parahydroxybenzoate (E217).

For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Capsule, soft.
Opaque pink, oval, soft gelatin capsule.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Recurrent or refractory testicular cancer
VEPESID is indicated in combination with other approved chemotherapeutic agents for the treatment of recurrent or refractory testicular cancer in adults.

Small cell lung cancer
VEPESID is indicated in combination with other approved chemotherapeutic agents for the treatment of small-cell lung cancer in adults.

Hodgkin's lymphoma
VEPESID is indicated in combination with other approved chemotherapeutic agents for the second line treatment of Hodgkin's lymphoma in adults.

Non-Hodgkin's lymphoma
VEPESID is indicated in combination with other approved chemotherapeutic agents for the treatment of relapsed or refractory non-Hodgkin's lymphoma in adults.

Acute myeloid leukaemia
VEPESID is indicated in combination with other approved chemotherapeutic agents for the treatment of relapsed or refractory acute myeloid leukaemia in adults.

Ovarian cancer
VEPESID is indicated in combination with other approved chemotherapeutic agents for the treatment of non-epithelial ovarian cancer in adults.

VEPESID is indicated for the treatment of platinum-resistant/refractory epithelial ovarian cancer in adults.

4.2 Posology and method of administration

VEPESID capsules should only be administered and monitored under the supervision of a qualified physician experienced in the use of anti-neoplastic medicinal products (see section 4.4).

Posology
The dose of VEPESID capsules is based on the recommended intravenous dose taking into account the dose-dependent bioavailability of VEPESID capsules. A 100 mg oral dose would be comparable to a 75 mg intravenous dose; a 400 mg oral dose would be comparable to a 200 mg intravenous dose. Within-patient variability in exposure (*i.e.* between cycles) is larger with oral administration than after intravenous administration (see section 4.4 and 5.2).

Monotherapy
The usual dose of VEPESID administered orally is 100 to 200 mg/m^2/day on days 1 to 5 or 200 mg/m^2/day on days 1, 3 and 5 every 3 to 4 weeks. Daily doses greater than 200 mg should be divided and given twice per day.

Combination therapy
The usual dose of VEPESID administered orally is 100 to 200 mg/m^2/day on days 1 to 5 or 200 mg/m^2/day on days 1, 3 and 5 every 3 to 4 weeks in combination with other drugs approved for use 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 radiotherapy or chemotherapy (see section 4.4), which may have compromised bone marrow reserve. The doses after the initial dose should be adjusted if neutrophil count is below 500 cells/mm^3 for more than 5 days. In addition the dose should be adjusted in case of occurrence of fever, infections, or at a thrombocyte count below 25,000 cells/mm^3, which is not caused by the disease. Follow up doses should be adjusted in case of occurrence of grade 3 or 4 toxicities or if renal creatinine clearance is below 50 ml/min. At decreased creatinine clearance of 15 to 50 mL/min a dose reduction by 25% is recommended.

Alternative dosage schedule
An alternative dosage schedule for VEPESID capsules is 50 mg/m^2/day for 2 to 3 weeks, with courses repeated after a one week rest period or upon recovery from myelosuppression.

Neutropenia and thrombocytopenia
Patients should not begin a new cycle of treatment with VEPESID if the neutrophil count is less than 1,500 cells/mm^3 or the platelet count is less than 100,000 cells/mm^3, unless caused by malignant disease.

Elderly population
No dosage adjustment is necessary in elderly patients (age > 65 years old), other than based on renal function (see section 5.2).

Paediatric population
The safety and efficacy of VEPESID in children below 18 years of age have not been established. Currently available data are described in section 5.2 but no recommendation on a posology can be made.

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 (see section 4.4). Since etoposide and its metabolites are not dialyzable, it can be administered pre- and post-haemodialysis (see section 4.9).

Method of administration
Capsules should be taken on an empty stomach.

4.3 Contraindications

Hypersensitivity to the active substance, sodium ethyl parahydroxybenzoate (E215), sodium propyl parahydroxybenzoate (E217) or to any of the excipients listed in section 6.1.

Concomitant use of yellow fever vaccine or other live vaccines is contraindicated in immunosuppressed patients (see section 4.5).

Lactation (see section 4.6)

4.4 Special warnings and precautions for use

VEPESID should only be administered and monitored under the supervision of a qualified physician experienced in the use of anti-neoplastic medicinal products. In all instances where the use of VEPESID is considered for chemotherapy, the physician must evaluate the need and usefulness of the drug against the risk of adverse reactions. Most such adverse reactions are reversible if detected early. If severe reactions occur, the drug should be reduced in dosage or discontinued and appropriate corrective measures should be taken according to the clinical judgment of the physician. Reinstitution of VEPESID therapy should be carried out with caution, and with adequate consideration of the further need for the drug and close attention to possible recurrence of toxicity.

Within-patient variability
The available efficacy data for etoposide in the different indications are generally based on studies in which etoposide was used intravenously. Within-patient variability in exposure (*i.e.* between cycles) is larger with oral administration than after intravenous administration. The coefficient of variation is around 30% after oral administration versus 10% after intravenous administration (between-patient variability is similar after intravenous or oral administration, *i.e.* 30 to 40%). Increased within-patient variability in exposure may lead to greater variability in the dose-response relationship, *i.e.*, leading to greater variability in patients' sensitivity to experience treatment-related toxicity from cycle to cycle, and potentially affecting overall efficacy of treatment in some patients. For this reason, it is critical that the advantages of the oral administration route are carefully weighed against the disadvantages of larger within-patient variability in exposure after oral administration. In case of curative intent the intravenous formulation should be used (see section 5.2).

Myelosuppression
Dose limiting bone marrow suppression is the most significant toxicity associated with VEPESID therapy. Fatal myelosuppression has been reported following etoposide administration. Patients being treated with VEPESID must be observed for myelosuppression carefully and frequently both during and after therapy. The following haematological parameters should be measured at the start of therapy and prior to each subsequent dose of VEPESID: platelet count, haemoglobin, white blood cell count and differential. If radiotherapy or chemotherapy has been given prior to starting etoposide treatment, an adequate interval should be allowed to enable the bone marrow to recover. VEPESID should not be administered to patients with neutrophil counts less than 1,500 cell/mm^3 or platelet counts less than 100,000cells/mm^3, unless caused by malignant disease. Doses subsequent to initial dose should be adjusted if neutrophil count less than 500 cells/mm^3 occurs for more than 5 days or is associated with fever or infection, if platelet count less than 25,000 cells/mm^3 occurs, if any grade 3 or 4 toxicity develops or if renal clearance is less than 50 ml/min.

Severe myelosuppression with resulting infection or haemorrhage may occur. Bacterial infections should be brought under control before treatment with VEPESID.

Secondary leukaemia
The occurrence of acute leukaemia, which can occur with or without myelodysplastic syndrome, has been described in patients that were treated with etoposide containing chemotherapeutic regimens. Neither the cumulative risk, nor the predisposing factors related to the development of secondary leukaemia are known. The roles of both administration schedules and cumulative doses of etoposide have been suggested but have not been clearly defined.

An 11q23 chromosome abnormality has been observed in some cases of secondary leukaemia in patients who have received epipodophyllotoxins. This abnormality has also been seen in patients developing secondary leukaemia after being treated with chemotherapy regimens not containing epipodophyllotoxins and in leukaemia occurring de novo. Another characteristic that has been associated with secondary leukaemia in patients who have received epipodophyllotoxins appears to be a short latency period, with average median time to development of leukaemia being approximately 32 months.

Hypersensitivity
Physicians should be aware of the possible occurrence of an anaphylactic reaction with VEPESID, manifested by chills, pyrexia, tachycardia, bronchospasm, dyspnoea and hypotension, which can be fatal. Treatment is symptomatic. VEPESID should be terminated immediately, followed by the administration of pressor agents, corticosteroids, antihistamines, or volume expanders at the discretion of the physician.

Low serum albumin
Low serum albumin is associated with increased exposure to etoposide. Therefore patients with low serum albumin may be at increased risk for etoposide-associated toxicities.

Impaired renal function
In patients with moderate (CrCl =15 to 50 mL/min), or severe (CrCl <15mL/min) renal impairment undergoing haemodialysis, etoposide should be administered at a reduced dose (see section 4.2). Haematological parameters should be measured and dose adjustments in subsequent cycles considered based on haematological toxicity and clinical effect in moderate and severe renal impaired patients.

Impaired hepatic function
Patients with impaired hepatic function should regularly have their hepatic function monitored due to the risk of accumulation.

Tumour lysis syndrome
Tumour lysis syndrome (sometimes fatal) has been reported following the use of etoposide in association with other chemotherapeutic drugs. Close monitoring of patients is needed to detect early signs of tumour lysis syndrome, especially in patients with risk factors such as bulky treatment-sensitive tumours, and renal insufficiency. Appropriate preventive measures should also be considered in patients at risk of this complication of therapy.

Mutagenic potential
Given the mutagenic potential of etoposide, an effective contraception is required for both male and female patients during treatment and up to 6 months after ending treatment. Genetic consultation is recommended if the patient wishes to have children after ending the treatment. As etoposide may decrease male fertility, preservation of sperm may be considered for the purpose of later fatherhood (see section 4.6).

Excipients
VEPESID contains sodium ethyl parahydroxybenzoate and sodium propyl parahydroxybenzoate

VEPESID capsules contain sodium ethyl parahydroxybenzoate and sodium propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).

VEPESID contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per soft capsule, that is to say essentially "sodium-free".

Paediatric population
Safety and effectiveness of VEPESID in paediatric patients has not been systematically studied.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other drugs on the pharmacokinetics of etoposide

High dose ciclosporin, resulting in plasma concentrations above 2000 ng/mL, administered with oral etoposide has led to an 80% increase in etoposide exposure (AUC) with a 38% decrease in total body clearance of etoposide compared to etoposide alone.

Concomitant cisplatin therapy is associated with reduced total body clearance of etoposide.

Concomitant phenytoin therapy is associated with increased etoposide clearance and reduced efficacy, and other enzyme-inducing antiepileptic therapy may be associated with increased VEPESID clearance and reduced efficacy.

In vitro plasma protein binding is 97%. Phenylbutazone, sodium salicylate, and acetylsalicyl acid may displace etoposide from plasma protein binding.

Effect of etoposide on the pharmacokinetics of other drugs

Co-administration of antiepileptic drugs and VEPESID can lead to decreased seizure control due to pharmacokinetic interactions between the drugs.

Co-administration of warfarin and etoposide may result in elevated international normalized ratio (INR). Close monitoring of INR is recommended.

Pharmacodynamic interactions

There is increased risk of fatal systemic vaccinal disease with the use of yellow fever vaccine. Live vaccines are contraindicated in immunosuppressed patients (see section 4.3).

Prior or concurrent use of other drugs with similar myelosuppressive action as etoposide may be expected to have additive or synergetic effects (see section 4.4).

Cross resistance between anthracyclines and etoposide has been reported in preclinical experiments.

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females
Women of childbearing potential should use appropriate contraceptive measures to avoid pregnancy during etoposide therapy. Etoposide has been shown to be teratogenic in mice and rats (see section 5.3). Given the mutagenic potential of etoposide, an effective contraceptive is required for both male and female patients during treatment and up to 6 months after ending treatment (see section 4.4). Genetic consultation is recommended if the patient wishes to have children after ending treatment.

Pregnancy
There are no or limited amount of data from the use of etoposide in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). In general etoposide can cause fetal harm when administered to pregnant women. VEPESID should not be used during pregnancy unless the clinical condition of the woman requires treatment with etoposide. Women of childbearing potential should be advised to avoid becoming pregnant. Women of childbearing potential have to use effective contraception during and up to 6 months after treatment. If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be informed of the potential hazard to the fetus.

Breastfeeding
Etoposide is excreted in human milk. There is the potential for serious adverse reactions in nursing infants from VEPESID. A decision must be made whether to discontinue breast-feeding or to discontinue VEPESID, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman (see section 4.3).

Fertility
As etoposide may decrease male fertility, preservation of sperm may be considered for the purpose of later fatherhood.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Etoposide may cause adverse reactions that affect the ability to drive and use machines such as fatigue, somnolence, nausea, vomiting, cortical blindness, hypersensitivity reactions with hypotension. Patients who experience such adverse reactions should be advised to avoid driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

Dose limiting bone marrow suppression is the most significant toxicity associated with VEPESID therapy. In clinical studies in which VEPESID was administered as a single agent either orally or by injection the most frequent adverse reactions of any severity were leukopenia (60 to 91%), thrombocytopenia (22 to 41%), nausea and/or vomiting (31 to 43%), and alopecia (8 to 66%).

Tabulated summary of adverse reactions

The following adverse reactions were reported from VEPESID clinical studies and post-marketing experience. These adverse reactions presented by system organ class and frequency, which is defined by the following categories: *very common* (≥1/10), *common* (≥1/100, <1/10), *uncommon* (≥1/1, 000, <1/100), *rare* (≥1/10, 000, <1/1,000), *not known* (cannot be estimated from the available data).

System Organ Class	**Frequency**	**Adverse Reaction (MedDRA Terms)**
Infections and infestations	not known	infection*
Neoplasms benign, malignant and unspecified (including cysts and polyps)	common	acute leukaemia
Blood and lymphatic system disorders	very common	anaemia , leukopenia, myelosuppression**, neutropenia, thrombocytopenia
Immune system disorders	rare	anaphylactic reactions
	not known	angioedema, bronchospasm
Metabolism and nutrition disorders	not known	tumour lysis syndrome
Nervous system disorders	common	dizziness
	uncommon	neuropathy peripheral
	rare	cortical blindness transient, neurotoxicities (*e.g.*, somnolence and fatigue), optic neuritis, seizure***
Cardiac disorders	common	arrythmia, myocardial infarction
Vascular disorders	common	hypertension
	not known	haemorrhage
Respiratory, thoracic and mediastinal disorders	rare	interstitial pneumonitis, pulmonary fibrosis
Gastrointestinal disorders	very common	abdominal pain, anorexia, constipation, nausea and vomiting
	common	diarrhoea, mucositis (including stomatitis and esophagitis)
	rare	dysgeusia, dysphagia
Hepatobiliary disorders	very common	hepatotoxicity
	not known	alanine aminotransferase increased, alkaline phosphatase increased, aspartate amino transferase increased, bilirubin increased
Skin and subcutaneous tissue disorders	very common	alopecia, pigmentation
	common	pruritus, rash, urticaria
	rare	radiation recall dermatitis, Stevens-Johnsons syndrome, toxic epidermal necrolysis
Reproductive system and breast disorders	not known	infertility
General disorders and administration	very common	asthenia, malaise

site conditions	rare	pyrexia

* including opportunistic infections like *pneumocystis jirovecii* pneumonia
** Myelosuppression with fatal outcome has been reported
***Seizure is occasionally associated with allergic reactions.

Description of selected adverse reactions

In the paragraphs below the incidences of adverse events, given as the mean percent, are derived from studies that utilized single agent VEPESID therapy.

Haematological Toxicity

Myelosuppression (see section 4.4) with fatal outcome has been reported following administration of etoposide. Myelosuppression is most often dose-limiting. Bone marrow recovery is usually complete by day 20, and no cumulative toxicity has been reported.Granulocyte and platelet nadirs tend to occur about 10 to 14 days after administration of etoposide depending on the way of administration and treatment scheme. Nadirs tend to occur earlier with intravenous administration compared to oral administration. Leukopenia and severe leukopenia (less than 1,000 cells/mm^3) were observed in 60 to 91% and 3 to 17%, respectively, for etoposide. Thrombocytopenia and severe thrombocytopenia (less than 50,000 platelets/mm^3) were seen in 22 to 41% and 1 to 20%, respectively, for etoposide. Reports of fever and infection were also very common in patients with neutropenia treated with etoposide.

Gastrointestinal Toxicity

Nausea and vomiting are the major gastrointestinal toxicities of etoposide. The nausea and vomiting can usually be controlled by antiemetic therapy.

Alopecia

Reversible alopecia, sometimes progressing to total baldness, was observed in up to 66% of patients treated with etoposide.

Hypertension

In clinical studies involving etoposide, episodes of hypertension have been reported. If clinically significant hypertension occurs in patients receiving etoposide, appropriate supportive therapy should be initiated.

Hypersensitivity

Anaphylactic reactions manifested by chills, fever, tachycardia, bronchospasm, dyspnoea, and hypotension which can be fatal can occur with the initial dose of etoposide. Acute fatal reactions associated with bronchospasm have been reported with etoposide. Syncope, face oedema, swelling face, tongue oedema and swelling tongue can also occur with etoposide.

Metabolic Complications

Tumour lysis syndrome (sometimes fatal) has been reported following the use of etoposidein association with other chemotherapeutic drugs (see section 4.4).

VEPESID contains sodium ethyl parahydroxybenzoate and sodium propyl parahydroxybenzoate

VEPESID capsules contain sodium ethyl parahydroxybenzoate and sodium propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).

Paediatric population

Safety and effectiveness of VEPESID in paediatric patients has not been systematically studied.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

4.9 Overdose

Total doses of 2.4 g/m^2 to 3.5 g/m^2 administered intravenously over three days have resulted in severe mucositis and myelotoxicity. Metabolic acidosis and cases of serious hepatic toxicity have been reported in patients receiving higher than recommended intravenous doses of etoposide. Similar toxicities can be expected with oral formulation. A specific antidote is not available. Treatment should therefore be symptomatic and supportive, and patients should be closely monitored. Etoposide and its metabolites are not dialyzable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cytostatics, plant alkaloids and other natural products, podophyllotoxin derivatives, ATC code: L01CB01

Mechanism of action
The main effect of etoposide appears to be at the late S and early G_2 portion of the cell cycle in mammalian cells. Two dose-dependent responses are seen: At high concentrations (10 mcg/mL or more), cells entering mitosis are lysed; at low concentrations (0.3 to 10 mcg/mL), cells are inhibited from entering prophase. Microtubule assembly is not affected. The predominant macromolecular effect of etoposide seems to be the rupture of the double strand by an interaction with DNA-topoisomerase II or by the formation of free radicals. Etoposide has been shown to cause metaphase arrest in chick fibroblasts.

5.2 Pharmacokinetic properties

Absorption
After either intravenous infusion or oral capsule administration, the C_{max} and AUC values exhibit marked intra- and inter-subject variability. The oral bioavailability is variable but averages 76% at the 100 mg oral dose and 48% at the 400 mg oral dose.

Distribution
The mean volumes of distribution at steady state fall in the range of 18 to 29 litres or 7 to 17 L/m^2. Etoposide shows low penetration into the CSF. *In vitro*, etoposide is highly protein bound (97%) to human plasma proteins.

Etoposide binding ratio correlates directly with serum albumin in cancer patients and normal volunteers (see section 4.4). Unbound fraction of etoposide correlates significantly with bilirubin in cancer patients.

Biotransformation
The hydroxyacid metabolite [4' dimethyl-epipodophyllic acid-9-(4,6 0-ethylidene-β-D-glucopyranoside)], formed by opening of the lactone ring, is found in the urine of adults and children. It is also present in human plasma, presumably as the trans isomer. Glucuronide and/or sulfate conjugates of etoposide are also excreted in human urine. In addition, O-demethylation of the dimethoxyphenol ring occurs through the CYP450 3A4 isoenzyme pathway to produce the corresponding catechol. There is no evidence of a hepatic first-pass effect for etoposide. No correlation exists between the absolute oral bioavailability of etoposide capsules and non-renal clearance. No evidence exists for any other differences in etoposide metabolism and excretion after administration of oral capsules as compared to intravenous infusion.

Elimination
On intravenous administration, the disposition of etoposide is best described as a biphasic process with a distribution half-life of about 1.5 hours and terminal elimination half-life ranging from 4 to 11 hours. Total body clearance values range from 33 to 48 mL/min or 16 to 36 mL/min/m^2 and, like the terminal elimination half-life, are independent of dose over a range 100 to 600 mg/m^2. After intravenous administration of ^{14}C etoposide (100 to 124 mg/m^2), mean recovery of radioactivity in the urine was 56% (45% of the dose was excreted as etoposide) and faecal recovery of radioactivity was 44% of the administered dose at 120 hours.

Linearity/non-linearity

Total body clearance and the terminal elimination half-life are independent of dose over a range 100 to 600 mg/m^2. Over the same dose range, the areas under the plasma concentration vs. time curves (AUC) and the maximum plasma concentration (C_{max}) values increase linearly with dose.

Renal impairment
Patients with impaired renal function receiving etoposide have exhibited reduced total body clearance, increased AUC and higher steady state volume of distribution (see section 4.2).

Hepatic impairment
In adult cancer patients with liver dysfunction, total body clearance of etoposide is not reduced.

Elderly population
Although minor differences in pharmacokinetic parameters between patients ≤65 years and >65 years of age have been observed, these are not considered clinically significant.

Paediatric population
In children, approximately 55% of the dose is excreted in the urine as etoposide in 24 hours. The mean renal clearance of etoposide is 7 to 10 mL/min/m^2 or about 35% of the total body clearance over a dose range of 80 to 600 mg/m^2. Etoposide, therefore, is cleared by both renal and nonrenal processes, ie, metabolism and biliary excretion. The effect of renal disease on plasma etoposide clearance is not known in children. In children, elevated SGPT levels are associated with reduced drug total body clearance. Prior use of cisplatin may also result in a decrease of etoposide total body clearance in children.

An inverse relationship between plasma albumin levels and etoposide renal clearance is found in children.

Gender
Although minor differences in pharmacokinetic parameters between genders have been observed, these are not considered clinically significant.

Drug interactions
In a study of the effects of other therapeutic agents on in vitro binding of ^{14}C etoposide to human serum proteins, only phenylbutazone, sodium salicylate, and aspirin displaced protein-bound etoposide at concentrations generally achieved in vivo (see section 4.5).

5.3 Preclinical safety data

Chronic toxicity
Anaemia, leukopenia, and thrombocytopenia were observed in rats and mice, while dogs had mild reversible deterioration of liver and kidney functions. The dose multiple (based on mg/m^2 doses) for these findings at the no-observed adverse-effect-level in the preclinical studies were ≥ approximately 0.05 times compared to the highest clinical dose. Historically, preclinical species have been more sensitive compared to humans towards cytotoxic agents. Testicular atrophy, spermatogenesis arrest, and growth retardation were reported in rats and mice.

Mutagenicity
Etoposide is mutagenic in mammalian cells.

Reproductive toxicity
In animal studies etoposide was associated with dose-related embryotoxicity and teratogenicity.

Carcinogenic potential
Given its mechanism of action, etoposide should be considered a possible carcinogen in humans.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content
Citric acid, anhydrous (E330)
Macrogol 400 (E1521)
Glycerol (85 per cent) (E422)

Water, purified

Capsule shell
Glycerol (85 per cent) (E422)
Gelatin (E441)
Sodium ethyl parahydroxybenzoate (E215)
Sodium propyl parahydroxybenzoate (E217)
Titanium dioxide (E171)
Red iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package.

6.5 Nature and contents of container

Pack of 20, 50 Capsules, softgels.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other 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. This includes appropriate equipment, such as wearing gloves and washing hands with soap and water after handling such products.If etoposide should contact the skin, mucosa or eyes, immediately wash the skin with soap and water and flush the mucosa or eyes with water.

Do not open any blister in which there is evidence of capsule leakage.

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

7 MARKETING AUTHORISATION HOLDER

Cheplapharm Arzneimittel GmbH
Ziegelhof 24
17489
Greifswald
Germany

8 MARKETING AUTHORISATION NUMBER

PA2239/006/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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