

New Zealand Datasheet

1 PRODUCT NAME

Etoposide Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Etoposide 100 mg/5 ml Solution for Injection

3 PHARMACEUTICAL FORM

Etoposide Injection is a sterile solution that is clear and colourless to pale yellow with a pH of 3–4.

Etoposide Injection is available in a 5 ml single-use clear glass vial containing 100 mg etoposide.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Small-cell lung cancer: Etoposide Solution for Injection is indicated for the first-line treatment of small-cell lung cancer with additional chemotherapeutic agents.

Hodgkin's disease

Malignant (non-Hodgkin's) lymphomas, particularly of the histiocytic variety

Acute non-lymphocytic leukaemia

Testicular tumours: Etoposide Solution for Injection is indicated both as the first-line combination regimens and for the treatment of refractory testicular tumours.

4.2 Dose and method of administration

Etoposide Solution for Injection must be diluted immediately prior to administration with either 5% Dextrose Injection or 0.9% Sodium Chloride Injection to give a solution concentration of 0.2 to 0.4 mg/ml of Etoposide (see Preparation for Administration).

Dosage in Adults

Etoposide Solution for Injection is to be administered slowly at a dosage of 50–100 mg/m² on days 1 to 5 every 3 or 4 weeks or 100 mg/m² on days 1, 3 and 5 every 3 or 4 weeks. Total dosage must be adapted based upon the myelosuppressive effects of combinations with other medicines and or the effects of previous chemotherapy or X-ray therapy which possibly could have compromised the reserves of the bone marrow.

Most patients undergo three or four treatment cycles with Etoposide Solution for Injection. Treatment cycles may be repeated and dosage adjusted (increased or decreased) depending on the individual patient's bone marrow reserve and tumour reserve. The optimum use of Etoposide Solution for Injection is in combination with other chemotherapeutic agents.

Dosage in Adults with Renal Impairment

The dosage of Etoposide Solution for Injection should be adjusted in patients with renal impairment according to measured creatinine clearance.

Patients with a measured creatinine clearance greater than 50 ml/min should receive 100% of the recommended Etoposide Solution for Injection dose.

Patients with a measured creatinine clearance 15ml/min to 50ml/min should receive 75% of the recommended Etoposide Solution for Injection dose.

Subsequent Etoposide Solution for Injection dosing should be based on patient tolerance and clinical effect. Equivalent dose adjustments of Etoposide Solution for Injection should be used.

Information is not readily available in patients that had creatinine clearances less than 15 ml/min. It is recommended that increased reduction must be taken into account for these patients.

Dosage in the Elderly

No dosage adjustment is necessary; however, total dosage per course should not exceed 400mg/m² intravenously.

Dosage in Children

The effectiveness and safety of Etoposide Solution for Injection has not been recognised in children due to inadequate clinical data.

Etoposide Solution for Injection contains polysorbate 80 and benzyl alcohol. In premature infants a life-threatening syndrome associated with injections which contain polysorbate 80 or benzyl alcohol have resulted in renal and hepatic failure, thrombocytopenia, pulmonary deterioration and ascites.

Preparation for Administration

Immediately before administration, the required dose of Etoposide Solution for Injection must be diluted with either 5% Dextrose Injection or 0.9% Sodium Chloride Injection to give a solution concentration of 0.2 to 0.4 mg/ml of Etoposide; it should then be given by intravenous infusion over a period of not less than 30 minutes. Higher concentrated solutions than 0.4mg/mL display crystal formation upon seeding or stirring (within 5 minutes) and must not be given intravenously.

Caution must be applied in handling and disposal of the Etoposide Solution for Injection. Gloves are recommended to prevent skin reactions that occur with accidental exposure of the solution to the skin. Any skin or mucosa that comes in contact with Etoposide Solution for Injection should be washed thoroughly with soap and cold water.

Polyvinyl chloride and clear neutral glass do not affect or absorb Etoposide Solution for Injection. Cracks and leaks have previously been reported when undiluted Etoposide has been used in plastic components made of ABS (a polymer composed of acrylonitrile, butadiene, and styrene) or acrylic. No such effect has been reported with diluted Etoposide.

Etoposide Solution for Injection is stable at room temperature (25°C) in 5% Dextrose Injection, or 0.9% Sodium Chloride Injection in concentrations of 0.2 or 0.4 mg/ml for 96 hours, and 12 hours respectively, under normal fluorescent light in both glass and plastic containers. However, it is recommended that the Etoposide Solution for Injection is administered as soon as the solution is reconstituted to reduce the risk of microbiological hazard.

Diluted Etoposide Injection is a clear solution that is colourless to pale yellow in colour. The reconstituted Etoposide Solution for Injection is to be examined for any discolouration or particulate material before administration. If there is any indication of precipitation the solution should be disposed of.

Etoposide Injection is for single use only and any unused portion should be discarded. Established guidelines on the proper handling and disposal of anticancer drugs should be followed.

Administration Precautions

CAUTION – ETOPOSIDE SOLUTION FOR INJECTION IS NOT TO BE ADMINISTERED BY RAPID INTRAVENOUS INFUSION.

Hypotension following rapid intravenous administration has been reported, hence, it is recommended that Etoposide Solution for Injection should be administered over a 30 to 60 minute period. Longer infusion times may be required based on patient tolerance.

Etoposide diluted to 0.4 mg/ml and administered through tubing connected to a pump with a peristaltic mechanism may precipitate out of solution in the tubing.

Administration of Etoposide Solution for Injection should not be by intra-cavity injection.

4.3 Contraindications

- Known hypersensitivity to Etoposide or any component of the Etoposide Injection preparation (see Excipients)
- Severe hepatic dysfunction.

4.4 Special warnings and precautions for use

Administration

An experienced physician in the use of oncological chemotherapy should supervise the administration of Etoposide Solution for Injection.

Etoposide Injection should be intravenously infused over a 30 to 60 minute period because rapid intravenous infusion may lead to hypotension. Etoposide Solution for Injection must not be administered by intra-cavity injection (See Administration Precautions).

Myelosuppression

Severe myelosuppression has previously been reported after the administration of Etoposide Solution for Injection resulting in bleeding and/or infection. Fatal myelosuppression has also been reported.

Myelosuppression that is dose-limiting is the most significant toxicity in relation to Etoposide.

Etoposide recipients should be monitored frequently for myelosuppression before and after treatment. Complete blood count with differential, haemoglobin level and leukocyte, neutrophil and platelet counts should be recorded at the beginning of therapy and reviewed prior to each following dose of Etoposide Solution for Injection.

Treatment with Etoposide should be withheld in patients with platelet counts $<50,000$ cells/mm³ or neutrophil counts <500 mm/m³ until blood counts have recovered sufficiently.

Treatment with Etoposide should be withheld in patients with infections until the infection is controlled. This is because of increased septicaemia risk as a consequence of the myelosuppressive effects of Etoposide.

Combination with other chemotherapeutic drugs may increase the likelihood of myelosuppression. Caution should be exercised when administering Etoposide in combination with other chemotherapy.

Caution should be exercised when administering Etoposide to patients with bone marrow reserve that may have been compromised by prior irradiation or chemotherapy, or with bone marrow function recovering from previous chemotherapy. Etoposide dosage should be adjusted as necessary.

Anaphylactic Reactions

Anaphylactic reactions, manifested by fever, bronchospasm, chills, dyspnoea, hypotension and tachycardia, have been reported during Etoposide infusion (see Adverse Effects). Coughing, cyanosis, diaphoresis, facial/tongue swelling, laryngospasm, loss of consciousness, back pain and tightness in throat have also been reported. Some reactions have been fatal.

If an anaphylactic reaction occurs, the infusion must be stopped without delay and symptomatic treatment applied (corticosteroids, pressor agents, volume expanders, antihistamines) at the discretion of the treating physician.

Injection Site Reactions

Injection site reactions have been reported during Etoposide infusion (see Adverse Effects). Etoposide Solution for Injection should only be administered after dilution via intravenous infusion. The infusion site should be monitored closely for possible infiltration throughout the administration of Etoposide Solution for Injection. In the case of extravasation, the infusion should be terminated immediately. Treatments specific for extravasation are not known.

Hepatic or Renal Impairment

Etoposide Solution for Injection is contraindicated in patients with severe hepatic dysfunction.

Etoposide Solution for Injection should be administered with caution in patients with hepatic or renal impairment. Dosage adjustments are recommended in patients with renal impairment (see Dosage and Administration).

General

If Etoposide is to be used as part of a chemotherapy regimen, the physician should weigh the necessity to use the drug against its potential risk and side effects.

Drug-related adverse events associated with Etoposide are generally reversible if identified early. If a patient presents with a serious adverse event, the dosage of Etoposide should be decreased or discontinued and the appropriate remedial treatment given. Caution should be exercised if Etoposide is re-initiated, with particular attention to the possible recurrence of the event.

Low serum albumin levels in patients may result in an increased risk of Etoposide associated toxicities.

Etoposide Solution for Injection contains 30.5% (v/v) ethanol. This may affect patients with liver disease, alcoholism, epilepsy, brain injury, brain disease or pregnant women. Benzyl

alcohol may also cause toxic and anaphylactic reactions in infants and children aged less than three years.

4.5 Interaction with other medicines and other forms of interaction

Do not physically mix Etoposide Solution for Injection with any other drug.

Exercise caution when administering Etoposide Solution for Injection with levamisole hydrochloride or other drugs that are recognised to reduce phosphatase activities. Concomitant administration of oral Etoposide with high-dose cyclosporine (concentrations above 2,000 mg/mL) resulted in an 80 percent Etoposide exposure increase (AUC) and a 38 percent decrease of Etoposide, in comparison with Etoposide only.

Decreased Etoposide total body clearance is associated with the administration of both Etoposide and cisplatin.

Etoposide along with phenytoin therapy is associated with an increase of Etoposide clearance and decreased effectiveness. Other anti-epileptic medication may also be associated with an increase of Etoposide clearance and decreased effectiveness.

Reduced seizure management can result from concomitant antiepileptic and Etoposide therapy due to the pharmacokinetic interactions between the medications.

Warfarin therapy alongside Etoposide may result in increased international normalized ratio (INR). Close observation is recommended of international normalized ratio.

Preclinical experiments have resulted in cross resistance between Etoposide and anthracyclines.

Risk of fatal systemic vaccine disease is increased with the co-administration of live vaccines with Etoposide. In immunosuppressed patients, live vaccinations are not recommended (see Warnings and Precautions, Vaccinations).

Vaccinations

During the use of Etoposide, normal human defence mechanisms can be reduced. The use of Etoposide alongside a live virus vaccine may potentially cause the reproduction of the virus in the vaccine to increase and or may potentially intensify the adverse effect of the vaccine virus.

Severe infection can result from administering Etoposide and a live vaccine concomitantly, therefore the use of live virus vaccines must be avoided and advice requested from an individual specialist.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category D

The effects of Etoposide in pregnant women are not known due to inadequate information being available. Etoposide administered in pregnancy has the potential to cause harm to the foetus. Caution should be given to women of childbearing potential to avoid pregnancy during treatment with Etoposide. If Etoposide is administered to a pregnant woman or a woman falls pregnant while being treated with Etoposide, the potential toxicity to the foetus should be explained fully to the patient.

Etoposide was teratogenic when administered to mice and rats.

Both men and women are required to use a contraceptive that is effective during the course of treatment and for six months after the treatment has ended due to the mutagenic potential of Etoposide Solution for Injection. After the treatment has ended, genetic consultation is suggested for patients who wish to have children in the future. Male fertility can decrease due to Etoposide administration, therefore for the intent of fatherhood after treatment, preservation of sperm should be considered.

Breast feeding

It is unknown whether Etoposide is secreted into breast milk; however, as numerous other medications are secreted into breast milk (and exposure to Etoposide has the likelihood of serious adverse effects), it is recommended that women treated with Etoposide Solution for Injection do not breastfeed their infants.

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 and use machines have been performed with etoposide. Fatigue, somnolence, nausea, vomiting and acute hypersensitivity reactions may occur due to a drop in blood pressure, and this may impair the ability to drive and use machines.

4.8 Undesirable effects

The following information on adverse effects with etoposide is sourced from data on intravenous and oral administration as an individual agent. Several dose schedules were used to treat a range of malignancies. Because etoposide phosphate is changed to etoposide, adverse events relating to the oral formulation may also occur in patients treated with the intravenous formulation.

Haematological

There have been reports of myelosuppression with fatal outcome in patients treated with etoposide (see Warnings and Precautions). In general, myelosuppression is dose-limiting with leukocyte, granulocyte and platelet nadirs occurring 15-22 days, 12-19 days and 10-15 days, respectively, after administration. Bone marrow normally recovers completely by day 21, with no reports of cumulative toxicity.

The main dose-limiting toxicity associated with etoposide is leukopenia (<4000 cells/mm³), occurring in 60-91% of patients treated with single-agent etoposide in clinical trials. Severe leukopenia (<1000 cells/mm³) has been reported in 7-17% of patients treated with single-agent etoposide.

Thrombocytopenia ($<100,000$ cells/m³) has been reported in 28-41% of patients treated with single-agent etoposide in clinical trials. Severe thrombocytopenia ($<50,000$ cells/mm³) has been reported in 9% of patients treated with single-agent etoposide.

Neutropenia (<2000 cells/m³) has been reported in 88% of patients treated with single-agent etoposide in clinical trials. Severe neutropenia (<500 cells/mm³) has been reported in 37% of patients treated with single-agent etoposide. Infection and fever have occurred in patients diagnosed with neutropenia.

Anaemia (haemoglobin <11 g/dL) has been reported in 72% of patients treated with single-agent etoposide in clinical trials. Severe anaemia (haemoglobin <8 g/dL) has been reported in 19% of patients treated with single-agent etoposide.

There have been rare reports of acute leukaemia, with or without a preleukaemic phase (myelodysplastic syndrome), in patients treated with etoposide in combination with other antineoplastic drugs (see Warnings and Precautions).

Neurological

Peripheral neuropathy has been reported in 0.7% of patients treated with etoposide. This may have been enhanced by concomitant use of vincristine sulphate.

Gastrointestinal

The main gastrointestinal toxicities associated with etoposide are nausea and vomiting, occurring in 31–43% of patients treated with intravenous etoposide in clinical trials. Nausea and vomiting are usually mild to moderate in severity and can usually be controlled with antiemetic therapy.

Other gastrointestinal toxicities associated with etoposide include anorexia (10–13%), mucositis (11%), constipation (8%), abdominal pain (7%), diarrhoea (1–13%), stomatitis (1–6%) and taste alteration (6%). Etoposide was discontinued in 1% of patients because of gastrointestinal toxicity.

Dermatological

Up to 44% of patients experienced reversible alopecia in clinical trials, occasionally advancing to overall baldness.

Extravasation or phlebitis has been reported in 5% of patients in clinical trials. Occasionally soft tissue toxicity has occurred following extravasation. Pain, swelling, necrosis (including necrosis of the skin) and cellulitis may occur as a consequence of etoposide infiltration (see Warnings and Precautions).

Allergic

Up to 3% of patients have reported anaphylactic-type reactions during or immediately after etoposide administration, characterised by fever, chills, dyspnoea, bronchospasm, tachycardia, and hypotension. There have also been reports of hypertension, flushing and seizures. Such reactions can occur with the initial dose of etoposide. Higher rates are reported in children administered etoposide at higher concentrations than recommended. It is unclear what role the rate of infusion or concentration of infusion solution plays in the development of anaphylactic-type reactions.

There have been reports of acute fatal bronchospasm in patients receiving etoposide (see Warnings and Precautions).

If an anaphylactic reaction occurs, the infusion should be terminated immediately and symptomatic treatment applied (antihistamines, pressor agents, volume expanders or corticosteroids at the discretion of the treating physician). Blood pressure typically normalises within several hours of stopping the infusion. After infusion discontinuation, there have been reports of apnoea with unprompted recommencement of breathing.

There have been infrequent reports of urticaria, rash, and/or pruritus at recommended doses of etoposide. Doses investigated have reported a widespread pruritic erythematous maculopapular rash, similar to perivasculitis.

Hepatic

There have been rare reports of hepatic toxicity with etoposide. These have generally occurred in patients treated with higher doses than recommended.

Cardiovascular

Approximately 1–2% of patients have experienced temporary hypotension following rapid intravenous administration of etoposide. This has not been related to electrocardiographic changes or cardiac toxicity, nor has delayed hypotension been reported. Etoposide should be administered by intravenous infusion over 30 or 60 minutes to prevent hypotension from developing. If clinically significant hypotension occurs, the infusion should be stopped and appropriate supportive therapy should be initiated. A lower infusion rate should be used when restarting the infusion.

Other

Asthenia and malaise were reported in 39% of patients treated with single-agent etoposide in clinical trials (severe in 3% of patients). Chills and/or fever were reported in 24% of patients and dizziness in 5% of patients.

There have been rare reports of the following events with etoposide: seizures (sometimes associated with allergic reactions), toxic epidermal necrolysis, interstitial pneumonitis/pulmonary fibrosis, central nervous system toxicity (somnolence and fatigue), aftertaste, Stevens-Johnson syndrome, liver toxicity, dysphagia, fever, transient cortical blindness, and one individual report of radiation recall dermatitis and optic neuritis.

Metabolic acidosis has been reported in patients receiving etoposide at higher than recommended doses.

Metabolic Complications

Following the administration of Etoposide in connection with other oncological medication, tumour lysis syndrome (occasionally fatal) has been reported.

Arrhythmia and myocardial infarction have been reported.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

4.9 Overdose

There is no known antidote for Etoposide Injection overdose.

Severe mucositis and myelotoxicity have been reported in patients receiving intravenous etoposide over three days at a total dose of 2.4 g/m² and 3.5 g/m².

Metabolic acidosis and serious hepatic toxicity have been reported with exposure to intravenous etoposide at higher than recommended doses.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antineoplastic agent—podophyllotoxin derivatives. ATC code: L01CB01

Mechanism of action

Etoposide is semi-synthetic derivative of podophyllotoxin. It is an antineoplastic agent that inhibits DNA synthesis. It acts by lysing cells entering mitosis (high concentrations; ≥ 10 mcg/ml) or by inhibiting cells from entering prophase (low concentrations; 0.3–10 mcg/ml). Etoposide has also been shown to cause metaphase arrest in chick fibroblasts. It does not affect microtubule assembly.

5.2 Pharmacokinetic properties

In humans, the plasma concentration of etoposide decays in a biphasic manner following intravenous administration. The distribution half-life is approximately 1.5 hours. The terminal elimination half-life is independent of dose (over a range of 100–600 mg/m²) and spans from 4 to 11 hours. Total body clearance is also independent of dose over a range of 100–600 mg/m² and ranges from 16 to 36 ml/min/m². The area underneath the plasma concentration versus time curve and the maximum plasma concentration (C_{max}) values linearly increase with dose over the same dose range. No accumulation in plasma has been reported with daily administration over 4 to 6 days of 100 mg/m² for 4 to 6 days.

At steady state, distribution mean volumes range from 18 to 29 litres. Although etoposide is detectable in the cerebrospinal fluid and intracerebral tumours, concentrations are less than in extracerebral plasmas and tumours. Etoposide levels are similar in normal tissues and primary tumours of the myometrium but are increased in normal lung tissue than lung metastases. In vitro, etoposide exhibits high binding to human plasma proteins (97%). In children, there is an inverse association between plasma albumin levels and etoposide renal clearance. Protein-bound etoposide is displaced by sodium sulcylate, phenyl butazone, and aspirin at concentrations attained in vivo.

Etoposide is cleared by both metabolism and biliary excretion. Mean radioactivity recovery at 120 hours following administration intravenously of ¹⁴C-etoposide (100–124 mg/m²) was 56% in the urine (45 percent that was excreted as etoposide) and 44% in the faeces. Within the dose range of 80–600 mg/m², mean renal clearance is 7–10 ml/min/m² (approximately 35 percent of the full body clearance). Approximately 55 percent of the dose is excreted in urine as etoposide within 24 hours in children. It is unclear what effect renal disease has on plasma etoposide clearance in children.

The Etoposide hydroxy acid metabolite [4'-demethyl epipodophyllic acid-9-(4,6-O-ethylidene- β -D-glucopyranoside)], developed by the opening of the lactone ring, is located in the urine of children and adults. This metabolite, probably as the trans isomer, is also found in human plasma, Mean radioactivity recovery of glucuronide and/or sulphate conjugates of etoposide at 120 hours after intravenous administration of ¹⁴C-etoposide is less than 8%. The corresponding catechol is formed through O-demethylation of the dimethoxyphenol ring via the CYP450 3A4 isoenzyme pathway.

Total body elimination of etoposide is associated with creatinine clearance, non renal clearance and low serum albumin concentration in adults. The total body elimination of etoposide in adult patients with cancer and with liver dysfunction is not decreased.

Decreased total body elimination of etoposide, increased AUC and increased steady state volume of distribution have been reported in patients with impaired renal function (see

Dosage and Administration). Reduced total body clearance has also been reported in children with elevated SGPT levels. Prior exposure to cisplatin may also decrease total body clearance of etoposide in children.

5.3 Preclinical safety data

Carcinogenicity/Mutagenicity

In vivo carcinogenicity tests have not been performed with etoposide. However, etoposide may have carcinogenic potential in humans because of its mechanism of action (see Mechanism of Action and Adverse Effects – Haematological Toxicity). There have been rare reports of acute leukaemia, with or without a preleukaemic phase (myelodysplastic syndrome), in patients treated with etoposide in combination with other antineoplastic drugs. In vitro studies have shown that etoposide has mutagenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each mL of Etoposide Solution for Injection contains 20 mg Etoposide (base) polyethylene glycol 300, polysorbate 80, benzyl alcohol, citric acid and 30.5 percent (v/v) ethanol.

Does not contain lactose or gluten.

6.2 Incompatibilities

Etoposide Injection must not be mixed with other drugs when administered.

This medicinal product must not be mixed with other medicinal products excepts those mentioned in section 4.2

6.3 Shelf life

The shelf life of Etoposide Injection when unopened is 36 months from date of manufacture when stored at or below 25°C and protected from light. The expiry date is given as the month and the year. The expiry date is that last day of the month given.

6.4 Special precautions for storage

Etoposide Solution for Injection should be stored at or below 25°C. Do not freeze.

The Solution for Injection should be protected from light. At 25°C or below, Etoposide will remain stable until the expiration date indicated on the package. Etoposide Solution for Injection is for single use only and any unused portion should be discarded.

Handling and disposal of Etoposide Solution for Injection should follow suitable cytotoxic guidelines.

6.5 Nature and contents of container

Etoposide Injection is available in a 5 ml glass vial containing 100 mg etoposide. Each carton contains 10 vials of Etoposide Injection.

6.6 Special precautions for disposal and other handling

Etoposide Injection should be handled in accordance with instruction for cytotoxic agents.

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

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.

Pregnant personnel are advised not to handle chemotherapeutic agents.

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.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

21 July 2011

10 DATE OF REVISION OF THE TEXT

17 September 2018

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.6	Fertility section added
4.7	Section added
4.8	Reporting of adverse events added
4.9	Poison information centre contact added
6.6	Section added