

**Approved**

**PROFESSIONAL INFORMATION FOR HUMAN USE**

**SCHEDULING STATUS**

**S4**

**PROPRIETARY NAME AND DOSAGE FORM**

Paclitaxel Fresenius 6 mg/ml (30 mg/5 ml), Concentrate for solution for infusion

Paclitaxel Fresenius 6 mg/ml (100 mg/16,7 ml), Concentrate for solution for infusion

Paclitaxel Fresenius 6 mg/ml (300 mg/50 ml), Concentrate for solution for infusion.

**WARNINGS**

Paclitaxel Fresenius (paclitaxel) should be administered under the supervision of a medical practitioner experienced in the use of cancer chemotherapeutic medicines.

Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

Severe hypersensitivity reactions characterised by dyspnoea, flushing, chest pain and tachycardia and hypotension requiring treatment, angioedema, and generalised urticaria have occurred in patients receiving Paclitaxel Fresenius. Patients receiving Paclitaxel Fresenius should be pre-treated with corticosteroids, promethazine, and H<sub>2</sub> antagonists to prevent these reactions (see DOSAGE AND DIRECTIONS FOR USE). Patients who experience severe hypersensitivity reactions to Paclitaxel Fresenius

should not be re-challenged with Paclitaxel Fresenius.

Paclitaxel Fresenius therapy should not be given to patients with baseline neutrophil counts of less than 1 500 cells/mm<sup>3</sup>. In order to monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving Paclitaxel Fresenius.

The poly-oxy-ethylated castor oil in Paclitaxel Fresenius can result in phthalate leaching from polyvinyl chloride (PVC) containers, at levels which increase with time and concentration. Consequently, the preparation, storage and administration of diluted Paclitaxel Fresenius should be carried out by using non-plasticised PVC-containing equipment.

## **COMPOSITION**

Each 1 ml of solution contains 6 mg paclitaxel.

### **Inactive ingredients:**

49,7 % v/v Ethanol anhydrous, macrogolglycerol ricinoleate (poly-oxy-ethylated castor oil), citric acid anhydrous, nitrogen.

## **PHARMACOLOGICAL CLASSIFICATION:**

A 26 Cytostatic agents

## **PHARMACOLOGICAL ACTION**

### **Pharmacodynamic properties**

Paclitaxel is an antimicrotubule substance that promotes the assembly of microtubules from tubulin dimers and stabilises microtubules by preventing

depolymerisation. This stability results in the inhibition of the normal dynamic reorganisation of the microtubule network that is essential for vital interphase and mitotic cellular functions. In addition, paclitaxel induces abnormal arrays or bundles of microtubules throughout the cell cycle and multiple asters of microtubules during mitosis.

### **Pharmacokinetic properties**

Following intravenous administration, paclitaxel exhibits a biphasic decline in plasma concentration. The initial rapid decline represents distribution to the peripheral compartment and elimination; the later phase is due, in part, to a relatively slow efflux of paclitaxel from the peripheral compartment. In patients treated with doses of 135 and 175 mg/m<sup>2</sup> given as 3 and 24 hour infusions, mean terminal half-life has ranged from 3,0 to 52,7 hours. Mean values for total body clearance ranged from 11,6 to 24 l/h/m<sup>2</sup>. Mean steady state volume of distribution has ranged from 198 to 688 l/m<sup>2</sup>, indicating extensive extravascular distribution and/or tissue binding.

The pharmacokinetics of paclitaxel are non-linear. There is a disproportionately large increase in C<sub>max</sub> and AUC with increasing dose, accompanied by an apparent dose-related decrease in total body clearance. These findings are most readily observed in patients in whom, high plasma concentrations of paclitaxel are achieved. Saturable processes in distribution and elimination/metabolism may account for these findings.

There was no evidence of accumulation of paclitaxel with multiple treatment course. In vitro studies of binding to human serum proteins, using paclitaxel concentrations ranging from 0,1 to 50 µg/ml, indicate that, on average, 89 % of paclitaxel is bound. The presence of cimetidine, ranitidine, dexamethasone or diphenhydramine did not affect protein binding of paclitaxel.

The disposition of paclitaxel has not been fully elucidated in humans. After intravenous administration of paclitaxel, mean values of cumulative urinary recovery of unchanged paclitaxel ranged from 1,3 to 12,6 % of the dose, indicating extensive non-renal clearance. Hepatic metabolism and biliary clearance may be the principal mechanism for disposition of paclitaxel. Paclitaxel is metabolised primarily by cytochrome P450 enzymes. Hydroxylated metabolites have been demonstrated to be the principal metabolites. The formation of 6 $\alpha$ -hydroxypaclitaxel, 3'-p- hydroxypaclitaxel and 6 $\alpha$ ,3'-p-dihydroxypaclitaxel is catalysed by CYP2C8, 3A4 and both 2C8 and 3A4 respectively. The effect of the renal or hepatic dysfunction on the disposition of paclitaxel has not been investigated. The clearance of paclitaxel is not affected by cimetidine pre-treatment. Ketoconazole may inhibit the metabolism of paclitaxel. Plasma levels of doxorubicin and doxorubicinol may be increased when paclitaxel and doxorubicin are used in combination.

## **INDICATIONS**

Paclitaxel Fresenius is indicated for:

1. The palliative treatment of Stage 3 or 4 advanced local carcinoma of the ovary after surgical resection, in combination with cisplatin.
2. The palliative management of metastatic carcinoma of the ovary after failure of first line or subsequent chemotherapy.
3. The treatment of metastatic carcinoma of the breast after failure of combination chemotherapy or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.

4. Palliative treatment of advanced non-small cell lung cancer in patients who are not candidates for potentially curative surgery and/or radiation therapy.

## **CONTRAINDICATIONS**

- Paclitaxel Fresenius is contraindicated in patients who have a history of severe hypersensitivity reactions to paclitaxel or other medicines formulated with poly-oxy-ethylated castor oil or any other ingredients of Paclitaxel Fresenius.
- Paclitaxel Fresenius should not be used in patients with baseline neutrophils  $<1\ 500/\text{mm}^3$ .
- Pregnancy and lactation (see PREGNANCY AND LACTATION).
- The safety and efficacy of Paclitaxel Fresenius in children have not been established.

## **WARNINGS AND SPECIAL PRECAUTIONS**

Paclitaxel Fresenius should be administered under the supervision of a medical practitioner experienced in the use of cancer chemotherapeutic medicines. Since severe hypersensitivity reactions may occur, appropriate supportive equipment should be available.

Paclitaxel Fresenius should be administered as a diluted infusion.

### **Hypersensitivity reactions**

Paclitaxel Fresenius should be given before cisplatin when used in combination. Patients should be pre-treated with corticosteroids, antihistamines and  $\text{H}_2$  antagonists before receiving Paclitaxel Fresenius. Anaphylaxis and severe hypersensitivity reactions, probably histamine-

mediated, characterised by dyspnoea, flushing, chest pain and tachycardia and hypotension requiring treatment, angioedema and generalised urticaria have occurred in patients receiving Paclitaxel Fresenius. Fatal reactions have occurred in patients despite pre-treatment. In cases of severe hypersensitivity reactions, Paclitaxel Fresenius infusion should be immediately discontinued, symptomatic therapy should be initiated and the patient should not be re-challenged with the Paclitaxel Fresenius.

Minor hypersensitivity reactions such as flushing, rash, do not require interruption of therapy.

### **Bone marrow suppression**

Bone marrow suppression (primary neutropenia) is the principal dose-limiting toxicity. Frequent monitoring of blood counts should be instituted during Paclitaxel Fresenius treatment. Patients should not be retreated until neutrophils recover to a level  $> 1\ 500/\text{mm}^3$  and platelets recover to a level  $> 100\ 000/\text{mm}^3$ . In cases of severe neutropenia ( $< 500\ \text{cells}/\text{mm}^3$ ) during a course of Paclitaxel Fresenius, a 20 % reduction in dose for subsequent courses of therapy is recommended. The incidence of neurotoxicity and severity of neutropenia increase with increased doses within a regimen.

### **Cardiovascular events**

Hypotension, hypertension and bradycardia have been observed during administration of Paclitaxel Fresenius. In severe cases Paclitaxel Fresenius infusions may need to be interrupted or discontinued at the discretion of the treating medical practitioner.

Frequent vital sign monitoring, particularly during the first hour of Paclitaxel Fresenius infusion, is recommended.

Severe cardiac conduction abnormalities have been reported. If patients develop significant conduction abnormalities during Paclitaxel Fresenius administration, appropriate therapy should be administered and continuous cardiac monitoring should be performed during subsequent therapy with Paclitaxel Fresenius. Continuous cardiac monitoring is not required except for patients with serious conduction abnormalities.

Severe cardiovascular events were observed more frequently in patients with non-small cell lung carcinoma than breast or ovarian carcinoma.

### **Fertility**

Paclitaxel Fresenius may have an antifertility effect, which could be irreversible. Male patients are therefore advised not to father a child during, and up to 6 months after, treatment and to seek advice on conservation of sperm prior to treatment.

### **Neurotoxicity**

Cross-study comparison of neurotoxicity suggests that when Paclitaxel Fresenius is given in combination with cisplatin 75 mg/m<sup>2</sup>, the incidence of severe neurotoxicity is more common at a Paclitaxel Fresenius dose of 175 mg/m<sup>2</sup> given by 3-hour infusion (21 %), than at a dose of 135 mg/m<sup>2</sup> given by 24-hour infusion (3 %).

The occurrence of peripheral neuropathy is frequent, and the development of moderate to severe symptomatology requires a dose reduction of 20 % for all subsequent courses of Paclitaxel Fresenius.

### **Hepatic impairment**

Patients with hepatic impairment may be at increased risk of toxicity particularly grade III-IV myelosuppression. Dose adjustment is

recommended (see DOSAGE AND DIRECTIONS FOR USE). Patients should be monitored closely for the development of profound myelosuppression.

Hepatic necrosis and hepatic encephalopathy leading to death have been reported.

Elevations in alkaline phosphatase and AST (SGOT) have been reported.

### **Injection site reaction**

A specific treatment for extravasation reactions is unknown at this time.

Given the possibility of extravasation, it is advisable to closely monitor the infusion site for possible infiltration during Paclitaxel Fresenius administration.

### **Paediatric use**

The safety and effectiveness of Paclitaxel Fresenius in children have not been established. There have been reports of central nervous system toxicity (associated with death) in a clinical trial in paediatric patients in which Paclitaxel Fresenius was infused intravenously over 3 hours at doses ranging from 350 mg/m<sup>2</sup> to 420 mg/m<sup>2</sup>.

### **Effects on ability to drive and use machines**

Patients should be advised that performance at skilled tasks, such as driving and operating machinery may be impaired due to the alcohol content of Paclitaxel Fresenius and some of its side effects (dizziness, vertigo and confusion - see SIDE EFFECTS). Patients should not be allowed to go home unaccompanied if these effects are observed.

### **Information on the excipients**

Paclitaxel Fresenius contains 49,7 % v/v anhydrous ethanol (393 mg/ml).

Consideration should be given to possible central nervous system and other effects of alcohol for all patients. Children may be more sensitive than adults to the effects of alcohol.

Paclitaxel Fresenius also contains poly-oxy-ethylated castor oil, which may cause serious allergic reaction in hypersensitive patients (see CONTRAINDICATIONS - "Hypersensitivity reactions").

### **INTERACTIONS**

The recommended regimen of Paclitaxel Fresenius administration for the primary treatment of ovarian carcinoma is for Paclitaxel Fresenius to be given before cisplatin. When Paclitaxel Fresenius is given before cisplatin; the safety profile of Paclitaxel Fresenius is consistent with that reported for single product use. When Paclitaxel Fresenius given after cisplatin, patients showed a more profound myelosuppression and an approximately 33 % decrease in paclitaxel clearance.

Medicines concomitantly administered with Paclitaxel Fresenius (e.g. corticosteroids, antihistamines, and H<sub>2</sub> antagonists) did not appear to interact adversely; however, possible interactions of Paclitaxel Fresenius with concomitantly administered medicines have not been formally investigated.

Based on *in vitro* data, there is the possibility of an inhibition of Paclitaxel Fresenius metabolism in patients treated with ketoconazole. As a result, caution should be exercised when treating patients with Paclitaxel Fresenius when they are receiving ketoconazole as concomitant therapy.

Plasma levels of doxorubicin and doxorubicinol may be increased when Paclitaxel Fresenius and doxorubicin are used in combination. Sequence effects characterised by more profound neutropenic and stomatitis episodes have been observed with combination use when Paclitaxel Fresenius is administered before doxorubicin and using longer than recommended infusion times.

The metabolism of Paclitaxel Fresenius is catalysed by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. Caution should be exercised when administering Paclitaxel Fresenius concomitantly with known substrates, inducers or inhibitors of these isoenzymes.

Contact of the undiluted concentrate with plasticised polyvinyl chloride (PVC) equipment or devices used to prepare solutions for infusion is not recommended. In order to minimise patient exposure to the plasticiser DEHP [di-2-ethylhexyl) phthalate], which may be leached from PVC infusion bags or sets, diluted Paclitaxel Fresenius solutions should preferably be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets. Paclitaxel Fresenius should be administered through an in-line filter with a microporous membrane not greater than 0,22 microns. Use of filter devices such as IVEX-2 filters which incorporate short inlet and outlet PVC-coated tubing has not resulted in significant leaching of DEHP.

## **HUMAN REPRODUCTION**

Paclitaxel Fresenius is contraindicated in pregnancy and lactation.

## **Pregnancy**

Paclitaxel Fresenius has been shown to be embryotoxic, fetotoxic and to decrease fertility in animal studies. Paclitaxel Fresenius may cause foetal harm when administered to pregnant women.

## **Women of childbearing potential**

Women of childbearing potential should be advised to avoid becoming pregnant during therapy with Paclitaxel Fresenius, and to inform the treating doctor immediately should this occur.

## **Lactation**

It is not known whether Paclitaxel Fresenius is excreted in human milk. Breastfeeding should be discontinued for the duration of Paclitaxel Fresenius therapy.

## **Fertility**

Paclitaxel Fresenius may have an antifertility effect, which could be irreversible. Male patients are therefore advised not to father a child during, and up to 6 months after, treatment and to seek advice on conservation of sperm prior to treatment.

## **DOSAGE AND DIRECTIONS FOR USE**

### **Indication 1:**

Palliative treatment of advanced ovarian carcinoma: a combination regimen consisting of Paclitaxel Fresenius 135 mg/m<sup>2</sup> administered over 24 hours, followed by cisplatin 75 mg/m<sup>2</sup>, every 3 weeks. Paclitaxel Fresenius should be administered before cisplatin.

Alternatively, a combination consisting of Paclitaxel Fresenius 175 mg/m<sup>2</sup> administered intravenously over 3 hours, followed by cisplatin 75 mg/m<sup>2</sup>, given every 3 weeks.

### **Indication 2 and 3:**

Secondary treatment of metastatic ovarian or breast carcinoma: Paclitaxel Fresenius at a dose of 175 mg/m<sup>2</sup> administered intravenously over 3 hours every 3 weeks has been shown to be effective in patients with metastatic carcinoma of the ovary or breast after the failure of first line or subsequent chemotherapy.

### **Indication 4:**

Palliative treatment of advanced non-small cell lung carcinoma: the recommended dose of Paclitaxel Fresenius is 175 mg/m<sup>2</sup> administered over a period of 3 hours; followed by a platinum compound, with a 3-week interval between courses.

### **All indications**

Paclitaxel Fresenius should not be re-administered until the neutrophil count is at least 1 500/mm<sup>3</sup> and the platelet count is at least 100 000/mm<sup>3</sup>. Patients who experience severe neutropenia (neutrophil count < 500/mm<sup>3</sup>) or moderate to severe peripheral neuropathy should receive a dose reduction of 20 % for subsequent courses (see WARNINGS AND SPECIAL PRECAUTIONS). The incidence and severity of neurotoxicity and haematologic toxicity increases with dose.

All patients must be pre-medicated with corticosteroids, antihistamines, and H<sub>2</sub> antagonists prior to Paclitaxel Fresenius administration, e.g. dexamethasone 20 mg orally approximately 12 and 6 hours before Paclitaxel Fresenius or 20 mg IV dexamethasone approximately 30 to 60

minutes before Paclitaxel Fresenius, promethazine 25 mg IV 30 to 60 minutes prior to Paclitaxel Fresenius and IV cimetidine 300 mg or ranitidine 50 mg 30 to 60 minutes before Paclitaxel Fresenius.

Paclitaxel Fresenius should be administered through an in-line filter with a microporous membrane not greater than 0,22 µm.

**Hepatic impairment:** See WARNINGS AND SPECIAL PRECAUTIONS.

Dosage adjustment is recommended as shown below:

Degree of hepatic impairment		
Transaminase levels	Bilirubin Levels (a)	Recommended Paclitaxel Fresenius dose (b)
24 HOUR INFUSION		
<2xULN and	25,65 µmol/l	135 mg/m <sup>2</sup>
2-<10xULN and	25,65 µmol/l	100 mg/m <sup>2</sup>
<10xULN and	27,36 – 128,25 µmol/l	50 mg/m <sup>2</sup>
≥10xULN or	128,25 µmol/l	Not recommended
3 HOUR INFUSION		
<10xULN and	≤1,25xULN	175 mg/m <sup>2</sup>
<10xULN and	1,26-2,0xULN	135 mg/m <sup>2</sup>
<10xULN and	2,01-5,0xULN	90 mg/m <sup>2</sup>
≥10xULN or	>5,0xULN	Not recommended

(a) Differences in criteria for bilirubin levels between the 3- and 24- hour infusion are due to differences in clinical trial design.

(b) Dosage recommendations are for the first course of therapy: further dose reduction in subsequent courses should be based on individual tolerance.

ULN=upper limit of normal.

**Directions for use/handling**

**Handling:** Caution should be exercised when handling Paclitaxel Fresenius. Dilution should be carried out by trained personnel in a designated area. Adequate protective gloves should be worn. Precautions should be taken to avoid contact with the skin, and mucous membranes. Following topical exposure, tingling, burning and redness have been observed. In the event of contact with the skin, the area should be washed with soap and water. In the event of contact with the mucous membranes, these should be flushed thoroughly with water. Upon inhalation, dyspnoea, chest pain, burning eyes, sore throat and nausea have been reported.

Given the possibility of extravasation, it is advisable to closely monitor the injection site for possible infiltration during Paclitaxel Fresenius administration.

**Preparation for IV administration:**

Paclitaxel Fresenius must be diluted prior to infusion.

Paclitaxel Fresenius should be diluted in 0,9 % sodium chloride injection, or 5 % dextrose injection, or 5 % dextrose and 0,9 % sodium chloride injection, or 5 % dextrose in Ringer's injection to a final concentration of 0,3 to 1,2 mg/ml. The prepared solutions are physically and chemically stable for up to 27 hours at ambient temperature (approximately 25 °C) and room lighting conditions: infusions should be completed within this timeframe.

There have been reports of precipitation with longer than the recommended 3-hour infusion schedules. Excessive agitation, vibration or shaking may induce precipitation and should be avoided. Infusion sets should be flushed thoroughly with a compatible diluent before use. Devices with spikes should not be used with vials of Paclitaxel Fresenius since they can cause the

stopper to collapse resulting in loss of sterile integrity of the Paclitaxel Fresenius solution.

Parenteral medicines should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit.

Upon preparation, solutions may show haziness, which is attributed to the formulation vehicle. Paclitaxel Fresenius should be administered through an in-line filter with a microporous membrane not greater than 0,22 µm. No significant losses in potency have been noted following delivery of the solution through IV tubing containing an in-line filter. After dilution the solution is for single use only.

In order to minimise patient exposure to the plasticiser DEHP [di-(2-ethylhexyl) phthalate], which may be leached from plasticised PVC infusion bags or sets, diluted Paclitaxel Fresenius solutions should preferably be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets. Use of filter devices which incorporate short inlet and/or outlet plasticised PVC tubing has not resulted in significant leaching of DEHP.

**Disposal:** All items used for reconstitution, administration or otherwise coming into contact with Paclitaxel Fresenius should undergo disposal according to local guidelines for the handling of cytotoxic compounds.

## **SIDE EFFECTS**

The frequency and severity of adverse events are generally similar between patients receiving Paclitaxel Fresenius for the treatment of ovarian, breast or lung carcinoma.

**Infections and infestations:**

*Frequent:* Infection

*Less frequent:* Septic shock

**Blood and lymphatic disorders:**

*Frequent:* Anaemia, thrombocytopenia, leukopenia or neutropenia with or without infection, myelosuppression, fever, bleeding.

*Less frequent:* Febrile neutropenia, acute myeloid leukemia, myelodysplastic syndrome.

**Immune system disorders:**

*Frequent:* Hypersensitivity reactions (mainly flushing and rash)

*Less frequent:* Significant hypersensitivity reactions requiring therapy (e.g., hypotension, angioedema, respiratory distress, generalised urticaria, oedema, back pain, chills), anaphylactic reactions with fatal outcome, anaphylactic shock.

**Metabolism and nutrition disorders:**

*Less frequent:* Anorexia

**Psychiatric disorders:**

*Less frequent:* Confusional state.

**Nervous system disorders:**

*Frequent:* Peripheral neuropathy including paraesthesia occurs and is dose dependent.

*Less frequent:* Seizures, optic nerve disturbances and neuroencephalopathy, autonomic neuropathy (resulting in paralytic ileus and orthostatic hypotension), encephalopathy, dizziness, headache, ataxia.

**Eye disorders:**

*Less frequent:* Reversible visual disturbance (scintillating scotomata), particularly in patients who have received higher doses than recommended, photopsia, visual floaters.

**Ear and labyrinth disorders:**

*Less frequent:* Hearing loss, tinnitus, vertigo, ototoxicity.

**Cardiac disorders:**

*Frequent:* Abnormal ECG, bradycardia

*Less frequent:* Congestive heart failure and abnormal electrocardiogram, atrial fibrillation, supraventricular tachycardia, cardiomyopathy, asymptomatic ventricular tachycardia, tachycardia with bigeminy, AV block and syncope, myocardial infarction.

**Vascular disorders:**

*Frequent:* Hypotension

*Less frequent:* Hypertension, thrombosis, thrombophlebitis, shock.

**Respiratory, thoracic and mediastinal disorders:**

*Less frequent:* Dyspnoea, pleural effusion, respiratory failure, interstitial pneumonia, lung fibrosis, pulmonary embolism, cough.

**Gastro-intestinal disorders:**

*Frequent:* Diarrhoea, nausea, vomiting and mucositis.

*Less frequent:* Bowel obstructions/perforations and ischaemic colitis, pancreatitis, mesenteric thrombosis, pseudomembranous colitis, esophagitis, constipation, ascites.

**Hepato-biliary disorders:**

*Less frequent:* Elevated serum hepatic enzymes, hepatic necrosis and hepatic encephalopathy.

**Skin and subcutaneous tissue disorders:**

*Frequently:* Alopecia.

*Less frequent:* Transient and mild nail and skin changes and abnormalities (noted as pigmentation or discolouration), pruritus, rash, erythema, phlebitis, cellulitis, skin exfoliation, necrosis and fibrosis, radiation recall, Stevens-Johnson syndrome, epidermal necrolysis, erythema multiforme, exfoliative dermatitis, urticaria, onycholysis (patients on therapy should wear sun protection on hands and feet).

**Musculoskeletal, connective tissue and bone disorders:**

*Frequent:* Myalgia or arthralgia, usually consisting of pain in the large joints of the arms and legs.

**General disorders and administration site conditions:**

*Less frequent:* Extravasation, with phlebitis or cellulitis. Extravasation during intravenous administration may lead to oedema, pain, erythema and induration and ulceration. Extravasation can result in cellulitis. Recurrence of skin reactions at a site of previous extravasation following administration of Paclitaxel Fresenius at a different site i.e. "recall reaction" has been reported.

**Investigations:**

*Frequent:* Severe elevation in AST (SGOT), severe elevation in alkaline phosphatase.

*Less frequent:* Severe elevation in bilirubin, increase in blood creatinine.

## **KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT**

There is no antidote for Paclitaxel Fresenius overdose. The primary anticipated complications of overdose would consist of bone marrow suppression, peripheral neurotoxicity and mucositis. Treatment is symptomatic and supportive.

## **IDENTIFICATION**

Clear, slightly yellowish solution practically free from particles.

## **PRESENTATION**

Paclitaxel Fresenius (30 mg/5 ml) with concentration 6 mg/ml, is packed in a 5 ml transparent glass vial with a white flip-off cap, with a fill volume of 5 ml. Pack sizes are 1 or 5 vials per outer cardboard carton.

Paclitaxel Fresenius (100 mg/16,7 ml) with concentration 6 mg/ml, is packed in a 50 ml transparent glass vial with a lilac flip-off cap, with a fill volume of 16,7 ml. Pack sizes are 1 or 5 vials per outer cardboard carton.

Paclitaxel Fresenius (300 mg/50 ml) with concentration 6 mg/ml, is packed in a 50 ml transparent glass vial with a red flip-off cap, with a fill volume of 50 ml. Pack sizes are 1 or 5 vials per outer cardboard carton.

## **STORAGE INSTRUCTIONS**

Store at or below 25 °C.

Store in the original package in order to protect from light.

After opening before dilution the product may be stored for 28 days at 25 °C.

After dilution in 5 % glucose solution, 0,9 % sodium chloride solution, 5 % glucose solution in Ringer solution, and 5 % glucose solution / 0,9 % sodium chloride solution the product may be stored for 24 hours at 25 °C protected from light. Discard any unused portion.

KEEP OUT OF REACH OF CHILDREN.

### **REGISTRATION NUMBERS**

Paclitaxel Fresenius 6 mg/ml (30 mg/5 ml) 43/26/0237

Paclitaxel Fresenius 6 mg/ml (100 mg/16,7 ml) 43/26/0244

Paclitaxel Fresenius 6 mg/ml (300 mg/50 ml) 43/26/0239

### **NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION**

Fresenius Kabi South Africa (Pty) Limited

Stand 7, Growthpoint Park,

2 Tonetti Street,

Halfway House, 1685,

South Africa

### **DATE OF PUBLICATION OF THIS PROFESSIONAL INFORMATION**

Date of registration: 15 August 2013

Date of last approval: 3 May 2018