141.0 mm

Dotaxol Injection

(Docetaxel)

ڈوٹیکزول انجیکشن

(ڈوسی ٹیکسل)

206.0 mm

COMPOSITION

Dotaxol Injection 20mg/0.5ml

Each 0.5ml contains:

Docetaxel (as trihydrate)…….....……..…20mg

(USP Specifications)

Dotaxol Injection 80mg/2ml

Each 2ml contains:

Docetaxel (as trihydrate)…….....……..…80mg

(USP Specifications)

Solvent:

Diluent for Dotaxol 20mg

Each vial contains:

Ethanol 95%.....13% v/v

Water for injection…….....…….87% v/v

(Innovator's Specification)

Diluent for Dotaxol 80mg

Each vial contains:

Ethanol 95%.....13% v/v

Water for injection…….....…….87% v/v

(Innovator's Specification)

DESCRIPTION

Docetaxel is an antineoplastic agent belonging to the taxoid family. It is prepared by semi synthesis beginning with a precursor extracted from the renewable needle biomass of yew plants.

Docetaxel is a clinically well-established anti-mitotic chemotherapy medication used mainly for the treatment of breast, ovarian, and non-small cell lung cancer. Docetaxel reversibly binds to tubulin with high affinity in a 1:1 stoichiometric ratio.

MECHANISM OF ACTION

Docetaxel is an antineoplastic agent that acts by disrupting the micro tubular network in cells that is essential for mitotic and interphase cellular functions. Docetaxel binds to free tubulin and promotes the assembly of tubulin into stable microtubules while simultaneously inhibiting their disassembly. This leads to the production of microtubule bundles without normal function and to the stabilization of microtubules, which results in the inhibition of mitosis in cells. Docetaxel's binding to microtubules does not alter the number of protofilaments in the bound microtubules, a feature which differs from most spindle poisons currently in clinical use.

INDICATIONS

Breast Cancer

Docetaxel injection concentrate is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.

Docetaxel injection concentrate in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.

Non-Small Cell Lung Cancer

Docetaxel injection concentrate as a single agent is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based chemotherapy.

Docetaxel injection concentrate in combination with cisplatin is indicated for the treatment of patients with unrespectable, locally advanced or metastatic non-small cell lung cancer who have not previously received chemotherapy for this condition.

Prostate Cancer

Docetaxel injection concentrate in combination with prednisone is indicated for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.

Gastric Adenocarcinoma

Docetaxel injection concentrate in combination with cisplatin and fluorouracil is indicated for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.

Head and Neck Cancer

Docetaxel injection concentrate in combination with cisplatin and fluorouracil is indicated for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN).

DOSAGE & ADMINISTRATION

For all indications, toxicities may warrant dosage adjustments. Administer in a facility equipped to manage possible complications (e.g. anaphylaxis).

Breast Cancer

For locally advanced or metastatic breast cancer after failure of prior chemotherapy, the recommended dose of docetaxel injection concentrate is 60 mg/m^2 to 100 mg/m^2 administered intravenously over 1 hour every 3 weeks.

For the adjuvant treatment of operable node-positive breast cancer, the recommended docetaxel injection concentrate dose is 75 mg/m^2 administered 1 hour after doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 every 3 weeks for 6 courses. Prophylactic G-CSF may be used to mitigate the risk of hematological toxicities.

Non-Small Cell Lung Cancer

For treatment after failure of prior platinum-based chemotherapy, docetaxel injection concentrate was evaluated as monotherapy, and the recommended dose is 75 mg/m^2 administered. intravenously over 1 hour every 3 weeks. A dose of 100 mg/m^2 in patients previously treated with chemotherapy was associated with increased hematologic toxicity, infection, and treatment-related mortality in randomized, controlled trials.

For chemotherapy-naïve patients, docetaxel injection concentrate was evaluated in combination with cisplatin. The recommended dose of docetaxel injection concentrate is 75 mg/m^2 administered intravenously over 1 hour immediately followed by cisplatin 75 mg/m^2 over 30 to 60 minutes every 3 weeks.

Prostate Cancer

For hormone-refractory metastatic prostate cancer, the recommended dose of docetaxel injection concentrate is 75 mg/m^2 every 3 weeks as a 1 hour intravenous infusion. Prednisone 5 mg orally twice daily is administered continuously.

Gastric Adenocarcinoma

For gastric adenocarcinoma, the recommended dose of docetaxel injection concentrate is 75mg/m^2 as a 1 hour intravenous infusion, followed by cisplatin 75 mg/m^2, as a 1 to 3 hour intravenous infusion (both on day 1 only), followed by fluorouracil 750 mg/m^2 per day given as a 24-hour continuous intravenous infusion for 5 days, starting at the end of the cisplatin infusion. Treatment is repeated every three weeks. Patients must receive premedication with anti-emetics and appropriate hydration for cisplatin administration.

Head and Neck Cancer

Patients must receive premedication with anti-emetics, and appropriate hydration (prior to and after cisplatin administration). Prophylaxis for neutropenic infections should be administered. All patients treated on the docetaxel injection concentrate containing arms of the TAX323 and TAX324 studies received prophylactic antibiotics.

Induction chemotherapy followed by radiotherapy (TAX323)

For the induction treatment of locally advanced inoperable SCCHN, the recommended dose of docetaxel injection concentrate is 75 mg/m^2 as a 1 hour intravenous infusion followed by cisplatin 75 mg/m^2 intravenously over 1 hour, on day one, followed by fluorouracil as a continuous intravenous infusion at 750 mg/m^2 per day for five days. This regimen is

administered every 3 weeks for 4 cycles. Following chemotherapy, patients should receive radiotherapy.

Induction chemotherapy followed by chemo radiotherapy (TAX324)

For the induction treatment of patients with locally advanced (unresectable, low surgical cure, or organ preservation) SCCHN, the recommended dose of docetaxel injection concentrate is 75 mg/m^2 as a 1 hour intravenous infusion on day 1, followed by cisplatin 100 mg/m^2 administered as a 30-minute to 3 hour infusion, followed by fluorouracil 1000 mg/m^2/day as a continuous infusion from day 1 to day 4. This regimen is administered every 3 weeks for 3 cycles. Following chemotherapy, patients should receive chemo radiotherapy.

Premedication Regimen

All patients should be pre-medicated with oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg twice daily) for 3 days starting 1 day prior to docetaxel injection concentrate administration in order to reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions.

For hormone-refractory metastatic prostate cancer, given the concurrent use of prednisone, the recommended premedication regimen is oral dexamethasone 8 mg, at 12 hours, 3 hours and 1 hour before the docetaxel injection concentrate infusion.

PHARMACODYNAMICS

Docetaxel was found to be cytotoxic in vitro against various murine and human tumor cell lines and against freshly excised human tumor cells in clonogenic assays.Docetaxel achieves high intracellular concentrations with a long cell residence time. In addition, docetaxel was found to be active on some but not all cell lines overexpressing the p-glycoprotein which is encoded by the multidrug resistance gene. In vivo, docetaxel is schedule independent and has a broad spectrum of experimental antitumor activity against advanced murine and human grafted tumors.

PHARMACOKINETICS

Absorption: The pharmacokinetics of docetaxel have been evaluated in cancer patients after administration of 20 mg/m^2 to 115 mg/m^2 in phase 1 studies. The area under the curve (AUC) was dose proportional following doses of 70 mg/m^2 to 115 mg/m^2 with infusion times of 1 to 2 hours. Docetaxel's pharmacokinetic profile is consistent with a three-compartment pharmacokinetic model, with half-lives for the α, β, and γ phases of 4 min, 36 min, and 11.1 hr. respectively. Mean total body clearance was 21 L/h/m^2.

Distribution: The initial rapid decline represents distribution to the peripheral compartments and the late (terminal) phase is due, in part, to a relatively slow efflux of docetaxel from the peripheral compartment. Mean steady state volume of distribution was 113 L. In vitro studies showed that docetaxel is about 94% protein bound, mainly to α1-acid glycoprotein, albumin, and lipoproteins. In three cancer patients, the in vitro binding to plasma proteins was found to be approximately 97%. Dexamethasone does not affect the protein binding of docetaxel.

Metabolism: In vitro drug interaction studies revealed that docetaxel is metabolized by the CYP3A4 iso-enzyme, and its metabolism may be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 3A4.

Elimination: A study of ^{14}C-docetaxel was conducted in three cancer patients. Docetaxel was eliminated in both the urine and feces following oxidative metabolism of the tert-butyl ester group, but fecal excretion was the main elimination route. Within 7 days, urinary and fecal excretion accounted for approximately 6% and 75% of the administered radioactivity, respectively. About 80% of the radioactivity recovered in feces is excreted during the first 48 hours as 1 major and 3 minor metabolites with very small amounts (less than 8%) of unchanged drug.

WARNINGS AND PRECAUTIONS

Toxic Deaths

Breast Cancer: Docetaxel injection concentrate administered at 100 mg/m^2 was associated with deaths considered possibly or probably related to treatment in 2.0% of metastatic breast cancer patients, both previously treated and untreated, with normal baseline liver function and in 11.5% of patients with various tumor types who had abnormal baseline liver function (AST and/or ALT >1.5 times ULN together with AP >2.5 times ULN). Among patients dosed at 60 mg/m^2, mortality related to treatment occurred in 0.6% of patients with normal liver function, and in 3 of 7 patients with abnormal liver function. Approximately half of these deaths occurred during the first cycle. Sepsis accounted for the majority of the deaths.

Non-Small Cell Lung Cancer : Docetaxel injection concentrate administered at a dose of 100 mg/m^2 in patients with locally advanced or metastatic non-small cell lung cancer who had a history of prior platinum-based chemotherapy was associated with increased treatment-related mortality (14% and 5% in two randomized, controlled studies). There were 2.8% treatment-related deaths among the 176 patients treated at the 75 mg/m^2 dose in the randomized trials. Among patients who experienced treatment-related mortality at the 75 mg/m^2 dose level, 3 of 5 patients had an ECOG PS of 2 at study entry.

Hepatic Impairment

Patients with combined abnormalities of transaminases and alkaline phosphatase should not be treated with docetaxel injection concentrate.

Hematologic Effects

Perform frequent peripheral blood cell counts on all patients receiving docetaxel injection concentrate. Patients should not be retreated with subsequent cycles of docetaxel injection concentrate until neutrophils recover to a level >1500 cells/mm^3 and platelets recover to a level > 100,000 cells/mm^3. A 25% reduction in the dose of docetaxel injection concentrate is recommended during subsequent cycles following severe neutropenia (<500 cells/mm^3) lasting 7 days or more, febrile neutropenia, or a grade 4 infection in a docetaxel injection concentrate cycle. Neutropenia (<2000 neutrophils/mm^3) occurs in virtually all patients given 60 mg/m^2 to 100 mg/m^2 of docetaxel injection concentrate and grade 4 neutropenia (<500 cells/mm^3) occurs in 85% of patients given 100 mg/m^2 and 75% of patients given 60 mg/m^2. Frequent monitoring of blood counts is, therefore, essential so that dose can be adjusted. Docetaxel injection concentrate should not be administered to patients with neutrophils <1500 cells/mm^3. Febrile neutropenia occurred in about 12% of patients given 100 mg/m^2 but was very uncommon in patients given 60 mg/m^2. Hematologic responses, febrile reactions and infections, and rates of septic death for different regimens are dose related.

Three breast cancer patients with severe liver impairment (bilirubin >1.7 times ULN) developed fatal gastrointestinal bleeding associated with severe drug-induced thrombocytopenia. In gastric cancer patients treated with docetaxel in combination with cisplatin and fluorouracil, febrile neutropenia and/or neutropenic infection occurred in 12% of patients receiving G-CSF compared to 28% who did not. Patients receiving this regime should be closely monitored during the first and subsequent cycles for febrile neutropenia and neutropenic infection.

Hypersensitivity Reactions

Patients should be observed closely for hypersensitivity reactions, especially during the first and second infusions. Severe hypersensitivity reactions characterized by generalized rash/erythema, hypotension and/or bronchospasm, or very rarely fatal anaphylaxis, have been reported in patients pre-medicated with 3 days of corticosteroids. Severe hypersensitivity reactions require immediate discontinuation of the docetaxel injection concentrate infusion and aggressive therapy. Patients with a history of severe hypersensitivity reactions should not be rechallenged with docetaxel injection concentrate. Hypersensitivity reactions may occur within a few minutes following initiation of a docetaxel injection concentrate infusion. If minor reactions such as flushing or localized skin reactions occur, interruption of therapy is not required. All patients should be pre-medicated with an oral corticosteroid prior to the initiation of the infusion of docetaxel injection concentrate.

Fluid Retention

Severe fluid retention has been reported following docetaxel injection concentrate therapy. Patients should be pre-medicated with oral corticosteroids prior to each docetaxel injection concentrate administration to reduce the incidence and severity of fluid retention. Patients with pre-existing effusions should be closely monitored from the first dose for the possible exacerbation of the effusions. When fluid retention occurs, peripheral edema usually starts in the lower extremities and may become generalized with a median weight gain of 2 kg. Among 92 breast cancer patients pre-medicated with 3-day

corticosteroids, moderate fluid retention occurred in 27.2% and severe fluid retention in 6.5%. The median cumulative dose to onset of moderate or severe fluid retention was 819 mg/m^2. Nine of 92 patients (9.8%) of patients discontinued treatment due to fluid retention; 4 patients discontinued with severe fluid retention; the remaining 5 had mild or moderate fluid retention. The median cumulative dose to treatment discontinuation due to fluid retention was 1021 mg/m^2. Fluid retention was completely, but sometimes slowly, reversible with a median of 16 weeks from the last infusion of docetaxel injection concentrate to resolution (range: 0 to 42+ weeks). Patients developing peripheral edema may be treated with standard measures, e.g., salt restriction, oral diuretic.

Acute Myeloid Leukemia

Treatment-related acute myeloid leukemia (AML) or myelodysplasia has occurred in patients given anthracyclines and/or cyclophosphamide, including use in adjuvant therapy for breast cancer. In the adjuvant breast cancer trial AML occurred in 3 of 744 patients who received docetaxel injection concentrate,doxorubicin and cyclophosphamide and in 1 of 736 patients who received fluorouracil, doxorubicin and cyclophosphamide. In these patients, the risk of delayed myelodysplasia or myeloid leukemia requires hematological follow-up.

Cutaneous Reactions

Localized erythema of the extremities with edema followed by desquamation has been observed. In case of severe skin toxicity, an adjustment in dosage is recommended .The discontinuation rate due to skin toxicity was 1.6% for metastatic breast cancer patients. Among 92 breast cancer patients pre-medicated with 3-day corticosteroids, there were no cases of severe skin toxicity reported and no patient discontinued docetaxel injection concentrate due to skin toxicity.

Neurologic Reactions

Severe neurosensory symptoms (e.g. paresthesia, dysesthesia, pain) were observed in 5.5% of metastatic breast cancer patients, and resulted in treatment discontinuation in 6.1%. When these symptoms occur, dosage must be adjusted. If symptoms persist, treatment should be discontinued. Patients who experienced neurotoxicity in clinical trials and for whom follow-up information on the complete resolution of the event was available had spontaneous reversal of symptoms with a median of 9 weeks from onset (range: 0 to 106 weeks). Severe peripheral motor neuropathy mainly manifested as distal extremity weakness occurred in 4.4%.

Asthenia

Severe asthenia has been reported in 14.9% of metastatic breast cancer patients but has led to treatment discontinuation in only 1.8%. Symptoms of fatigue and weakness may last a few days up to several weeks and may be associated with deterioration of performance status in patients with progressive disease.

Use in Pregnancy

Pregnancy Category D

Docetaxel injection concentrate can cause fetal harm when administered to a pregnant woman. Docetaxel caused embryo fetal toxicities including intrauterine mortality when administered to pregnant rats and rabbits during the period of organogenesis. Embryo fetal effects in animals occurred at doses as low as 1/50 and 1/300 the recommended human dose on a body surface area basis. There are no adequate and well-controlled studies in pregnant women using docetaxel injection concentrate. If docetaxel injection concentrate is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant during therapy with docetaxel injection concentrate.

Nursing Mothers

It is not known whether docetaxel is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from docetaxel injection concentrate, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

SIDE EFFECTS

The most common adverse reactions across all docetaxel injection concentrate indications are infections, neutropenia, anemia, febrile neutropenia, hypersensitivity, thrombocytopenia, neuropathy, dysgeusia, dyspnea, constipation, anorexia, nail disorders, fluid retention, asthenia, pain, nausea, diarrhea, vomiting, mucositis, alopecia, skin reactions, and myalgia. Incidence varies depending on the indication.

Immune system disorders

Hypersensitivity reactions have generally occurred within a few minutes following the start of the infusion of docetaxel and were usually mild to moderate. The most frequently reported symptoms were flushing, rash with or without pruritus, chest tightness, back pain, dyspnea and fever or chills. Severe reactions were characterised by hypotension and/or bronchospasm or generalized rash/erythema.

Nervous system disorders

The development of severe peripheral neurotoxicity requires a reduction of dose. Mild to moderate neuro-sensory signs are characterised by paranesthesia, dysesthesia or pain including burning. Neuro-motor events are mainly characterised by weakness.

Skin and subcutaneous tissue disorders

Reversible cutaneous reactions have been observed and were generally considered as mild to moderate. Reactions were characterised by a rash including localized eruptions mainly on the feet and hands (including severe hand and foot syndrome), but also on the arms, face or thorax, and frequently associated with pruritus. Eruptions generally occurred within one week after the docetaxel infusion. Less frequently, severe symptoms such as eruptions followed by desquamation which rarely lead to interruption or discontinuation of docetaxel treatment were reported. Severe nail disorders are characterised by hypo- or hyperpigmentation and sometimes pain and onycholysis.

General disorders and administration site conditions

Infusion site reactions were generally mild and consisted of hyperpigmentation, inflammation, redness or dryness of the skin, phlebitis or extravasation and swelling of the vein.

Fluid retention includes events such as peripheral edema and less frequently pleural effusion, pericardial effusion, ascites and weight gain. The peripheral edema usually starts at the lower extremities and may become generalized with a weight gain of 3 kg or more. Fluid retention is cumulative in incidence and severity.

Gastrointestinal Reactions

Nausea, vomiting, and diarrhea were generally mild to moderate. Severe reactions occurred in 3 to 5% of patients with solid tumors and to a similar extent among metastatic breast cancer patients. The incidence of severe reactions was 1% or less for the 92 breast cancer patients pre-medicated with 3-day corticosteroids.

Cardiovascular Reactions

Hypotension occurred in 2.8% of patients with solid tumors; 1.2% required treatment. Clinically meaningful events such as heart failure, sinus tachycardia, atrial flutter, dysrhythmia, unstable angina, pulmonary edema, and hypertension occurred rarely. Seven of 86 (8.1%) of metastatic breast cancer patients receiving docetaxel injection concentrate 100 mg/m^2 in a randomized trial and who had serial left ventricular ejection fractions assessed developed deterioration of LVEF by $\geqslant$10% associated with a drop below the institutional lower limit of normal.

Hepatic Reactions

In patients with normal LFTs at baseline, bilirubin values greater than the ULN occurred in 8.9% of patients. Increases in AST or ALT >1.5 times the ULN, or alkaline phosphatase >2.5 times ULN, were observed in 18.9% and 7.3% of patients, respectively. While on docetaxel injection concentrate, increases in AST and/or ALT >1.5 times ULN concomitant with alkaline phosphatase >2.5 times ULN occurred in 4.3% of patients with normal LFTs at baseline. Whether these changes were related to the drug or underlying disease has not been established.

Post-Marketing Experiences

The following adverse reactions have been identified from clinical trials and/or post-marketing surveillance. Because they are reported from a

population of unknown size, precise estimates of frequency cannot be made.

Body as a whole: diffuse pain, chest pain, radiation recall phenomenon.

Cardiovascular: atrial fibrillation, deep vein thrombosis, ECG abnormalities, thrombophlebitis, pulmonary embolism, syncope, tachycardia, myocardial infarction.

Cutaneous: very rare cases of cutaneous lupus erythematosus and rare cases of bullous eruptions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and Scleroderma-like changes usually preceded by peripheral lymphedema. In some cases multiple factors may have contributed to the development of these effects. Severe hand and foot syndrome has been reported.

Gastrointestinal: abdominal pain, anorexia, constipation, duodenal ulcer, esophagitis, gastrointestinal hemorrhage, gastrointestinal perforation, ischemic colitis, colitis, intestinal obstruction, ileus, neutropenic enterocolitis and dehydration as a consequence to gastrointestinal events have been reported.

Hematologic: bleeding episodes. Disseminated intravascular coagulation (DIC), often in association with sepsis or multi-organ failure, has been reported.Cases of acute myeloid leukemia and myelodysplasic syndrome have been reported in association with docetaxel injection concentrate when used in combination with other chemotherapy agents and/or radiotherapy.

Hypersensitivity: rare cases of anaphylactic shock have been reported. Very rarely these cases resulted in a fatal outcome in patients who received premedication.

Hepatic: rare cases of hepatitis, sometimes fatal primarily in patients with pre-existing liver disorders, have been reported.

Neurologic: confusion, rare cases of seizures or transient loss of consciousness have been observed, sometimes appearing during the infusion of the drug.

Ophthalmologic: conjunctivitis, lacrimation or lacrimation with or without conjunctivitis. Excessive tearing which may be attributable to lacrimal duct obstruction has been reported. Rare cases of transient visual disturbances (flashes, flashing lights, scotomata) typically occurring during drug infusion and in association with hypersensitivity reactions have been reported. These were reversible upon discontinuation of the infusion.

Hearing: rare cases of ototoxicity, hearing disorders and/or hearing loss have been reported, including cases associated with other ototoxic drugs.

Respiratory: dyspnea, acute pulmonary edema, acute respiratory distress syndrome, interstitial pneumonia. Pulmonary fibrosis has been rarely reported. Rare cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy.

Renal: renal insufficiency and renal failure have been reported, the majority of these cases were associated with concomitant nephrotoxic drugs.

DRUG INTERACTIONS

• Docetaxel is a CYP3A4 substrate. *In vitro* studies have shown that the metabolism of docetaxel may be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 3A4.

• *In vivo* studies showed that the exposure of docetaxel increased 2.2-fold when it was co-administered with ketoconazole, a potent inhibitor of CYP3A4. Protease inhibitors, particularly ritonavir, may increase the exposure of docetaxel. Concomitant use of docetaxel injection concentrate and drugs that inhibit CYP3A4 may increase exposure to docetaxel and should be avoided. In patients receiving treatment with docetaxel injection concentrate, close monitoring for toxicity and a docetaxel injection, dose reduction could be considered if systemic administration of a potent CYP3A4 inhibitor cannot be avoided.

• Docetaxel pharmacokinetics in the presence of prednisone was studied in patients with metastatic prostate cancer. Docetaxel is metabolised by CYP3A4 and prednisone is known to induce CYP3A4. No statistically significant effect of prednisone on the pharmacokinetics of docetaxel was observed. Docetaxel is highly protein bound (>95%). Although the possible in vivo interaction of docetaxel with concomitantly administered medicinal product has not been investigated formally, in vitro interactions with tightly protein-bound agents such as erythromycin, diphenhydramine, propranolol, propafenone, phenytoin, salicylate, sulfamethoxazole and sodium valproate did not affect protein binding of docetaxel. In addition, dexamethasone did not affect protein binding of docetaxel. Docetaxel did not influence the binding of digitoxin.

• The pharmacokinetics of docetaxel,doxorubicin and cyclophosphamide were not influenced by their co-administration. Limited data from a single uncontrolled study were suggestive of an interaction between docetaxel and carboplatin. When combined to docetaxel, the clearance of carboplatin was about 50% higher than values previously reported for carboplatin monotherapy.

OVERDOSE

There is no known antidote for docetaxel injection concentrate over dosage. In case of over dosage, the patient should be kept in a specialized unit where vital functions can be closely monitored. Anticipated complications of over dosage include: bone marrow suppression, peripheral neurotoxicity, and mucositis. Patients should receive therapeutic G-CSF as soon as possible after discovery of overdose. Other appropriate symptomatic measures should be taken, as needed.

CONTRAINDICATIONS

•Docetaxel injection concentrate is contraindicated in patients who have a history of severe hypersensitivity reactions to docetaxel or to other drugs formulated with polysorbate 80. Severe reactions, including anaphylaxis, have occurred.

•Docetaxel injection concentrate should not be used in patients with neutrophil counts of <1500 cells/mm^3

STORAGE & INSTRUCTIONS

Store between 2-25°C.

Protect from heat, sunlight and moisture. Do not freeze.

Keep away from the reach of children.

To be sold on the prescription of a registered oncologist or on demand from cancer hospitals and institutions only.

HOW SUPPLIED

Dotaxol Injection 20mg/0.5ml

1 vial + solvent for Dotaxol 20mg (1.5ml)

Dotaxol Injection 80mg/2ml

1 vial + solvent for Dotaxol 80mg (6ml)

ہدایات:

دوا کو ۲-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔

دھوپ، گرمی، نمی سے محفوظ اور منجمد ہونے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند اونکولوجسٹ یا کینسر ہسپتال کے نسخہ پر فروخت کریں۔

Manufactured by:

PHARMASOL

PRIVATE LIMITED

Plot # 549,Sundar Industrial Estate,

Lahore, Pakistan.