Docetor® IV injection

Docetaxel USP Injection

DESCRIPTION

Docetor® IV injection is a preparation of Docetaxel. Docetaxel is an antineoplastic agent, which acts by disrupting the microtubular network in cells that is essential for vital mitotic and interphase cellular functions. Docetaxel promotes the assembly of tubulin into stable microtubules while simultaneously inhibiting their disassembly. Docetaxel binds to free tubulin thereby decreasing the critical intracellular concentration of tubulin. The promoted polymerization of microtubules leads to the production of microtubule bundles without normal function and to the stabilization of microtubules, resulting in the inhibition of mitosis in cells. The binding of Docetaxel to microtubules does not alter the number of protofilaments in the bound microtubules; in that, it differs from other spindle poisons.

INDICATIONS

- **Breast Cancer:** Docetaxel 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 is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer in monotherapy or in combination with platinum derivatives.
- **Ovarian Cancer:** Docetaxel is indicated for the treatment of metastatic carcinoma of the ovary after failure of first-line or subsequent chemotherapy.
- **Prostate Cancer:** Docetaxel in combination with prednisone or prednisolone is indicated for the treatment of patients with androgen-independent (hormone-refractory) metastatic prostate cancer.
- **Squamous Cell Carcinoma of the Head and Neck:** Docetaxel is indicated as monotherapy in the treatment of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck after failure of a previous chemotherapy regimen.

DOSAGE AND ADMINISTRATION

Recommended Dose-

- **Metastatic Breast Cancer, Non-Small Cell Lung Cancer, Ovarian Cancer, and Squamous Cell Carcinoma of the Head and Neck:** The recommended dosage is 100 mg/m2 administered as a one-hour infusion every 3 weeks. When used in combination, Docetaxel is administered at the recommended dosage of 75 mg/m2.
- **Prostate Cancer:** The recommended dosage is 75 mg/m2 administered as a one-hour infusion every 3 weeks. Concomitant treatment with prednisone or prednisolone 5 mg orally twice daily is administered continuously.
- Adjuvant Treatment of Operable Node-Positive Breast Cancer: The dose is 75 mg/m2 administered 1 hour after doxorubicin 50 mg/m2 and cyclophosphamide 500 mg/m2 every 3 weeks for 6 courses.

Premedication-

- **Premedication Regimen:** In order to reduce the incidence and severity of fluid retention, all patients should be pretreated with oral corticosteroids. The recommended premedication should consist only of oral corticosteroids, such as dexamethasone 16 mg per day (e.g. 8 mg BID), for 3 days starting one day prior to each Docetaxel administration. Antihistamines have not been shown to be useful in controlling fluid retention.
- **Premedication Regimen for Prostate Cancer:** For prostate cancer, given the concurrent use of prednisone or prednisolone, the recommended premedication regimen is oral dexamethasone 8 mg at 12 hours, 3 hours and 1 hour before the Docetaxel infusion.

Other Dosing Considerations-

- **Prophylactic Use of Antibiotics:** In order to reduce the incidence of febrile neutropenia and infections, the prophylactic use of antibiotics is recommended for patients treated for head and neck cancer. The treatment should consist of oral fluoroquinolone antibiotics, or equivalent oral or intravenous antibiotics, for 10 days starting on day 5 of each cycle of Docetaxel Injection USP administration.
- **Prophylactic Use of Granulocyte-Colony Stimulating Factor (G-CSF):** Prophylactic G-CSF may be used to mitigate the risk of hematological toxicities. In addition to G-CSF, the prophylactic use of antibiotics may provide additional benefit.
- **Geriatrics:** Based on the population pharmacokinetics, there are no special instructions for the use in the elderly.

Administration-

Precautions: Docetaxel must be administered intravenously. It is extremely important that the intravenous needle or catheter be properly positioned before any Docetaxel is injected. Leakage into surrounding tissue during intravenous administration of

Docetaxel may cause considerable irritation, local tissue necrosis and/or thrombophlebitis. If extravasation occurs, the injection should be discontinued immediately, and any remaining portion of the dose should be introduced into another vein.

Docetaxel solution must be diluted directly in 0.9% Sodium chloride solution or 5% dextrose solution prior to administration.

Preparation of the Infusion Solution-

- If the vials are stored under refrigeration, allow the required number of Docetaxel vials to stand at room temperature for approximately 5 minutes.
- Aseptically withdraw the required amount of Docetaxel (10 mg/mL) with a calibrated syringe and inject the required volume into a 250 mL infusion bag or bottle of either 0.9% Sodium Chloride solution or 5% Dextrose solution to produce a final concentration of 0.3 to 0.74 mg/mL.
- Thoroughly mix the infusion by manual rotation, until a clear homogenous solution is obtained.
- As with all parenteral products, Docetaxel should be inspected visually for particulate matter or discoloration prior to administration whenever the solution and container permit. If it is not clear or appears to have precipitation, the solution should be discarded. Discard unused portion.

Dosing Adjustment-

- **Patients with Neutropenia, Cutaneous Reactions or Peripheral Neuropathy:** Careful monitoring of neutrophil counts is an essential part of Docetaxel therapy. Docetaxel should not be administered until the neutrophil count is at least 1,500 cells/ mm^3. Patients who experience either febrile neutropenia, severe neutropenia (neutrophil <500 cells/mm^3 for more than one week), severe or cumulative cutaneous reaction, or severe neurosensory signs and/or sympt during Docetaxel therapy should have their dosage of Docetaxel reduced from 100 mg/m^2 to 75 mg/m^2. When Docetaxel is given in combination, the dose of Docetaxel should be reduced from 75 mg/m^2 to 60 mg/m^2. If the patient continues to experience these reactions at 60 mg/ m^2, the treatment should be discontinued. Alternatively, prophylactic G-CSF may be used in patients with either prior febrile neutropenia or severe infection in order to maintain dose intensity.
- **Patients with Hepatic Impairment:** Docetaxel Injection USP should not be used in patients with serum bilirubin > ULN. Also, Docetaxel Injection USP should not be used in patients who have ALT and/or AST > 1.5 x ULN concomitant with alkaline phosphatase > 2.5 x ULN.
- **Concomitant use with a potent CYP3A4 inhibitor:** if systemic administration of a potent CYP3A4 inhibitor cannot be avoided, a dose reduction of Docetaxel Injection USP should be considered and close monitoring for toxicity is recommended.

Docetaxel Injection USP in Combination with Capecitabine-

	Grade 2	Grade 3	Grade 4
1st appearance	Interrupt treatment until resolved to grade 0-1 then continue at same doses with prophylaxis where possible.	Grade 3 at time Docetaxel treatment due: interrupt treatment and delay for a maximum of two weeks until grade 0-1 then continue at 75% of original Capecitabine dose and at 55 mg/m^2 of Docetaxel with prophylaxis where possible. If no recovery to grade 0-1 within two weeks delay, patient will stop Docetaxel therapy but may restart Capecitabine at 75% of original Capecitabine dose when grade 0-1. Grade 3 occurring between cycles with recovery to grade 0-1 by the time the next treatment due: continue at 75% of original Capecitabine dose and at 55 mg/m^2 of Docetaxel with prophylaxis where possible.	Discontinue Capecitabine and Docetaxel treatment unless treating physician considers it to be in the best interest of the patient to continue with Capecitabine monotherapy at 50% of original dose.
2nd appearance of same toxicity	Interrupt treatment until resolved to grade 0-1, then continue at 75% of original Capecitabine dose and at 55 mg/m2 of Docetaxel.	Discontinue Docetaxel Injection USP treatment and interrupt Capecitabine treatment until resolved to grade 0-1, then continue at 50% of original Capecitabine dose.	
3rd appearance of same toxicity	Interrupt treatment until resolved to grade 0-1, then continue at 50% of original Capecitabine dose and discontinue Docetaxel.	Discontinue treatment.	
4th appearance of same toxicity	Discontinue treatment.		

CONTRAINDICATIONS

- Hypersensitivity
- Patients with baseline neutrophil counts of < 1,500 cells/mm3

SIDE EFFECTS

- Neutropenia, thrombocytopenia, anemia
- Nausea, diarrhea, stomatitis

WARNING AND PRECAUTION

Docetaxel should be given under the supervision of a doctor experienced in the use of anticancer drugs. There is a higher risk of developing severe adverse reactions, which may be life-threatening, in patients with liver disease. Docetaxel should not be used if you have liver disease. Docetaxel should not be used if you have a white blood cell (neutrophil) count of less than 1,500 cells/mm3. Docetaxel may cause severe allergic reactions which require you to immediately stop taking the treatment. A possible serious side effect that may occur is acute myeloid leukemia. No studies have been conducted to find out if Docetaxel could cause cancer.

USE IN PREGNANCY AND LACTATION

Therefore, Docetaxel must not be used during pregnancy. Women of childbearing age and receiving Docetaxel should be advised to avoid becoming pregnant, and to inform the treating physician immediately should this occur. Should Docetaxel be 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.

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, breastfeeding must be discontinued during Docetaxel therapy.

PHARMACEUTICAL PRECAUTION

(Will be confirmed later)

PACKAGING

Docetor® IV injection

SK+F ONCOLOGY

Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
RUPGANJ, NARAYANGANJ, BANGLADESH
® REGD. TRADEMARK
R/PM0533 V01