Docetor™ IV Injection

Docetaxel Injection USP

DESCRIPTION

Docetor™ IV injection is a preparation of Docetaxel Trihydrate. 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; a feature which differs from other spindle poisons.

INDICATIONS

- **Breast Cancer: Docetor™** 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: Docetor™** 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: Docetor™** is indicated for the treatment of metastatic carcinoma of the ovary after failure of first-line or subsequent chemotherapy.
- **Prostate Cancer: Docetor™** 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: Docetor™** 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

Breast Cancer

- For locally advanced or metastatic breast cancer after failure of prior chemotherapy, the recommended dose of **Docetor™** 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 **Docetor™** dose is 75 mg/m^2 administered 1 hour after doxorubicin 50 mg/m^2 and cyclophosphamide 50 mg/m^2 every 3 weeks for 6 courses.

Non-small Cell Lung Cancer

Monotherapy with Docetor™ for NSCLC treatment after failure of prior Platinum based chemotherapy:

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.

Combination therapy of Docetor™ & Cisplatin in NSCLC treatment

The recommended dose of **Docetor™** is 75 mg/m^2 administered intravenously over 1 hour immediately followed by cisplatin 75 mg/m^2 over 30-60 minutes every 3 weeks.

Prostate Cancer

For metastatic castration-resistant prostate cancer, the recommended dose of **Docetor™** is 75 mg/m^2 every 3 weeks as a 1-hour intravenous infusion.

Gastric Adenocarcinoma

The recommended dose of **Docetor™** is 75 mg/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.

Head and Neck Cancer

Induction Chemotherapy followed by Radiotherapy: For the induction treatment of locally advanced inoperable Squamous cell carcinoma of head & neck, the recommended dose of **Docetor™** 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 5 days.

Induction Chemotherapy followed by Chemoradiotherapy: For the induction treatment of patients with locally advanced (unresectable, low surgical cure, or organ preservation) SCCHN, the recommended dose of **Docetor™** 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.

Dosage Adjustments during Treatment

Breast Cancer:

Patients who are dosed initially at 100 mg/m^2 and who experience either febrile neutropenia, neutrophils <500 cells/mm^3 for more than 1 week, or severe or cumulative cutaneous reactions during **Docetor™** therapy should have the dosage adjusted from 100 mg/m^2 to 75 mg/m^2, can be decreased upto to 55 mg/m^2 if the patient continues to experience these reactions, or the treatment should be discontinued.

Combination Therapy with Docetor™ in the Adjuvant Treatment of Breast Cancer:

Docetor™ in combination with doxorubicin and cyclophosphamide should be administered when the neutrophil count is ≥ 1,500 cells/mm^3. Patients who experience febrile neutropenia should receive G-CSF in all subsequent cycles and have their **Docetor™** dose reduced to 60 mg/m^2.

Non-small Cell Lung Cancer:

Monotherapy with Docetor™ for NSCLC treatment after failure of prior platinum-based chemotherapy:

Patients who are dosed initially at 75 mg/m^2 and who experience either febrile neutropenia, neutrophils <500 cells/mm^3 for more than one week, severe or cumulative cutaneous reactions, or other grade 3/4 non-hematological toxicities during **Docetor™** treatment should have treatment withheld until resolution of the toxicity and then resumed at 55 mg/m^2. Patients who develop ≥ grade 3 peripheral neuropathy should have **Docetor™** treatment discontinued entirely.

Prostate Cancer:

Docetor™ should be administered when the neutrophil count is ≥ 1,500 cells/mm^3. Patients who experience either febrile neutropenia, neutrophils <500 cells/mm^3 for more than one week, severe or cumulative cutaneous reactions or moderate neurosensory signs and/or symptoms during **Docetor™** therapy should have the dosage of **Docetor™** reduced from 75 mg/m^2 to 60 mg/m^2.

Gastric or Head and Neck Cancer:

Patients treated with **Docetor™** in combination with cisplatin and fluorouracil must receive antiemetics and appropriate hydration according to current institutional guidelines.

Recommended Dose Modifications for Toxicities in Patients Treated with Docetor™ in Combination with Cisplatin and Fluorouracil

Toxicity	Dosage adjustment
Diarrhea grade 3	First episode: Reduce fluorouracil dose by 20%. Second episode: Then reduce **Docetor™** dose by 20%.
Diarrhea grade 4	First episode: Reduce **Docetor™** and fluorouracil doses by 20%. Second episode: Discontinue treatment
Stomatitis/mucositis grade 3	First episode: Reduce fluorouracil dose by 20%. Second episode: Stop fluorouracil only, at all subsequent cycles. Third episode: Reduce **Docetor™** dose by 20%.
Stomatitis/mucositis grade 4	First episode: Stop fluorouracil only, at all subsequent cycles. Second episode: Reduce **Docetor™** dose by 20%.

CONTRAINDICATIONS

- Hypersensitivity to docetaxel or polysorbate 80
- Patients with baseline neutrophil counts of < 1,500 cells/mm^3

ADVERSE REACTION

Most common adverse reactions across all **Docetor™** 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.

WARNING AND PRECAUTION

- **Second primary malignancies:** In patients treated with **Docetor™** containing regimens, monitor for delayed AML, MDS, NHL, and renal cancer.
- **Cutaneous reactions:** Reactions including erythema of the extremities with edema followed by desquamation may occur. Severe cutaneous adverse reactions have been reported. Severe skin toxicity may require dose adjustment or permanent treatment discontinuation.
- **Neurologic reactions:** Reactions including paresthesia, dysesthesia, and pain may occur. Severe neurosensory symptoms require dose adjustment or discontinuation if persistent.
- **Eye disorders:** Cystoid macular edema (CME) has been reported and requires treatment discontinuation.
- **Asthenia:** Severe asthenia may occur and may require treatment discontinuation.
- **Embryo-fetal toxicity:** Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.
- **Alcohol content:** The alcohol content in a dose of **Docetor™** injection may affect the central nervous system. This may include impairment of a patient's ability to drive or use machines immediately after infusion.

USE IN PREGNANCY & LACTATIONS

Docetor™ can cause fetal harm when administered to a pregnant woman. **Docetor™** contains alcohol which can interfere with neurobehavioral development. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with **Docetor™** and for 1 week after the last dose.

PHARMACEUTICAL PRECAUTIONS

Do not store above 25 °C temperature. Keep away from light & wet place. Keep out of reach of children.

PREPARATION FOR INTRAVENOUS INFUSION

Docetor™ injection requires no prior dilution with diluent and is ready to add to the infusion solution.

1. **Docetor™** vials should not be stored above 25 °C temperature. If the vials are stored under refrigeration, allow the appropriate number of vials of **Docetor™** injection vials to stand at room temperature for approximately 5 minutes before use.
2. Using only a 21 gauge needle, aseptically withdraw the required amount of **Docetor™** injection (20 mg docetaxel/mL) with a calibrated syringe and inject via a single injection (one shot) 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 mg/mL to 0.74 mg/mL. If a dose greater than 200 mg of **Docetor™** is required, use a larger volume of the infusion vehicle so that a concentration of 0.74 mg/mL **Docetor™** is not exceeded.
3. Thoroughly mix the infusion by gentle manual rotation.
4. As with all parenteral products, **Docetor™** should be inspected visually for particulate matter or discoloration prior to administration whenever the solution and container permit. If the **Docetor™** dilution for intravenous infusion is not clear or appears to have precipitation, it should be discarded.
5. **Docetor™** infusion solution is supersaturated, therefore may crystallize over time. If crystals appear, the solution must no longer be used and shall be discarded. The **Docetor™** dilution for infusion should be administered intravenously as a 1-hour infusion under ambient room temperature (below 25 °C) and lighting conditions.

STABILITY

Docetor™ final dilution for infusion, if stored between 2 °C and 25°C (36 °F and 77 °F) is stable for 6 hours. **Docetor™** final dilution for infusion (in either 0.9% Sodium Chloride solution or 5% Dextrose solution) should be used within 6 hours (including the 1 hour intravenous administration).

PRECAUTIONS FOR SAFE HANDLING AND DISPOSAL

Product should be used in a controlled work area and with adequate ventilation. To minimize hazards from accidental breakage or spills of containers and to simplify clean-up, product should be stored and transported within secondary containers, pans or trays. Disposable protective coatings and/or barrier sheeting should be used in areas where possibility of spillage exists to simplify cleanup. Hands should be washed thoroughly after handling. Disposal should be in accordance with applicable regional, national and local laws and regulations. Wastes should be double contained (e.g. double sealed bags) and labeled indicating contents to ensure safe handling and disposal. Incineration of waste product is recommended.

PACKAGING

Docetor™ 20 IV Injection: Each box contains one single-dose vial of Docetaxel Trihydrate USP equivalent to Docetaxel 20 mg/1 mL injection.

Docetor™ 80 IV Injection: Each box contains one single-dose vial of Docetaxel Trihydrate USP equivalent to Docetaxel 80 mg/4 mL injection.

SK+F ONCOLOGY

Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
RUPGANJ, NARAYANGANJ, BANGLADESH
TM TRADEMARK
R/PM0839 V01