# Doxel


## Doxel 20 mg vial containing concentrated solution for IV infusion
## Doxel 40 mg vial containing concentrated solution for IV infusion
## Doxel 80 mg vial containing concentrated solution for IV infusion
## Doxel 160 mg vial containing concentrated solution for IV infusion

**COMPOSITION:** Each vial containing concentrated solution contains 20 mg, 40 mg, 80 mg and 160 mg docetaxel. It contains pre-mix solution to give a vial containing concentrated solution for Doxel 20 mg IV infusion (40 mg/mL) , a vial containing concentrated solution for Doxel 40 mg IV infusion (40 mg/mL), a vial containing concentrated solution for Doxel 80 mg IV infusion (40 mg/mL) and a vial containing concentrated solution for Doxel 160 mg IV infusion (40 mg/mL) and diluent vial containing Ethanol (96 % v/v).

**PHARMACOLOGICAL PROPERTIES:** Docetaxel is a taxan group antineoplastic agent which shows its effect by disrupting the microtubular cycle which is required for vital mitotic and interphase cellular functions.

**INDICATIONS:** Doxel is indicated, in combination with doxorubicin and cyclophosphamide administered concomitantly, in adjuvant therapy of patients with operable node-positive breast cancer; in combination with doxorubicin as first-line therapy in patients who have not received cytotoxic therapy previously and who have locally advanced or metastatic breast cancer; patients with locally advanced or metastatic breast cancer in whom the previous chemotherapy has failed, the previous chemotherapy should have included antracycline or alkyllizer; in combination with trastuzumab, in treatment of metastatic breast cancer patients who have excessive HER-2 tumors and who have not received previous chemotherapy for metastatic disease; in combination with capecytabine, in patients with locally advanced or metastatic breast cancer in whom the previous cytotoxic chemotherapy has failed; the previous treatment should have included antracycline; in patients with locally advanced or metastatic non-small cell lung carcinoma who have not responded to platinum-based therapy and in whom the previous chemotherapy has failed; in combination with cisplatin, patients with non-resectable locally advanced or metastatic non-small cell lung cancer and who have not received previous chemotherapy for this disease; in combination with prednisone or prednisolone, in treatment of hormon-refractor metastatic prostate cancer; and in patients with metastatic gastric adenocarcinoma including metastatic gastro-esophageal combination adenocarcinoma and who have not received previous chemotherapy for metastatic disease. It is used in combination with platinum group in treatment of locally advanced, recurrent and metastatic head neck cancers, in first line treatment of epithelial ovary cancers. Doxel is indicated in platinum-sensitive or platinum-refractor recurrent ovary cancers.

**CONTRAINDICATIONS:** In patients who have shown hypersensitivity to other drugs containing doxel or polysorbate 80, in patients with a neutrophyl count <1500 cells/mm3. Docetaxel should not be used in pregnant or lactating women. Since there is no data on this subject, docetaxel should not be used in patients with severe liver failure.

**WARNINGS AND PRECAUTIONS:** All patients should receive pre-treatment with corticosteroids such as dexamethasone to reduce fluid retension or the severity of hypersensitivity reactions. Neutropenia is the most frequent adverse effect of docetaxel therapy. Patients should not be given doxel treatment until the neutrophyl count reaches ? 1500 cells/mm$^3$.

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In cases of severe neutropenia during docetaxel treatment, dose should be reduced and appropriate symptomatic therapy should be administered.

Patients receiving TCF treatment should be given prophylactic G-CSF to alleviate the risk of neutropenic complications (febrile neutropenia, continuous neutropenia or neutropenic infection). In cases of mild reactions such as flushing or localized skin reactions, discontinuation of docetaxel therapy is not required. However, in severe reactions requiring treatment, Doxel infusion should be discontinued immediately and aggresive treatment should be initiated. It is reported that treatment should be discontiued or delayed when serious symptoms such as eruptions and then desquamations occur. Patients with serious fluid retension such as pleural effusion, pericardial effusion and ascitis should be closely monitored. In patients with high liver function test results (LFT), the recommended docetaxel dosage is 75 mg/m$^2$ and LFT should be evaluated at baseline and prior to each treatment cycle. In patients with bilirubin levels above normal and/or ALT and AST values more than 3.5 times the upper limit of normal value with accompanying phosphatase levels more than 6 times the upper limit of normal, no dosage reduction is recommended and docetaxel is not to be used in these patients unless clearly indicated. In a pivotal study evaluating the cisplatinum-5-flourouracil combination for treatment of patients with gastric adenocarcinoma, patients with ALT and/or AST levels more than 1.5 times the upper limit of normal with accompanying alkaline phosphatase levels more than 2.5 times the upper limit of normal and bilirubin levels 1 times the upper limit of normal were excluded. No dosage adjustment is recommended for these patients and docetaxel should not be used. There are no data on use of docetaxel combination therapies in patients with liver insufficiency. There are no data on use of docetaxel therapy in patients with severe renal failure. Serious peripheral neuropathy development requires dosage reduc- tion. Patients to be treated with Doxel in combination with trastuzumab should be evaluated for basic cardiac functions. Cardiac function should be monitored during treatment to detect patients in whom cardiac impairments can develop. Contraceptive measures should be employed for at least 3 months fol- lowing the end of treatment. In adjuvant therapy of breast cancer, symptoms such as abdominal pain and sensitivity, fever and diarrhea that appear in early phase with or without neutropenia can be early manifestations of serious gastrointestinal toxicity; these symptoms should be evaluated immediately and treated. Patients should be monitored for symptoms of congestive heart failure during treatment and the follow-up period. Elderly patients receiving Doxel treatment should be closely monitored. Since Doxel contains ethanol, possible CSS and other effects should be carefully monitored; it can be harmful for alcohol addicts. Care should be axercised in pregnant or lactating women, children and in high risk patients such as those with liver disease or epilepsy.

Pregnancy and lactation: **Pregnancy category is D**. Doxel is contraindicated during lactatlon.

**Effects on driving and machine use:** The amount of alcohol in this pharmaceutical product can effect your ability in driving and machine use.

**SIDE EFFECTS/ADVERSE EFFECTS:** The most common adverse effects of Doxel administered alone are neutropenia, anemia, alopecia, nausea, vomiting, stomatitis, diarrhea and asthenia. The se- verity of side effects can be increased when Doxel is given in combination with other chemo- therapeutic agents.

Immune system: Flushing, eruptions with or withour itching, respiratory problems, back pain, dyspnea and drug fever or tremors are seen. Severe symptoms were characterized.

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Nervous system: Neurosensory signs, paresthesia, disesthesia or neuromotor events, generalized weakness, taste disturbances. Skin and sub-cutaneous tissue: Severe hand and foot syndrome, eruptions localized on arms, face or chest which are frequently itchy, de-squamations, nail reactions, erythema multiforme, Stevens-Johnson syndrome, cutanous lupus erythematosus such as toxic epidermal necrosis and bulluous erythema cases were reported. General impairments and condition of the administration site: Hyperpigmentation, inflammation, dry and red skin, phlebitis or extravasation and vein swelling. Fluid retension: Peripheral edema, pleural effusion, ascitis, pericardial effusion, pulmonary edema. Blood and lymp system: Anemia, febrile neutropenia, thrombocytopenia. Metabolic: Anorexia. Cardiovascular disturbances: Arythmia, hypotension, hypertension, bleeding, dispnea. Other: Stomatitis, diarrhea, nausea, vomiting, alopecia, skin reactions, nail impairments, increase in blood bilirubin levels, increase in alkaline phosphatase, increased AST, increased ALT, in.

**DRUG INTERACTIONS:** It interacts with drugs such as cyclosporin, terfenadine, ketoconazole, erythromycin and troleandomycin. Docetaxel is highly protein-bound.

**DOSAGE AND ADMINISTRATION:** Docetaxel is administered 75-100 mg/m$^2$ as a 1-hour infusion every 3 weeks. In adjuvant treatment of operable node-positive breast cancer the recommended docetaxel dose is 75 mg/m$^2$ and it is administered every 3 weeks 1 hour following doxorubicin 50 mg/m$^2$ and cyclophosphamide 500 mg/m$^2$ for 6 cycles. The recommended docetaxel dose in combination with trastuzumab is 100 mg/m$^2$ every 3 weeks and trastuzumab is administered weekly. The recommended doxetaxel dose in combination iwth capecitabine is 75 mg/m$^2$ every 3 weeks and capecitabine is administered 1250 mg/m$^2$ bid for 2 weeks; this is followed by a 2-week resting period.

Non-small cell lung cancer: Patients are given docetaxel as a 1-hour infusion every 3 weeks. The recommended dosage regimen for patients who received no chemotherapy previously is docetaxel 75 mg/m$^2$ and immediately following this, cisplatin 75 mg/m$^2$ within 30-60 minutes. In cases where the previous platinum-based chemotherapy was unsuccessful, the recommended dosage is 75 mg/m$^2$ as single agent. Ovary carcinoma: The recommended Doxel dose is 100 mg/m$^2$ given in a 1-hour infusion every 3 weeks. When administered in combination with a platinum -group drug, the recommended docetaxel dose is 75 mg/m$^2$. Head and neck cancers: In patients with non-operable, locally advanced, squam-cell carcinoma of the head and neck where radiotherapy was administered following induction chemotherapy, the recommended docetaxel dose for induction therapy is 75 mg/m$^2$ given in a 1-hour infusion. On Day1, following this, 75 mg/m$^2$ cisplatin is administered. Then 750 mg/m$^2$ 5-flourouracil is administered daily as continuous infusion for 5 days. This dosage regimen is administered every 3 weeks for 4 cycles. In patients with locally advanced squamous- cell carcinoma of head and neck, the recommended dosage for docetaxel induction therapy is 75 mg/m$^2$.given as a 1-hour intravenous infusion on Day 1. Then, from Day 1 to Day 4, this dose is followed by 100 mg/m$^2$ cisplatin infusion given within 30 min-3 hours and following this, 1000 mg/m$^2$/day 5-flourouracil is given as a continous infusion. This dosage regimen is administered every 3 weeks for 3 cycles. Gastric carcinoma: Given 75 mg/m$^2$ as a 1 hour infusion and then 75 mg/m$^2$ cisplatin given as a 1-3 hour infusion (both only on Day 1); following this, starting at the end of the cisplatin infusion, 750 mg/m$^2$/day 5-flourouracil is administered as continous infusion for 5 days. This regimen is repeated every 3 weeks. Prostate cancer: The recommended Doxel dose is 75 mg/m$^2$ infusion given in 1 hour every 3 weeks. Oral prednisone or prednisolone 5 mg bid is administered continously.

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**STORAGE CONDITIONS:** Intact vials should be kept at room temperature (<25°C), in its original package and away from light.

**AVAILABLE FORMS:**

DOXEL 20 mg IV Vial containing concentrated solution for infusion, in protective blister with 1 concentrate solution vial and 1 diluent vial in a package.

DOXEL 40 mg IV Vial containing concentrated solution for infusion, in protective blister with 1 concentrate solution vial and 1 diluent vial in a package.

DOXEL 80 mg IV Vial containing concentrated solution for infusion, in protective blister with 1 concentrate solution vial and 1 diluent vial in a package.

DOXEL 160 mg IV Vial containing concentrated solution for infusion, in protective blister with 1 concentrate solution vial and 1 diluent vial in a package.

Sold under prescription. Please refer to our company for further details.

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