TAXELDO (Docetaxel Concentrate for Solution for Infusion 20mg/ml)

NAME AND STRENGTH OF ACTIVE INGREDIENT
Each ml of concentrate contains 20 mg docetaxel (as trihydrate).

TAXELDO (Docetaxel Concentrate for Solution for Infusion 20mg/ml):
One vial of 1 ml of concentrate contains 20 mg of docetaxel.

Excipients with known effect:
Each vial of concentrate contains 0.5 ml of ethanol anhydrous (0.395 g).

TAXELDO (Docetaxel Concentrate for Solution for Infusion 80mg/4ml):
One vial of 4 ml of concentrate contains 80 mg of docetaxel.

Excipients with known effect:
Each vial of concentrate contains 2 ml of ethanol anhydrous (1.58 g).

TAXELDO (Docetaxel Concentrate for Solution for Infusion 160mg/8ml):
One vial of 8 ml of concentrate contains 160 mg of docetaxel.

Excipients with known effect:
Each vial of concentrate contains 4 ml of ethanol anhydrous (3.16 g).

For a full list of excipients, see section list of excipients.

PHARMACEUTICAL FORM
Concentrate for solution for infusion (sterile concentrate).
The concentrate is a brownish yellow to pale yellow colour solution.

PHARMACODYNAMICS
Pharmacotherapeutic group: Taxanes, ATC Code: L01CD02

Mechanism of Action
Docetaxel is an antineoplastic agent which acts by promoting the assembly of tubulin into stable microtubules and inhibits their disassembly which leads to a marked decrease of free tubulin. The binding of docetaxel to microtubules does not alter the number of protofilaments.
Docetaxel has been shown in vitro to disrupt the microtubular network in cells which is essential for vital mitotic and interphase cellular functions.

Pharmacodynamic Effects
Docetaxel was found to be cytotoxic in vitro against various murine and human tumour cell lines and against freshly excised human tumour 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 over expressing the pglycoprotein which is encoded by the multidrug resistance gene. In vivo, docetaxel is schedule independent and has a broad spectrum of experimental anti-tumour activity against advanced murine and human grafted tumours.

PHARMACOKINETICS
Absorption
The pharmacokinetics of docetaxel have been evaluated in cancer patients after administration of 20 - 115 mg/m^2 in phase I studies. The kinetic profile of docetaxel is dose independent and consistent with a three-compartment pharmacokinetic model with half lives for the α, β and γ (terminal) phases of 4 min, 36 min and between 11.1 h and 17.5 h, respectively, when sampled up to 24 hours. An additional study assessing the pharmacokinetics of docetaxel at similar doses (75 – 100 mg/m^2) in patients, but over a longer time interval (over 22 days) found a longer mean terminal elimination half-life between 91 and 120 hours. The late phase is due, in part, to a relatively slow efflux of docetaxel from the peripheral compartment.

Distribution
Following the administration of a 100 mg/m^2 dose given as a one-hour infusion a mean peak plasma level of 3.7 µg/ml was obtained with a corresponding AUC of 4.6 h.µg/ml. Mean values for total body clearance and steady-state volume of distribution were 21 liter/h/m^2 and 113 liter, respectively. Inter individual variation in total body clearance was approximately 50%. Docetaxel is more than 95% bound to plasma proteins.

Elimination

A study of ^{14}C-docetaxel has been conducted in three cancer patients. Docetaxel was eliminated in both the urine and faeces following cytochrome P450-mediated oxidative metabolism of the tert-butyl ester group, within seven days, the urinary and faecal excretion accounted for about 6% and 75% of the administered radioactivity, respectively. About 80% of the radioactivity recovered in faeces is excreted during the first 48 hours as one major inactive metabolite and 3 minor inactive metabolites and very low amounts of unchanged medicinal product.

Special Populations

Age and Gender

A population pharmacokinetic analysis has been performed with docetaxel in 577 patients. Pharmacokinetic parameters estimated by the model were very close to those estimated from phase I studies. The pharmacokinetics of docetaxel were not altered by the age or sex of the patient.

Hepatic Impairment

In a small number of patients with clinical chemistry data suggestive of mild to moderate liver function impairment (ALT, AST ≥ 1.5 times the ULN associated with alkaline phosphatase ≥ 2.5 times the ULN), total clearance was lowered by 27% on average.

Fluid Retention

Docetaxel clearance was not modified in patients with mild to moderate fluid retention and there are no data available in patients with severe fluid retention.

Combination Therapy

Doxorubicin

When used in combination, docetaxel does not influence the clearance of doxorubicin and the plasma levels of doxorubicinol (a doxorubicin metabolite). The pharmacokinetics of docetaxel, doxorubicin and cyclophosphamide were not influenced by their coadministration.

Capecitabine

Phase I study evaluating the effect of capecitabine on the pharmacokinetics of docetaxel and vice versa showed no effect by capecitabine on the pharmacokinetics of docetaxel (C_{max} and AUC) and no effect by docetaxel on the pharmacokinetics of a relevant capecitabine metabolite 5'-DFUR.

Cisplatin

Clearance of docetaxel in combination therapy with cisplatin was similar to that observed following monotherapy. The pharmacokinetic profile of cisplatin administered shortly after docetaxel infusion is similar to that observed with cisplatin alone.

Cisplatin and 5-fluorouracil

The combined administration of docetaxel, cisplatin and 5-fluorouracil in 12 patients with solid tumours had no influence on the pharmacokinetics of each individual medicinal product.

Prednisone and Dexamethasone

The effect of prednisone on the pharmacokinetics of docetaxel administered with standard dexamethasone premedication has been studied in 42 patients.

Prednisone

No effect of prednisone on the pharmacokinetics of docetaxel was observed.

INDICATION

Breast Cancer

TAXELDO in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with:

- operable node-positive breast cancer.
- operable node-negative breast cancer.

For patients with operable node-negative breast cancer, adjuvant treatment should be restricted to patients eligible to receive chemotherapy according to internationally established criteria for primary therapy of early breast cancer.

TAXELDO in combination with doxorubicin is indicated for the treatment of patients with locally advanced or metastatic breast cancer who have not previously received cytotoxic therapy for this condition.
TAXELDO in combination with capecitabine is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of cytotoxic chemotherapy. Previous therapy should have included an anthracycline.
TAXELDO monotherapy is indicated for the treatment of patients with locally advanced or metastatic breast cancer in whom previous therapy has failed. Prior therapy should have included an anthracycline unless clinically contraindicated.

Non-Small Cell Lung Cancer
TAXELDO is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior chemotherapy.
TAXELDO in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic non-small cell lung cancer, in patients who have not previously received chemotherapy for this condition. TAXELDO in combination with carboplatin represents a treatment option to cisplatin-based therapy.

Ovarian Cancer
TAXELDO is indicated for the treatment of metastatic carcinoma of the ovary after failure of first-line or subsequent chemotherapy.

Squamous Cell Carcinoma of the Head and Neck
TAXELDO 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.

Prostate Cancer
TAXELDO in combination with prednisone or prednisolone is indicated for the treatment of patients with hormone refractory metastatic prostate cancer.

Gastric Adenocarcinoma
TAXELDO in combination with cisplatin and 5-fluorouracil is indicated for the treatment of patients with metastatic gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for metastatic disease.

Head and Neck Cancer
TAXELDO in combination with cisplatin and 5-fluorouracil is indicated for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck.

POSOLOGY AND METHOD OF ADMINISTRATION
The use of docetaxel should be confined to units specialised in the administration of cytotoxic chemotherapy and it should only be administered under the supervision of a physician qualified in the use of anticancer chemotherapy.

Recommended Dose
For breast, non-small cell lung, gastric, and head and neck cancers, premedication consisting of an oral corticosteroid, such as dexamethasone 16 mg per day (e.g., 8 mg BID) for 3 days starting 1 day prior to docetaxel administration, unless contraindicated, can be used.

For prostate cancer, given the concurrent use of prednisone or prednisolone the recommended premedication regimen is oral dexamethasone 8 mg, 12 hours, 3 hours and 1 hour before the docetaxel infusion.

Docetaxel is administered as a one-hour infusion every three weeks.

Prophylactic G-CSF may be used to mitigate the risk of haematological toxicities.

Breast Cancer
In the adjuvant treatment of operable node-positive and node negative breast cancer, the recommended dose of docetaxel is 75 mg/m^2 administered 1-hour after doxorubicin 50mg/m^2 and cyclophosphamide 500 mg/m^2 every 3 weeks for 6 cycles (TAC regimen) (See also section Dose adjustments during treatment). For the treatment of patients with locally advanced or metastatic breast cancer, the recommended dosage of docetaxel is 100mg/m^2 in monotherapy. In first-line treatment, docetaxel 75 mg/m^2 is given in combination therapy with doxorubicin (50 mg/m^2).
In combination with capecitabine, the recommended dose of docetaxel is 75 mg/m^2 every three weeks, combined with capecitabine at 1250 mg/m^2 twice daily (within 30 minutes after a meal) for 2 weeks followed by a 1-week rest period. For capecitabine dose calculation according to body surface area, see capecitabine summary of product characteristics.

Non-small Cell Lung Cancer
In chemotherapy naïve patients treated for non-small cell lung cancer, the recommended dose regimen is docetaxel 75 mg/m^2 immediately followed by cisplatin 75 mg/m^2 over 30 - 60 minutes. For treatment after failure of prior platinum-based chemotherapy, the recommended dosage is 75 mg/m² as a single agent.

Prostate Cancer
The recommended dose of docetaxel is 75 mg/m^2. Prednisone or prednisolone 5 mg orally twice daily is administered continuously.

Gastric Adenocarcinoma
The recommended dose of docetaxel is 75 mg/m^2 as a 1 hour infusion, followed by cisplatin 75 mg/m^2, as a 1 to 3 hour infusion (both on day 1 only), followed by 5-fluorouracil 750 mg/m^2 per day given as a 24-hour continuous infusion for 5 days, starting at the end of the cisplatin infusion. Treatment is repeated every three weeks. Patients must receive premedication with antiemetics and appropriate hydration for cisplatin administration. Prophylactic G-CSF should be used to mitigate the risk of haematological toxicities (See also section Dose adjustments during treatment)

Head and Neck Cancer

Patients must receive premedication with antiemetics and appropriate hydration (prior to and after cisplatin administration). Prophylactic G-CSF may be used to mitigate the risk of haematological toxicities.

- *Induction chemotherapy followed by radiotherapy*
  For the induction treatment of inoperable locally advanced squamous cell carcinoma of the head and neck (SCCHN), the recommended dose of docetaxel is 75 mg/m^2 as a 1 hour infusion followed by cisplatin 75 mg/m^2 over 1 hour, on day one, followed by 5-fluorouracil as a continuous 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 chemoradiotherapy*
  For the induction treatment of patients with locally advanced (technically unresectable, low probability of surgical cure, and aiming at organ preservation) squamous cell carcinoma of the head and neck (SCCHN), the recommended dose of docetaxel 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 5-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 chemoradiotherapy.

For cisplatin and 5-fluorouracil dose modifications, see the corresponding summary of product characteristics.

Ovarian Cancer

The recommended dosage is 100 mg/m^2 administered as one hour infusion every three weeks. When use in combination, docetaxel is administered at the recommended dosage of 75mg/m^2.

Squamous Cell Carcinoma of the Head and Neck

The recommended dosage is 100mg/m^2 administered as one hour infusion every three weeks. When use in combination, docetaxel is administered at the recommended dosage of 75mg/m^2.

Dose Adjustments During Treatment

General

Docetaxel should be administered when the neutrophil count is ≥ 1,500 cells/mm^3. In patients who experienced either febrile neutropenia, neutrophil count < 500 cells/mm^3 for more than one week, severe or cumulative cutaneous reactions or severe peripheral neuropathy during docetaxel therapy, the dose of docetaxel should be reduced from 100 mg/m^2 to 75 mg/m^2 and/or from 75 to 60 mg/m^2. If the patient continues to experience these reactions at 60 mg/m^2, the treatment should be discontinued.

Adjuvant Therapy for Breast Cancer

Primary G-CSF prophylaxis should be considered in patients who receive docetaxel, doxorubicin and cyclophosphamide (TAC) adjuvant therapy for breast cancer. Patients who experience febrile neutropenia and/or neutropenic infection should have their docetaxel dose reduced to 60 mg/m^2 in all subsequent cycles. Patients who experience Grade 3 or 4 stomatitis should have their dose decreased to 60 mg/m^2.

In Combination with Cisplatin

For patients who are dosed initially at docetaxel 75 mg/m^2 in combination with cisplatin and whose nadir of platelet count during the previous course of therapy is < 25,000 cells/mm^3, or in patients who experience febrile neutropenia, or in patients with serious non-haematologic toxicities, the docetaxel dose in subsequent cycles should be reduced to 65 mg/m^2. For cisplatin dose adjustments, see the corresponding summary of product characteristics.

In Combination with Capecitabine

- For capecitabine dose modifications, see capecitabine summary of product characteristics.
- For patients developing the first appearance of Grade 2 toxicity, which persists at the time of the next docetaxel/capecitabine treatment, delay treatment until resolved to Grade 0 - 1, and resume at 100% of the original dose.
- For patients developing the second appearance of Grade 2 toxicity, or the first appearance of Grade 3 toxicity, at any time during the treatment cycle, delay treatment until resolved to Grade 0 - 1 and then resume treatment with docetaxel 55 mg/m^2.
- For any subsequent appearances of toxicities, or any Grade 4 toxicities, discontinue the docetaxel dose.

In Combination with Cisplatin and 5-fluorouracil

If an episode of febrile neutropenia, prolonged neutropenia or neutropenic infection occurs despite G-CSF use, the docetaxel dose should be reduced from 75 to 60 mg/m^2. If subsequent episodes of complicated neutropenia occur the docetaxel dose should be reduced from 60 to 45 mg/m^2. In case of Grade 4 thrombocytopenia the docetaxel dose should be reduced from 75 to 60 mg/m^2. Patients should not be retreated with subsequent cycles of docetaxel until neutrophils recover to a level > 1,500 cells/mm^3 and platelets recover to a level > 100,000 cells/mm^3. Discontinue treatment if these toxicities persist.

Recommended dose modifications for toxicities in patients treated with docetaxel in combination with cisplatin and 5-fluorouracil (5-FU):

Toxicity	Dose Adjustment
Diarrhoea grade 3	First episode: reduce 5-FU dose by 20%. Second episode: then reduce docetaxel dose by 20%.
Diarrhoea grade 4	First episode: reduce docetaxel and 5-FU doses by 20%. Second episode: discontinue treatment.
Stomatitis/mucositis grade 3	First episode: reduce 5-FU dose by 20%. Second episode: stop 5-FU only, at all subsequent cycles. Third episode: reduce docetaxel dose by 20%.
Stomatitis/mucositis grade 4	First episode: stop 5-FU only, at all subsequent cycles. Second episode: reduce docetaxel dose by 20%.

For cisplatin and 5-fluorouracil dose adjustments, see the corresponding summary of product characteristics.
In the pivotal SCCHN studies patients who experienced complicated neutropenia (including prolonged neutropenia, febrile neutropenia, or infection), it was recommended to use G-CSF to provide prophylactic coverage (e.g., day 6 - 15) in all subsequent cycles.

Special Populations

Patients with Hepatic Impairment

Based on pharmacokinetic data with docetaxel at 100 mg/m² as single agent, patients who have both elevations of transaminase (ALT and/or AST) greater than 1.5 times the upper limit of the normal range (ULN) and alkaline phosphatase greater than 2.5 times the ULN, the recommended dose of docetaxel is 75 mg/m^2. For those patients with serum bilirubin > ULN and/or ALT and AST > 3.5 times the ULN associated with alkaline phosphatase > 6 times the ULN, no dose reduction can be recommended and docetaxel should not be used unless strictly indicated.
In combination with cisplatin and 5-fluorouracil for the treatment of patients with gastric adenocarcinoma, the pivotal clinical study excluded patients with ALT and/or AST > 1.5 × ULN associated with alkaline phosphatase > 2.5 × ULN, and bilirubin > 1 x ULN; for these patients, no dose-reductions can be recommended and docetaxel should not be used unless strictly indicated. No data are available in patients with hepatic impairment treated by docetaxel in combination in the other indications.

Paediatric Population

The safety and efficacy of TAXELDO in nasopharyngeal carcinoma in children aged 1 month to less than 18 years have not been established.
There is no relevant use of TAXELDO in the paediatric population in the indications breast cancer, non-small cell lung cancer, prostate cancer, gastric carcinoma and head and neck cancer, not including type II and III less differentiated nasopharyngeal carcinoma.

Older people

Based on a population pharmacokinetic analysis, there are no special instructions for use in older people.
In combination with capecitabine, for patients 60 years of age or more, a starting dose reduction of capecitabine to 75% is recommended.

ROUTE OF ADMINISTRATION

Intravenous

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed in section List of Excipients.
Patients with baseline neutrophil count of < 1,500 cells/mm^3.
Patients with severe liver impairment.
Contraindications for other medicinal products also apply, when combined with docetaxel.

WARNING AND PRECAUTIONS

For breast and non-small cell lung cancers, premedication consisting of an oral corticosteroid, such as dexamethasone 16 mg per day (e.g., 8 mg BID) for 3 days starting 1 day prior to docetaxel administration, unless contraindicated, can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. For prostate cancer, the premedication is oral dexamethasone 8 mg, 12 hours, 3 hours and 1 hour before the docetaxel infusion.

Haematology

Neutropenia is the most frequent adverse reaction of docetaxel. Neutrophil nadirs occurred at a median of 7 days but this interval may be shorter in heavily pre-treated patients. Frequent monitoring of complete blood counts should be conducted on all patients receiving docetaxel. Patients should be retreated with docetaxel when neutrophils recover to a level ≥ 1,500 cells/mm^3.

In the case of severe neutropenia (< 500 cells/mm^3 for seven days or more) during a course of docetaxel therapy, a reduction in dose for subsequent courses of therapy or the use of appropriate symptomatic measures are recommended.

In patients treated with docet100MGaxel in combination with cisplatin and 5-fluorouracil (TCF), febrile neutropenia and neutropenic infection occurred at lower rates when patients received prophylactic G-CSF. Patients treated with TCF should receive prophylactic GCSF to mitigate the risk of complicated neutropenia (febrile neutropenia, prolonged neutropenia or neutropenic infection). Patients receiving TCF should be closely monitored.

In patients treated with docetaxel in combination with doxorubicin and cyclophosphamide (TAC), febrile neutropenia and/or neutropenic infection occurred at lower rates when patients received primary G-CSF prophylaxis. Primary G-CSF prophylaxis should be considered in patients who receive adjuvant therapy with TAC for breast cancer to mitigate the risk of complicated neutropenia (febrile neutropenia, prolonged neutropenia or neutropenic infection). Patients receiving TAC should be closely monitored.

Gastrointestinal reactions

Caution is recommended for patients with neutropenia, particularly at risk for developing gastrointestinal complications. Although majority of cases occurred during the first or second cycle of docetaxel containing regimen, enterocolitis could develop at any time, and could lead to death as early as on the first day of onset. Patients should be closely monitored for early manifestations of serious gastrointestinal toxicity.

Hypersensitivity Reactions

Patients should be observed closely for hypersensitivity reactions especially during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of docetaxel, thus facilities for the treatment of hypotension and bronchospasm should be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localized cutaneous reactions do not require interruption of therapy. However, severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate therapy. Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel. Patients who have previously experienced a hypersensitivity reaction to paclitaxel may be at risk to develop hypersensitivity reaction to docetaxel, including more severe hypersensitivity reaction. These patients should be closely monitored during initiation of docetaxel therapy.

Cutaneous Reactions

Localised skin erythema of the extremities (palms of the hands and soles of the feet) with oedema followed by desquamation has been observed. Severe symptoms such as eruptions followed by desquamation which lead to interruption or discontinuation of docetaxel treatment were reported.

Severe Cutaneous Adverse Reactions (SCARs) such as Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and Acute Generalized Exanthematous Pustulosis (AGEP) have been reported with docetaxel treatment. Patients should be informed about the signs and symptoms of serious skin manifestations and closely monitored. If signs and symptoms suggestive of these reactions appear discontinuation of docetaxel should be considered.

Fluid Retention

Patients with severe fluid retention such as pleural effusion, pericardial effusion and ascites should be monitored closely.

Respiratory Disorders

Acute respiratory distress syndrome, interstitial pneumonia/pneumonitis, interstitial lung disease, pulmonary fibrosis and respiratory failure have been reported and may be associated with fatal outcome. Cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy.

If new or worsening pulmonary symptoms develop, patients should be closely monitored, promptly investigated, and appropriately treated. Interruption of docetaxel therapy is recommended until diagnosis is available. Early use of supportive care measures may help improve the condition. The benefit of resuming docetaxel treatment must be
carefully evaluated.

Patients with Liver Impairment

In patients treated with docetaxel at 100 mg/m^2 as single agent who have serum transaminase levels (ALT and/or AST) greater than 1.5 times the ULN concurrent with serum alkaline phosphatase levels greater than 2.5 times the ULN, there is a higher risk of developing severe adverse reactions such as toxic deaths including sepsis and gastrointestinal haemorrhage which can be fatal, febrile neutropenia, infections, thrombocytopenia, stomatitis and asthenia. Therefore, the recommended dose of docetaxel in those patients with elevated liver function test (LFTs) is 75 mg/m^2 and LFTs should be measured at baseline and before each cycle.

For patients with serum bilirubin levels > ULN and/or ALT and AST > 3.5 times the ULN concurrent with serum alkaline phosphatase levels > 6 times the ULN, no dose reduction can be recommended and docetaxel should not be used unless strictly indicated.

In combination with cisplatin and 5-fluorouracil for the treatment of patients with gastric adenocarcinoma, the pivotal clinical study excluded patients with ALT and/or AST > 1.5 × ULN associated with alkaline phosphatase > 2.5 × ULN, and bilirubin > 1 x ULN; for these patients, no dose-reductions can be recommended and docetaxel should not be used unless strictly indicated. No data are available in patients with hepatic impairment treated by docetaxel in combination in the other indications.

Patients with Renal Impairment

There are no data available in patients with severely impaired renal function treated with docetaxel.

Nervous System
The development of severe peripheral neurotoxicity requires a reduction of dose.

Cardiac Toxicity
Heart failure has been observed in patients receiving docetaxel in combination with trastuzumab, particularly following anthracycline (doxorubicin or epirubicin)-containing chemotherapy. This may be moderate to severe and has been associated with death.
When patients are candidates for treatment with docetaxel in combination with trastuzumab, they should undergo baseline cardiac assessment. Cardiac function should be further monitored during treatment (e.g., every three months) to help identify patients who may develop cardiac dysfunction. For more details see summary of product characteristics of trastuzumab.
Ventricular arrhythmia including ventricular tachycardia (sometimes fatal) has been reported in patients treated with docetaxel in combination regimens including doxorubicin, 5-fluorouracil and/ or cyclophosphamide. Baseline cardiac assessment is recommended.

Eye Disorders
Cystoid macular oedema (CMO) has been reported in patients treated with docetaxel. Patients with impaired vision should undergo a prompt and complete ophthalmologic examination. In case CMO is diagnosed, docetaxel treatment should be discontinued and appropriate treatment initiated.

Second primary malignancies
Second primary malignancies have been reported when docetaxel was given in combination with anticancer treatments known to be associated with second primary malignancies. Second primary malignancies (including acute myeloid leukemia, myelodysplastic syndrome and non-Hodgkin lymphoma) may occur several months or years after docetaxel-containing therapy. Patients should be monitored for second primary malignancies.

Tumour Lysis Syndrome
Tumour lysis syndrome has been reported with docetaxel after the first or the second cycle. Patients at risk of tumour lysis syndrome (e.g., with renal impairment, hyperuricemia, bulky tumour, rapid progression) should be closely monitored. Correction of dehydration and treatment of high uric acid levels are recommended prior to initiation of treatment.

Others
Women of childbearing potential must use contraceptive measures during treatment and for 2 months after cessation of treatment with docetaxel. Men must use contraceptive measures during treatment and for 4 months after cessation of treatment with docetaxel. The concomitant use of docetaxel with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole) should be avoided.

Additional Cautions for Use in Adjuvant Treatment of Breast Cancer
Complicated Neutropenia
For patients who experience complicated neutropenia (prolonged neutropenia, febrile neutropenia or infection), G-CSF and dose reduction should be considered.

Gastrointestinal Reactions
Symptoms such as early abdominal pain and tenderness, fever, diarrhoea, with or without neutropenia, may be early manifestations of serious gastrointestinal toxicity and should be evaluated and treated promptly.

Congestive Heart Failure (CHF)
Patients should be monitored for symptoms of congestive heart failure during therapy and during the follow up period. In patients treated with the TAC regimen for node positive breast cancer, the risk of CHF has been shown to be higher during the first year after treatment.

Patients with 4+ Nodes
As the benefit observed in patient with 4+ nodes was not statistically significant on disease-free survival (DFS) and overall survival (OS), the positive benefit/risk ratio for TAC in patients with 4+ nodes was not fully demonstrated at the final analysis.

Older People
There are limited data available in patients > 70 years of age on docetaxel use in combination with doxorubicin and cyclophosphamide.
Older people treated with TCF should be closely monitored.

Excipients
TAXELDO 20 mg/1 ml concentrate for solution for infusion contains 50 vol % ethanol anhydrous (alcohol), i.e., up to 0.395 g ethanol anhydrous per vial, equivalent to 10 ml of beer or 4 ml wine.
TAXELDO 80 mg/4 ml concentrate for solution for infusion contains 50 vol % ethanol anhydrous (alcohol), i.e., up to 1.58 g ethanol anhydrous per vial, equivalent to 40 ml of beer or 17 ml wine.

TAXELDO (Docetaxel Concentrate for Solution for Infusion 20mg/ml)

TAXELDO 160 mg/8 ml concentrate for solution for infusion contains 50 vol % ethanol anhydrous (alcohol), i.e., up to 3.16 g ethanol anhydrous per vial, equivalent to 80 ml of beer or 34 ml wine.
Harmful for those suffering from alcoholism.
To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease, or epilepsy.
Consideration should be given to possible effects on the central nervous system.

INTERACTION WITH OTHER MEDICAMENTS
The amount of alcohol in this medicinal product may alter the effects of other medicinal products.

Metabolism of docetaxel may be modified by the concomitant administration of compounds which induce, inhibit or are metabolised by (and thus may inhibit the enzyme competitively) cytochrome P450-3A such as ciclosporine, ketoconazole and erythromycin. As a result, caution should be exercised when treating patients with these medicinal products as concomitant therapy since there is a potential for a significant interaction.

In case of combination with CYP3A4 inhibitors, the occurrence of docetaxel adverse reactions may increase, as a result of reduced metabolism. If the concomitant use of a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, clarithromycin, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole) cannot be avoided, a close clinical surveillance is warranted and a dose-adjustment of docetaxel may be suitable during the treatment with the strong CYP3A4 inhibitor. In a pharmacokinetic study with 7 patients, the co-administration of docetaxel with the strong CYP3A4 inhibitor ketoconazole leads to a significant decrease in docetaxel clearance by 49%.

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.

PREGNANCY AND LACTATION
Women of childbearing potential/ Contraception in males and females
Women of childbearing potential and men receiving docetaxel should be advised to avoid becoming pregnant, and not to father a child and to inform the treating physician immediately should this occur.
Due to the genotoxic risk of docetaxel, women of childbearing potential must use effective method of contraception during treatment and for 2 months after cessation of treatment with docetaxel. Men must use effective method of contraception during treatment and for 4 months after cessation of treatment with docetaxel.

Pregnancy
There is no information on the use of docetaxel in pregnant women. Docetaxel has been shown to be both embryotoxic and foetotoxic in rabbits and rats. As with other cytotoxic medicinal products, docetaxel may cause foetal harm when administered to pregnant women. Therefore, docetaxel must not be used during pregnancy unless clearly indicated.

Breast-feeding
Docetaxel is a lipophilic substance but it is not known whether it is excreted in human milk. Consequently, because of the potential for adverse reactions in nursing infants, breast feeding must be discontinued for the duration of docetaxel therapy.

Fertility
Studies in animals have shown that docetaxel may alter male fertility. Therefore, males being treated with docetaxel must seek advice on conservation of sperm prior to treatment.

SIDE EFFECTS
Summary of the Safety Profile for All Indications
The adverse reactions considered to be possibly or probably related to the administration of docetaxel have been obtained in:

- 1312 and 121 patients who received 100 mg/m² and 75 mg/m² of docetaxel as a single agent respectively.
- 258 patients who received docetaxel in combination with doxorubicin.
- 406 patients who received docetaxel in combination with cisplatin.
- 92 patients treated with docetaxel in combination with trastuzumab.

Font size: 7

- 255 patients who received docetaxel in combination with capecitabine.
- 332 patients who received docetaxel in combination with prednisone or prednisolone (clinically important treatment related adverse events are presented).
- 1276 patients (744 and 532 in TAX 316 and GEICAM 9805 respectively) who received docetaxel in combination with doxorubicin and cyclophosphamide (clinically important treatment related adverse events are presented).
- 300 gastric adenocarcinoma patients (221 patients in the phase III part of the study and 79 patients in the phase II part) who received docetaxel in combination with cisplatin and 5-fluorouracil (clinically important treatment related adverse events are presented).
- 174 and 251 head and neck cancer patients who received docetaxel in combination with cisplatin and 5-fluorouracil (clinically important treatment related adverse events are presented).

These reactions were described using the NCI Common Toxicity Criteria (grade 3 = G3; grade 3 - 4 = G3/4; grade 4 = G4), the COSTART and the MedDRA terms.
Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The most commonly reported adverse reactions of docetaxel alone are: neutropenia (which was reversible and not cumulative; the median day to nadir was 7 days and the median duration of severe neutropenia (< 500 cells/mm3) was 7 days), anaemia, alopecia, nausea, vomiting, stomatitis, diarrhoea and asthenia. The severity of adverse events of docetaxel may be increased when docetaxel is given in combination with other chemotherapeutic agents.

For combination with trastuzumab, adverse events (all grades) reported in > 10% are displayed. There was an increased incidence of SAEs (40% vs. 31%) and Grade 4 AEs (34% vs. 23%) in the trastuzumab combination arm compared to docetaxel monotherapy.

For combination with capecitabine, the most frequent treatment-related undesirable effects (≥ 5%) reported in a phase III study in breast cancer patients failing anthracycline treatment are presented (see capecitabine summary of product characteristics).
The following adverse reactions are frequently observed with docetaxel: 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, dyspnoea 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 paraesthesia, 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 localised 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 hyper pigmentation, inflammation, redness or dryness of the skin, phlebitis or extravasation and swelling of the vein.
Fluid retention includes events such as peripheral oedema and less frequently pleural effusion, pericardial effusion, ascites and weight gain. The peripheral oedema usually starts at the lower extremities and may become generalised with a weight gain of 3 kg or more. Fluid retention is cumulative in incidence and severity.

Tabulated List of Adverse Reactions in Breast Cancer for TAXELDO 100 mg/m² Single Agent

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
Infections and Infestations	Infections (G3/4: 5.7%; including sepsis and pneumonia, fatal in 1.7%)	Infection associated with G4 neutropenia (G3/4: 4.6%)	
Blood and Lymphatic System Disorders	Neutropenia (G4: 76.4%); Anaemia (G3/4: 8.9%); Febrile neutropenia	Thrombocytopenia (G4: 0.2%)	
Immune System Disorders	Hypersensitivity (G3/4: 5.3%)		

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
Metabolism and Nutrition Disorders	Anorexia		
Nervous System Disorders	Peripheral sensory neuropathy (G3: 4.1%); Peripheral motor neuropathy (G3/4: 4%); Dysgeusia (severe: 0.07%)		
Cardiac Disorders		Arrhythmia (G3/4: 0.7%)	Cardiac failure
Vascular Disorders		Hypotension; Hypertension; Haemorrhage	
Respiratory, Thoracic and Mediastinal Disorders	Dyspnoea (severe: 2.7%)		
Gastrointestinal Disorders	Stomatitis (G3/4: 5.3%); Diarrhoea (G3/4: 4%); Nausea (G3/4: 4%); Vomiting (G3/4: 3%)	Constipation (severe: 0.2%); Abdominal pain (severe: 1%); Gastrointestinal haemorrhage (severe: 0.3%)	Oesophagitis (severe: 0.4%)
Skin and Subcutaneous Tissue Disorders	Alopecia; Skin reaction (G3/4: 5.9%); Nail disorders (severe: 2.6%)		
Musculoskeletal and Connective Tissue Disorders	Myalgia (severe: 1.4%)	Arthralgia	
General Disorders and Administration Site Conditions	Fluid retention (severe: 6.5%); Asthenia (severe: 11.2%); Pain	Infusion site reaction; Non-cardiac chest pain (severe: 0.4%)	
Investigations		G3/4 Blood bilirubin increased (< 5%); G3/4 Blood alkaline phosphatase increased (< 4%); G3/4 AST increased (< 3%); G3/4 ALT increased (< 2%)	

Description of Selected Adverse Reactions in Breast Cancer for TAXELDO 100 mg/m^2 Single Agent

Blood and Lymphatic System Disorders
Rare: bleeding episodes associated with grade 3/4 thrombocytopenia.

Nervous System Disorders
Reversibility data are available among 35.3% of patients who developed neurotoxicity following docetaxel treatment at 100 mg/m² as single agent. The events were spontaneously reversible within 3 months.

Skin and Subcutaneous Tissue Disorders
Very rare: one case of alopecia non-reversible at the end of the study. 73% of the cutaneous reactions were reversible within 21 days.

General Disorders and Administration Site Conditions
The median cumulative dose to treatment discontinuation was more than 1,000 mg/m^2 and the median time to fluid retention reversibility was 16.4 weeks (range 0 to 42 weeks). The onset of moderate and severe retention is delayed (median cumulative dose: 818.9 mg/m^2) in patients with premedication compared with patients without premedication (median cumulative dose: 489.7 mg/m^2); however, it has been reported in some patients during the early courses of therapy

Tabulated List of Adverse Reactions in Non-Small Cell Lung Cancer for Docetaxel 75 mg/m² Single Agent

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions
Infections and Infestations	Infections (G3/4: 5%)	
Blood and Lymphatic System Disorders	Neutropenia (G4: 54.2%); Anaemia (G3/4: 10.8%); Thrombocytopenia (G4: 1.7%)	Febrile neutropenia
Immune System Disorders		Hypersensitivity (no severe)
Metabolism and Nutrition Disorders	Anorexia	
Nervous System Disorders	Peripheral sensory neuropathy (G3/4: 0.8%)	Peripheral motor neuropathy (G3/4: 2.5%)

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions
Cardiac Disorders		Arrhythmia (no severe)
Vascular Disorders		Hypotension
Gastrointestinal Disorders	Nausea (G3/4: 3.3%); Stomatitis (G3/4: 1.7%); Vomiting (G3/4: 0.8%); Diarrhoea (G3/4: 1.7%)	Constipation
Skin and Subcutaneous Tissue Disorders	Alopecia; Skin reaction (G3/4: 0.8%)	Nail disorders (severe: 0.8%)
Musculoskeletal and Connective Tissue Disorders		Myalgia
General Disorders and Administration Site Conditions	Asthenia (severe: 12.4%); Fluid retention (severe: 0.8%); Pain	
Investigations		G3/4 Blood bilirubin increased (< 2%)

Tabulated List of Adverse Reactions in Breast Cancer for TAXELDO 75 mg/m² in Combination with Doxorubicin

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
Infections and Infestations	Infection (G3/4: 7.8%)		
Blood and Lymphatic System Disorders	Neutropenia (G4: 91.7%); Anaemia (G3/4: 9.4%); Febrile neutropenia; Thrombocytopenia (G4: 0.8%)		
Immune System Disorders		Hypersensitivity (G3/4: 1.2%)	
Metabolism and Nutrition Disorders		Anorexia	
Nervous System Disorders	Peripheral sensory neuropathy (G3: 0.4%)	Peripheral motor neuropathy (G3/4: 0.4%)	
Cardiac Disorders		Cardiac failure; Arrhythmia (no severe)	
Vascular Disorders			Hypotension
Gastrointestinal Disorders	Nausea (G3/4: 5%); Stomatitis (G3/4: 7.8%); Diarrhoea (G3/4: 6.2%); Vomiting (G3/4: 5%); Constipation		
Skin and Subcutaneous Tissue Disorders	Alopecia; Nail disorders (severe: 0.4%); Skin reaction (no severe)		
Musculoskeletal and Connective Tissue Disorders		Myalgia	
General Disorders and Administration Site Conditions	Asthenia (severe: 8.1%); Fluid retention (severe: 1.2%); Pain	Infusion site reaction	
Investigations		G3/4 Blood bilirubin increased (< 2.5%); G3/4 Blood alkaline phosphatase increased (<2.5%)	G3/4 AST increased (< 1%); G3/4 ALT increased (<1%)

Tabulated List of Adverse Reactions in Non-Small Cell Lung Cancer for TAXELDO 75 mg/m² in Combination with Cisplatin

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
Infections and Infestations	Infection (G3/4: 5.7%)		
Blood and Lymphatic System Disorders	Neutropenia (G4: 51.5%); Anaemia (G3/4: 6.9%); Thrombocytopenia (G4: 0.5%)	Febrile neutropenia	
Immune System Disorders	Hypersensitivity (G3/4: 2.5%)		

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
Metabolism and Nutrition Disorders	Anorexia		
Nervous system Disorders	Peripheral sensory neuropathy (G3: 3.7%); Peripheral motor neuropathy (G3/4: 2%)		
Cardiac Disorders		Arrhythmia (G3/4: 0.7%)	Cardiac failure
Vascular Disorders		Hypotension (G3/4: 0.7%)	
Gastrointestinal Disorders	Nausea (G3/4: 9.6%); Vomiting (G3/4: 7.6%); Diarrhoea (G3/4: 6.4%); Stomatitis (G3/4: 2%)	Constipation	
Skin and Subcutaneous Tissue Disorders	Alopecia; Nail disorders (severe: 0.7%); Skin reaction (G3/4: 0.2%)		
Musculoskeletal and Connective Tissue Disorders	Myalgia (severe: 0.5%)		
General Disorders and Administration Site Conditions	Asthenia (severe: 9.9%); Fluid retention (severe: 0.7%); Fever (G3/4: 1.2%)	Infusion site reaction; Pain	
Investigations		G3/4 Blood bilirubin increased (2.1%); G3/4 ALT increased (1.3%)	G3/4 AST increased (0.5%); G3/4 Blood alkaline phosphatase increased (0.3%)

Tabulated List of Adverse Reactions in Breast Cancer for TAXELDO 100 mg/m² in Combination with Trastuzumab

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions
Blood and Lymphatic System Disorders	Neutropenia (G3/4: 32%); Febrile neutropenia (includes neutropenia associated with fever and antibiotic use) or neutropenic sepsis	
Metabolism and Nutrition Disorders	Anorexia	
Psychiatric Disorders	Insomnia	
Nervous System Disorders	Paraesthesia; Headache; Dysgeusia; Hypoaesthesia	
Eye Disorders	Lacrimation increased; Conjunctivitis	
Cardiac Disorders		Cardiac failure
Vascular Disorders	Lymphoedema	
Respiratory, Thoracic and Mediastinal Disorders	Epistaxis; Pharyngolaryngeal pain; Nasopharyngitis; Dyspnoea; Cough; Rhinorrhoea	
Gastrointestinal Disorders	Nausea; Diarrhoea; Vomiting; Constipation; Stomatitis; Dyspepsia; Abdominal pain	
Skin and Subcutaneous Tissue Disorders	Alopecia; Erythema; Rash; Nail Disorders	
Musculoskeletal and Connective Tissue Disorders	Myalgia; Arthralgia; Pain in extremity; Bone pain; Back pain	
General Disorders and Administration Site Conditions	Asthenia; Oedema peripheral; Pyrexia; Fatigue; Mucosal inflammation; Pain; Influenza like illness; Chest pain; Chills	Lethargy
Investigations	Weight increased	

Description of Selected Adverse Reactions in Breast Cancer for TAXELDO 100 mg/m² in Combination with Trastuzumab

Blood and Lymphatic System Disorders

Very common: Haematological toxicity was increased in patients receiving trastuzumab and docetaxel, compared with docetaxel alone (32% grade 3/4 neutropenia versus 22%, using NCI-CTC criteria). Note that this is likely to be an underestimate since docetaxel alone at a dose of 100 mg/m² is known to result in neutropenia in 97% of patients, 76% grade 4, based on nadir blood counts. The incidence of febrile neutropenia/neutropenic sepsis was also increased in patients treated with Herceptin plus docetaxel (23% versus 17% for patients treated with docetaxel alone).

Cardiac Disorders

Symptomatic cardiac failure was reported in 2.2% of the patients who received docetaxel plus trastuzumab compared to 0% of patients given docetaxel alone. In the docetaxel plus trastuzumab arm, 64% had received a prior anthracycline as adjuvant therapy compared with 55% in the docetaxel arm alone.

Tabulated List of Adverse Reactions in Breast Cancer for TAXELDO 75 mg/m² in Combination with Capecitabine

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions
Infections and Infestations		Oral candidiasis (G3/4: < 1%)
Blood and Lymphatic System Disorders	Neutropenia (G3/4: 63%); Anaemia (G3/4: 10%)	Thrombocytopenia (G3/4: 3%)
Metabolism and Nutrition Disorders	Anorexia (G3/4: 1%); Decreased appetite	Dehydration (G3/4: 2%)
Nervous System Disorders	Dysgeusia (G3/4: < 1%); Paraesthesia (G3/4: < 1%)	Dizziness; Headache (G3/4: < 1%); Neuropathy peripheral
Eye Disorders	Lacrimation increased	
Respiratory, Thoracic and Mediastinal Disorders	Pharyngolaryngeal pain (G3/4: 2%)	Dyspnoea (G3/4: 1%); Cough (G3/4: < 1%); Epistaxis (G3/4: < 1%)
Gastrointestinal Disorders	Stomatitis (G3/4: 18%); Diarrhoea (G3/4: 14%); Nausea (G3/4: 6%); Vomiting (G3/4: 4%); Constipation (G3/4: 1%); Abdominal pain (G3/4: 2%); Dyspepsia	Abdominal pain upper; Dry mouth
Skin and Subcutaneous Tissue Disorders	Hand-foot syndrome (G3/4: 24%); Alopecia (G3/4: 6%); Nail disorders (G3/4: 2%)	Dermatitis; Rash erythematous (G3/4: < 1%); Nail discolouration; Onycholysis (G3/4: 1%)
Musculoskeletal and Connective Tissue Disorders	Myalgia (G3/4: 2%); Arthralgia (G3/4: 1%)	Pain in extremity (G3/4: < 1%); Back pain (G3/4: 1%)
General Disorders and Administration Site Conditions	Asthenia (G3/4: 3%); Pyrexia (G3/4:1%); Fatigue/weakness (G3/4: 5%); Oedema peripheral (G3/4: 1%)	Lethargy; Pain
Investigations		Weight decreased; G3/4 Blood bilirubin increased (9%)

Tabulated List of Adverse Reactions in Prostate Cancer for TAXELDO 75 mg/m² in Combination with Prednisone or Prednisolone

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions
Infections and Infestations	Infection (G3/4: 3.3%)	
Blood and Lymphatic System Disorders	Neutropenia (G3/4: 32%); Anaemia (G3/4: 4.9%)	Thrombocytopenia (G3/4: 0.6%); Febrile neutropenia
Immune System Disorders		Hypersensitivity (G3/4: 0.6%)
Metabolism and Nutrition Disorders	Anorexia (G3/4: 0.6%)	
Nervous System Disorders	Peripheral sensory neuropathy (G3/4: 1.2%); Dysgeusia (G3/4: 0%)	Peripheral motor neuropathy (G3/4: 0%)
Eye Disorders		Lacrimation increased (G3/4: 0.6%)
Cardiac Disorders		Cardiac left ventricular function decrease (G3/4: 0.3%)
Respiratory, Thoracic and Mediastinal Disorders		Epistaxis (G3/4: 0%); Dyspnoea (G3/4: 0.6%); Cough (G3/4: 0%)
Gastrointestinal Disorders	Nausea (G3/4: 2.4%); Diarrhoea (G3/4: 1.2%); Stomatitis/Pharyngitis (G3/4: 0.9%); Vomiting (G3/4: 1.2%)	
Skin and Subcutaneous Tissue Disorders	Alopecia; Nail disorders (no severe)	Exfoliative rash (G3/4: 0.3%)
Musculoskeletal and Connective Bone Disorders		Arthralgia (G3/4: 0.3%); Myalgia (G3/4: 0.3%)

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions
General Disorders and Administration Site Conditions	Fatigue (G3/4: 3.9%); Fluid retention (severe: 0.6%)	

Tabulated List of Adverse Reactions in Breast Cancer for Adjuvant Therapy with TAXELDO 75 mg/m² in Combination with Doxorubicin and Cyclophosphamide in Patients with Node-positive (TAX 316) and Node-negative (GEICAM 9805) Breast Cancer – Pooled Data

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
Infections and Infestations	Infection (G3/4: 2.4%); Neutropenic infection (G3/4: 2.6%).		
Blood and Lymphatic System Disorders	Anaemia (G3/4: 3%); Neutropenia (G3/4: 59.2%); Thrombocytopenia (G3/4: 1.6%); Febrile neutropenia (G3/4: NA)		
Immune System Disorders		Hypersensitivity (G3/4: 0.6%)	
Metabolism and Nutrition Disorders	Anorexia (G3/4: 1.5%)		
Nervous System Disorders	Dysgeusia (G3/4: 0.6%); Peripheral sensory neuropathy (G3/4: < 0.1%)	Peripheral motor neuropathy (G3/4: 0%);	Syncope (G3/4: 0%) Neutrotoxiticy (G3/4: 0%); Somnolence (G3/4: 0%)
Eye Disorders	Conjunctivitis (G3/4: < 0.1%)	Lacrimation increased (G3/4: < 0.1%);	
Cardiac Disorders		Arrhythmia (G3/4: 0.2%);	
Vascular Disorders	Hot flush (G3/4: 0.5%)	Hypotension (G3/4: 0%) Phlebitis (G3/4: 0%)	Lymphoedema (G3/4: 0%)
Respiratory, Thoracic and Mediastinal Disorders		Cough (G3/4: 0%)	
Gastrointestinal Disorders	Nausea (G3/4: 5.0%); Stomatitis (G3/4: 6.0%); Vomiting (G3/4: 4.2%); Diarrhoea (G3/4: 3.4%); Constipation (G3/4: 0.5%)	Abdominal pain (G3/4: 0.4%)	
Skin and Subcutaneous Tissue Disorders	Alopecia (persisting < 3%); Skin disorder (G3/4: 0.6%); Nail disorders (G3/4: 0.4%)		
Musculoskeletal and Connective Tissue Disorders	Myalgia (G3/4: 0.7%); Arthralgia (G3/4: 0.2%)		
Reproductive System and Breast Disorders	Amenorrhoea (G3/4: NA)		
General Disorders and Administration Site Conditions	Asthenia (G3/4: 10.0%); Pyrexia (G3/4: NA); Oedema peripheral (G3/4: 0.2%)		
Investigations		Weight increased (G3/4: 0%) Weight decreased (G3/4: 0.2%)	

Description of Selected Adverse Reactions for Adjuvant Therapy with TAXELDO 75 mg/m² in Combination with Doxorubicin and Cyclophosphamide in Patients with Node- positive (TAX 316) and Node-negative (GEICAM 9805) Breast Cancer

Nervous System Disorders

In study TAX316 peripheral sensory neuropathy started during the treatment period and persisted into the follow-up period in 84 patients (11.3%) in TAC arm and 15 patients (2 %) in FAC arm. At the end of the follow-up period (median follow-up time of 8 years), peripheral sensory neuropathy was observed to be ongoing in 10 patients (1.3%) in TAC arm, and in 2 patients (0.3%) in FAC arm.

In GEICAM 9805 study peripheral sensory neuropathy that started during the treatment period persisted into the follow-up period in 10 patients (1.9%) in TAC arm and 4 patients (0.8 %) in FAC arm. At the end of the follow-up period (median follow-up time of 10 years and 5 months), peripheral sensory neuropathy was observed to be ongoing in 3 patients (0.6%) in TAC arm, and in 1 patient (0.2%) in FAC arm.

Cardiac Disorders
In study TAX316, 26 patients (3.5%) in the TAC arm and 17 patients (2.3%) in the FAC arm experienced congestive heart failure. All except one patient in each arm were diagnosed with CHF more than 30 days after the treatment period. Two patients in the TAC arm and 4 patients in the FAC arm died because of cardiac failure.
In GEICAM 9805 study, 3 patients (0.6 %) in TAC arm and 3 patients (0.6 %) in FAC arm developed congestive heart failure during the follow-up period. At the end of the follow-up period (actual median follow-up time of 10 years and 5 months), no patients had CHF in TAC arm and 1 patient in TAC arm died because of dilated cardiomyopathy, and CHF was observed to be ongoing in 1 patient (0.2%) in FAC arm.

Skin and Subcutaneous Tissue Disorders
In study TAX316, alopecia persisting into the follow-up period after the end of the chemotherapy was reported in 687 of 744 TAC patients (92.3%) and 645 of 736 FAC patients (87.6%).
At the end of the follow-up period (actual median follow-up time of 8 years), alopecia was observed to be ongoing in 29 TAC patients (3.9%) and 16 FAC patients (2.2%).

In GEICAM 9805 study, alopecia that started during the treatment period and persisted into the follow-up period was observed to be ongoing in 49 patients (9.2 %) in TAC arm and 35 patients (6.7 %) in FAC arm. Alopecia related to study drug started or worsened during the follow-up period in 42 patients (7.9 %) in TAC arm and 30 patients (5.8 %) in FAC arm. At the end of the follow-up period (median follow-up time of 10 years and 5 months), alopecia was observed to be ongoing in 3 patients (0.6%) in TAC arm, and in 1 patient (0.2%) in FAC arm.

Reproductive System and Breast Disorders
In TAX316 amenorrhoea that started during the treatment period and persisted into the follow-up period after the end of chemotherapy was reported in 202 of 744 TAC patients (27.2%) and 125 of 736 FAC patients (17.0%). Amenorrhoea was observed to be ongoing at the end of the follow-up period (median follow-up time of 8 years) in 121 of 744 TAC patients (16.3%) and 86 FAC patients (11.7%).

In GEICAM 9805 study, amenorrhoea that started during the treatment period and persisted into the follow-up period was observed to be ongoing in 18 patients (3.4 %) in TAC arm and 5 patients (1.0 %) in FAC arm. At the end of the follow-up period (median follow-up time of 10 years and 5 months), amenorrhoea was observed to be ongoing in 7 patients (1.3%) in TAC arm, and in 4 patients (0.8%) in FAC arm.

General Disorders and Administration Site Conditions
In study TAX316, peripheral oedema that started during the treatment period and persisted into the follow-up period after the end of chemotherapy was observed in 119 of 744 TAC patients (16.0%) and 23 of 736 FAC patients (3.1%). At the end of the follow- up period (actual median follow-up time of 8 years), peripheral oedema was ongoing in19 TAC patients (2.6%) and 4 FAC patients (0.5%).
In study TAX316 lymphoedema that started during the treatment period and persisted into the follow-up period after the end of chemotherapy was reported in 11 of 744 TAC patients (1.5%) and 1 of 736 FAC patients (0.1%). At the end of the follow-up period (actual median follow-up time of 8 years), lymphoedema was observed to be ongoing in 6 TAC patients (0.8%) and 1 FAC patient (0.1%).
In study TAX316 asthenia that started during the treatment period and persisted into the follow-up period after the end of chemotherapy was reported in 236 of 744 TAC patients (31.7%) and 180 of 736 FAC patients (24.5%). At the end of the follow-up period (actual median follow-up time of 8 years), asthenia was observed to be ongoing in 29 TAC patients (3.9%) and 16 FAC patients (2.2%).

In study GEICAM 9805 peripheral oedema that started during the treatment period persisted into the follow-up period in 4 patients (0.8%) in TAC arm and in 2 patients (0.4%) in FAC arm. At the end of the follow-up period (median follow-up time of 10 years and 5 months), no patients (0%) in TAC arm had peripheral oedema and it was observed to be ongoing in 1 patient (0.2%) in FAC arm.
Lymphoedema that started during the treatment period persisted into the follow-up period in 5 patients (0.9%) in TAC arm and 2 patients (0.4 %) in FAC arm. At the end of the follow-up period, lymphoedema was observed to be ongoing in 4 patients (0.8%) in TAC arm, and in 1 patient (0.2%) in FAC arm.
Asthenia that started during the treatment period and persisted into the follow-up period was observed to be ongoing in 12 patients (2.3 %) in TAC arm and 4 patients (0.8 %) in FAC arm. At the end of the follow-up period, asthenia was observed to be ongoing in 2 patients (0.4%) in TAC arm, and in 2 patients (0.4%) in FAC arm.

Acute Leukaemia/Myelodysplastic Syndrome
After 10 years of follow up in study TAX316, acute leukaemia was reported in 3 of 744 TAC patients (0.4%) and in 1 of 736 FAC patients (0.1%). One TAC patient (0.1%) and 1 FAC patient (0.1%) died due to AML during the follow-up period (median follow-up time of 8 years). Myelodysplastic syndrome was reported in 2 of 744 TAC patients (0.3%) and in 1 of 736 FAC patients (0.1%).

After 10 years of follow-up in GEICAM 9805 study, acute leukaemia occurred in 1 of 532 (0.2%) patients in TAC arm . No cases were reported in patients in FAC arm. No patient was diagnosed with myelodysplastic syndrome in either treatment groups.

Neutropenic Complications
Table below shows that the incidence of Grade 4 neutropenia, febrile neutropenia and neutropenic infection was decreased in patients who received primary G-CSF prophylaxis after it was made mandatory in the TAC arm – GEICAM study.

Neutropenic Complications in Patients Receiving TAC With or Without Primary G-CSF Prophylaxis (GEICAM 9805)

	Without Primary G-CSF Prophylaxis (n = 111) n (%)	**With Primary G-CSF Prophylaxis (n = 421) n (%)**
Neutropenia (Grade 4)	104 (93.7)	135 (32.1)
Febrile Neutropenia	28 (25.2)	23 (5.5)
Neutropenic Infection	14 (12.6)	21 (5.0)
Neutropenic Infection (Grade 3 – 4)	2 (1.8)	5 (1.2)

Tabulated List of Adverse Reactions in Gastric Adenocarcinoma Cancer for TAXELDO 75 mg/m² in combination with Cisplatin and 5-fluorouracil

MedDRA System Organ Classes	**Very Common Adverse Reactions**	**Common Adverse Reactions**
Infections and Infestations	Neutropenic infection; Infection (G3/4: 11.7%)	
Blood and Lymphatic System Disorders	Anaemia (G3/4: 20.9%); Neutropenia (G3/4: 83.2%); Thrombocytopenia (G3/4: 8.8%); Febrile neutropenia	
Immune System Disorders	Hypersensitivity (G3/4: 1.7%)	
Metabolism and Nutrition Disorders	Anorexia (G3/4: 11.7%)	
Nervous System Disorders	Peripheral sensory neuropathy (G3/4: 8.7%)	Dizziness (G3/4: 2.3%); Peripheral motor neuropathy (G3/4: 1.3%)
Eye Disorders		Lacrimation increased (G3/4: 0%)
Ear and Labyrinth Disorders		Hearing impaired (G3/4: 0%)
Cardiac Disorders		Arrhythmia (G3/4: 1.0%)
Gastrointestinal Disorders	Diarrhoea (G3/4: 19.7%); Nausea (G3/4: 16%); Stomatitis (G3/4: 23.7%); Vomiting (G3/4: 14.3%)	Constipation (G3/4: 1.0%); Gastrointestinal pain (G3/4: 1.0%); Oesophagitis/dysphagia/odynophagia (G3/4: 0.7%)
Skin and Subcutaneous Tissue Disorders	Alopecia (G3/4: 4.0%)	Rash pruritus (G3/4: 0.7%); Nail disorders (G3/4: 0.7%); Skin exfoliation (G3/4: 0%)
General Disorders and Administration Site Conditions	Lethargy (G3/4: 19.0%); Fever (G3/4: 2.3%); Fluid retention (severe/life-threatening: 1%)	

Description of Selected Adverse Reactions in Gastric Adenocarcinoma Cancer for TAXELDO 75 mg/m² in Combination with Cisplatin and 5-Fluorouracil

Blood and Lymphatic System Disorders
Febrile neutropenia and neutropenic infection occurred in 17.2% and 13.5% of patients respectively, regardless of G-CSF use. G-CSF was used for secondary prophylaxis in 19.3% of patients (10.7% of the cycles). Febrile neutropenia and neutropenic infection occurred respectively in 12.1% and 3.4% of patients when patients received prophylactic G-CSF, in 15.6% and 12.9% of patients without prophylactic G-CSF.

Tabulated List of Adverse Reactions in Head and Neck Cancer for TAXELDO 75 mg/m² in combination with cisplatin and 5-fluorouracil

- Induction chemotherapy followed by radiotherapy (TAX 323)

MedDRA System Organ Classes	**Very Common Adverse Reactions**	**Common Adverse Reactions**	**Uncommon Adverse Reactions**
Infections and Infestations	Infection (G3/4: 6.3%); Neutropenic infection		

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
Neoplasms Benign, Malignant and Unspecified (incl cysts and polyps)		Cancer pain (G3/4: 0.6%)	
Blood and Lymphatic System Disorders	Neutropenia (G3/4: 76.3%); Anaemia (G3/4: 9.2%); Thrombocytopenia (G3/4: 5.2%)	Febrile neutropenia	
Immune System Disorders		Hypersensitivity (no severe)	
Metabolism and Nutrition Disorders	Anorexia (G3/4: 0.6%)		
Nervous System Disorders	Dysgeusia/Parosmia; Peripheral sensory neuropathy (G3/4: 0.6%)	Dizziness	
Eye Disorders		Lacrimation increased; Conjunctivitis	
Ear and Labyrinth Disorders		Hearing impaired	
Cardiac Disorders		Myocardial ischemia (G3/4:1.7%)	Arrhythmia (G3/4: 0.6%)
Vascular Disorders		Venous disorder (G3/4: 0.6%)	
Gastrointestinal Disorders	Nausea (G3/4: 0.6%); Stomatitis (G3/4: 4.0%); Diarrhoea (G3/4: 2.9%); Vomiting (G3/4: 0.6%)	Constipation; Esophagitis/dysphagia/ odynophagia (G3/4: 0.6%); Abdominal pain; Dyspepsia; Gastrointestinal haemorrhage (G3/4: 0.6%)	
Skin and Subcutaneous Tissue Disorders	Alopecia (G3/4: 10.9%)	Rash pruritic; Dry skin; Skin exfoliative (G3/4: 0.6%)	
Musculoskeletal and Connective Tissue Disorders		Myalgia (G3/4: 0.6%)	
General Disorders and Administration Site Conditions	Lethargy (G3/4: 3.4%); Pyrexia (G3/4: 0.6%); Fluid retention; Oedema		
Investigations		Weight increased	

- Induction chemotherapy followed by chemoradiotherapy (TAX 324)

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
Infections and Infestations	Infection (G3/4: 3.6%)	Neutropenic infection	
Neoplasms Benign, Malignant and Unspecified (incl cysts and polyps)		Cancer pain (G3/4: 1.2%)	
Blood and Lymphatic System Disorders	Neutropenia (G3/4: 83.5%); Anaemia (G3/4: 12.4%); Thrombocytopenia (G3/4: 4.0%); Febrile neutropenia		
Immune System Disorders			Hypersensitivity
Metabolism and Nutrition Disorders	Anorexia (G3/4: 12.0%)		
Nervous System Disorders	Dysgeusia/Parosmia (G3/4: 0.4%); Peripheral sensory neuropathy (G3/4: 1.2%)	Dizziness (G3/4: 2.0%); Peripheral motor neuropathy (G3/4: 0.4%)	
Eye Disorders		Lacrimation increased	Conjunctivitis
Ear and Labyrinth Disorders	Hearing impaired (G3/4: 1.2%)		
Cardiac Disorders		Arrhythmia (G3/4: 2.0%)	Ischemia myocardial
Vascular Disorders			Venous disorder
Gastrointestinal Disorders	Nausea (G3/4: 13.9%); Stomatitis (G3/4: 20.7%); Vomiting (G3/4: 8.4%);	Dyspepsia (G3/4: 0.8%);	

MedDRA System Organ Classes	Very Common Adverse Reactions	Common Adverse Reactions	Uncommon Adverse Reactions
	Diarrhoea (G3/4: 6.8%); Esophagitis/dysphagia/ odynophagia (G3/4: 12.0%); Constipation (G3/4: 0.4%)	Gastrointestinal pain (G3/4: 1.2%); Gastrointestinal haemorrhage (G3/4: 0.4%)	
Skin and Subcutaneous Tissue Disorders, Musculoskeletal, Connective Tissue Bone Disorders	Alopecia (G3/4: 4.0%); Rash pruritic	Dry skin ; Desquamation Myalgia (G3/4: 0.4%)	
General Disorders and Administration Site Conditions	Lethargy (G3/4: 4.0%); Pyrexia (G3/4: 3.6%); Fluid retention (G3/4: 1.2%); Oedema (G3/4: 1.2%)		
Investigations	Weight decreased		Weight increased

Post-marketing Experience

Neoplasms Benign, Malignant and Unspecified (incl. cysts and polyps)

Second primary malignancies (frequency not known), including non-Hodgkin lymphoma have been reported in association with docetaxel when used in combination with other anticancer treatments known to be associated with second primary malignancies. Acute myeloid leukemia and myelodysplastic syndrome have been reported (frequency uncommon) in pivotal clinical studies in breast cancer with TAC regimen.

Blood and Lymphatic System Disorders

Bone marrow suppression and other haematologic adverse reactions have been reported. Disseminated intravascular coagulation (DIC), often in association with sepsis or multiorgan failure, has been reported.

Immune System Disorders

Some cases of anaphylactic shock, sometimes fatal, have been reported.

Hypersensitivity reactions (frequency not known) have been reported with docetaxel in patients who previously experienced hypersensitivity reactions to paclitaxel.

Nervous System Disorders

Rare cases of convulsion or transient loss of consciousness have been observed with docetaxel administration. These reactions sometimes appear during the infusion of the medicinal product.

Eye Disorders

Very rare cases of transient visual disturbances (flashes, flashing lights, scotomata) typically occurring during infusion of the medicinal product and in association with hypersensitivity reactions have been reported. These were reversible upon discontinuation of the infusion. Cases of lacrimation with or without conjunctivitis, as cases of lacrimal duct obstruction resulting in excessive tearing have been rarely reported. Cases of cystoid macular oedema (CMO) have been reported in patients treated with docetaxel.

Ear and Labyrinth Disorders

Rare cases of ototoxicity, hearing impaired and/or hearing loss have been reported.

Cardiac Disorders

Rare cases of myocardial infarction have been reported.

Ventricular arrhythmia including ventricular tachycardia (frequency not known), sometimes fatal, has been reported in patients treated with docetaxel in combination regimens including doxorubicin, 5-fluorouracil and/ or cyclophosphamide.

Vascular Disorders

Venous thromboembolic events have rarely been reported.

Respiratory, Thoracic and Mediastinal Disorders

Acute respiratory distress syndrome and cases of interstitial pneumonia/ pneumonitis, interstitial lung disease, pulmonary fibrosis and respiratory failure sometimes fatal have rarely been reported. Rare cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy.

Gastrointestinal Disorders
Rare cases of enterocolitis, including colitis, ischemic colitis, and neutropenic enterocolitis, have been reported with a potential fatal outcome (frequency not known). Rare occurrences of dehydration as a consequence of gastrointestinal events, including enterocolitis and gastrointestinal perforation have been reported. Rare cases of ileus and intestinal obstruction have been reported.

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

Skin and Subcutaneous Tissue Disorders
Cases of cutaneous lupus erythematosus, bullous eruptions such as erythema multiforme and severe cutaneous adverse reactions such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and acute generalized exanthematous pustulosis (AGEP), have been reported with docetaxel. Scleroderma-like changes usually preceded by peripheral lymphoedema have been reported with docetaxel. Cases of permanent alopecia (frequency not known) have been reported.

Renal and Urinary Disorders
Renal insufficiency and renal failure have been reported. In about 20% of these cases there were no risk factors for acute renal failure such as concomitant nephrotoxic medicinal products and gastro-intestinal disorders.

General Disorders and Administration Site Conditions
Radiation recall phenomena have rarely been reported.
Injection site recall reaction (recurrence of skin reaction at a site of previous extravasation following administration of docetaxel at a different site) has been observed at the site of previous extravasation (frequency not known).
Fluid retention has not been accompanied by acute episodes of oliguria or hypotension.
Dehydration and pulmonary oedema have rarely been reported.

Metabolism and nutrition disorders
Cases of electrolyte imbalance have been reported. Cases of hyponatraemia have been reported, mostly associated with dehydration, vomiting and pneumonia. Hypokalaemia, hypomagnesaemia, and hypocalcaemia were observed, usually in association with gastrointestinal disorders and in particular with diarrhoea. Tumour lysis syndrome, potentially fatal, has been reported (frequency not known).

Musculoskeletal disorder
Myositis has been reported with docetaxel (frequency not known).

SYMPTOMS AND TREATMENT OF OVERDOSE
Overdose
There were a few reports of overdose. There is no known antidote for docetaxel overdose. In case of overdose, the patient should be kept in a specialised unit and vital functions closely monitored. In cases of overdose, exacerbation of adverse events may be expected. The primary anticipated complications of overdose would consist of 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.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
No studies on the effects on the ability to drive and use machines have been performed. The amount of alcohol in this medicinal product and the side effects of the product may impair the ability to drive or use machines. Therefore, patients should be warned of the potential impact of the amount of alcohol and the side effects of this medicinal product on the ability to drive or use machines, and be advised not to drive or use machines if they experience these side effects during treatment.

INSTRUCTIONS FOR USE
TAXELDO is an antineoplastic agent and, as with other potentially toxic compounds, caution should be exercised when handling it and preparing TAXELDO solutions. The use of gloves is recommended.
If TAXELDO concentrate or infusion solution should come into contact with skin, wash immediately and thoroughly with soap and water. If TAXELDO concentrate or infusion solution should come into contact with mucous membranes, wash immediately and thoroughly with water.

TAXELDO (Docetaxel Concentrate for Solution for Infusion 20mg/ml)

Preparation for the Intravenous Administration

Preparation of the Infusion Solution

DO NOT use other docetaxel medicinal products consisting of 2 vials (concentrate and solvent) with this medicinal product (TAXELDO 20 mg/1 ml concentrate for solution for infusion, which contains only 1 vial, TAXELDO 80 mg/4 ml concentrate for solution for infusion, which contains only 1 vial, TAXELDO 160 mg/8 ml concentrate for solution for infusion, which contains only 1 vial).

TAXELDO 20 mg/1 ml concentrate for solution for infusion, TAXELDO 80 mg/4 ml concentrate for solution for infusion and TAXELDO 160 mg/8 ml concentrate for solution for infusion require NO prior dilution with a solvent and are ready to add to the infusion solution.

Each vial is of single use and should be used immediately.

If the vials are stored under refrigeration, allow the required number of boxes of TAXELDO concentrate for solution for infusion to stand below 25°C for 5 minutes before use.

More than one vial of TAXELDO concentrate for solution for infusion may be necessary to obtain the required dose for the patient. Aseptically withdraw the required amount of TAXELDO concentrate for solution for infusion using a calibrated syringe fitted with a 21G needle.

In TAXELDO 20 mg /1 ml vial, TAXELDO 80 mg/4 ml vial and TAXELDO 160 mg/8 ml vial, the concentration of docetaxel is 20 mg/ml.

The required volume of TAXELDO concentrate for solution for infusion must be injected via a single injection (one shot) into a 250 ml infusion bag or bottle containing either 5% glucose solution or sodium chloride 9 mg/ml (0.9%) solution for infusion.

If a dose greater than 190 mg of docetaxel is required, use a larger volume of the infusion vehicle so that a concentration of 0.74 mg/ml docetaxel is not exceeded.

Mix the infusion bag or bottle manually using a rocking motion.

The infusion bag solution should be used within 6 hours below 25°C including the one-hour infusion to the patient.

As with all parenteral products, TAXELDO infusion solution should be visually inspected prior to use, solutions containing a precipitate should be discarded.

Any unused product or waste material should be disposed of in accordance with local requirements.

List of Excipients

Polysorbate 80

Ethanol Anhydrous

PACKAGING AVAILABLE:

Pack size 20 mg/1 mL

One vial of 5mL of glass vial with rubber stopper and flip off seal. 1 vial is packed into a paper outer carton with a piece of package insert.

Pack size 80 mg/4 mL

One vial of 5mL of glass vial with rubber stopper and flip off seal. 1 vial is packed into a paper outer carton with a piece of package insert.

Pack size 160 mg/8 mL

One vial of 15mL of glass vial with rubber stopper and flip off seal. 1 vial is packed into a paper outer carton with a piece of package insert

Each box contains one vial.

STORAGE CONDITION & SHELF LIFE

Unopened vial

Store under refrigeration between 2-8°C. Protect from light.

After opening of the vial

Each vial is for single use and should be used immediately after opening. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Once added to the infusion bag

From a microbiological point of view, reconstitution/dilution must take place incontrolled and aseptic conditions and the medicinal product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Once added as recommended into the infusion bag, the docetaxel infusion solution, if stored below 25°C, is stable for 6 hours. It should be used within 6 hours (including the one hour infusion IV administration).

In addition, physical and chemical in-use stability of the infusion solution prepared as recommended has been demonstrated in non-PVC bags up to 24 hours when stored between 2 to 8°C.

Font size: 7

TAXELDO (Docetaxel Concentrate for Solution for Infusion 20mg/ml)

Docetaxel infusion solution is supersaturated, therefore may crystallize over time. If crystals appear, the solution must no longer be used and shall be discarded.

NAME AND ADDRESS OF MANUFACTURER
Hetero Labs Limited
Unit VI, Sy. No. 410 & 411, TSIIC,
Pharma SEZ, Polepally Village,
Jadcherla Mandal, Mahaboob Nagar District,
Telangana - 509301, India.

PRODUCT REGISTRATION HOLDER
CAMBER LABORATORIES SDN BHD
Unit E-13A-02, Menara SUEZCAP 2, No. 2, KL Gateway,
Jalan Kerinchi, Gerbang Kerinchi Lestari,
59200 Kuala Lumpur, Malaysia.

DATE OF REVISION
11 November 2024

Font size: 7