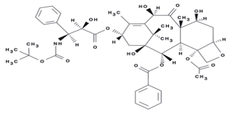
DOCETAXEL KEMEX
Docetaxel 20 mg/0.5 ml and 80 mg/2.0 ml
Injectable Solution
FOR INTRAVENOUS USE ONLY
Rx Only

Formula
Each vial contains:
DOCETAXEL KEMEX 20 mg/0.5 ml
Docetaxel..... 20.00 mg
Polisorbate 80 q.s..... 0.50 ml
Each vial of solvent for docetaxel 20 mg contains:
Absolute Ethanol..... 0.185 ml
Water for injection q.s..... 1.5 ml
DOCETAXEL KEMEX 80 mg/2.0 ml
Docetaxel..... 80.00 mg
Polisorbate 80 q.s..... 2.00 ml
Each vial of solvent for docetaxel 80 mg contains:
Absolute Ethanol..... 0.74 ml
Water for injection q.s..... 6.0 ml

Therapeutic action
Antineoplastic.

Properties
Pharmaco-therapeutic class: cytostatic (L: antineoplastic and inmunomodulating agent).
Docetaxel is an antineoplastic agent that acts by promoting the assembly of tubulin into stable microtubules and inhibits their disassembly wich 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 wich is essential for vital mitotic and interface cellular functions. Docetaxel was found to be cytotoxic in vitro against various murine and human tumor cell lines and against freshly excised human tumor cells in clonogenic assays. Docetaxel achieves high intracellular concentrations with a long cell residence time. Docetaxel was found to be active on some but not all cell lines overexpressing the p-glycoprotein which is encoded by the multidrug resistance gene.
At doses of 20 to 115 mg/m2 in Phase I studies, the kinetic profile of docetaxel is dose independent and consistent with a three-compartment pharmacokinetics model, with half-lives for the a, b, and d phases of 4 min, 36 min, and 11.1 hr, respectively. Following the administration of a 100 mg/m2 dose given as a one-hour infusion a mean peak 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 l/h/m2 and 113 l, respectively. A population pharmacokinetic analysis has been performed in 577 patients receiving docetaxel. . 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. In a small number of patients (n=23) with clinical chemistry data suggestive of mild to moderate liver function impairment (Alanine transaminase (ALT), Aspartate transaminase (AST) >1.5 times the upper limit of normal (ULN) associated with alkaline phosphatase >2.5 times the upper limit of normal), total clearance was lowered by 27% on average (see "how should this drug be used").
Docetaxel is more than 95% protein bound. Docetaxel was eliminated in both the urine and feces following cytochrome P450-mediated oxidative metabolism of the tert-butyl ester group within 7 days. When used in combination, docetaxel does not influence the clearance of doxorubicin and the plasma levels of doxorubicinol (a doxorubicin metabolite). On the other hand, the clearance of docetaxel was increased while the efficacy is maintained. Phase I studies evaluating the effect of capecitabine on the pharmacokinetics of docetaxel and the effect of docetaxel on the pharmacokinetics of capecitabine showed no effect by capecitabine on the pharmacokinetics of docetaxel (Cmax and AUC) and no effect of docetaxel on the pharmacokinetics of 5'-DFUR (the most important metabolite of capecitabine).
Clearance of docetaxel in combination therapy with cisplatin or carboplatin 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.



When should this drug be used (Therapeutic Indications)
Breast cancer: DOCETAXEL KEMEX 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.
DOCETAXEL KEMEX monotherapy is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of cytotoxic therapy. Previous chemotherapy should have included an anthracycline or an alkylating agent.
DOCETAXEL KEMEX 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.
Non-small cell lung cancer: DOCETAXEL KEMEX is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior chemotherapy.
DOCETAXEL KEMEX 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. DOCETAXEL KEMEX in combination with carboplatin represents a treatment option to cicplatin-beased therapy.
Ovarian cancer: DOCETAXEL KEMEX is indicated for the treatment of patients whit metastatic carcinoma of the ovary after failure of first-line or subsequent chemotherapy.
How should this drug be used
Recommended dosage
The recommended dosage of docetaxel in breast cancer and ovarian cancer is 100 mg/m2 administered as a one-hour infusion every three weeks. The recommended dosage of docetaxel, is 75 mg/m2 every three weeks, when combined with capecitabine administered orally at a dose of 1250 mg/m2 twice daily (within 30 minutes after a meal) for 2 weeks followed by 1 - week rest period. For capecitabine dose calculation according to body surface area, see local package insert. In first-line treatment for breast cancer, docetaxel 75 mg/m2 is given in combination therapy with doxorubicin (50 mg/m2) administered as a one-hour infusion every three weeks.
In non-small cell lung cancer, docetaxel is administered as a one-hour intravenous infusion every three weeks.
For chemotherapy naïve patients, the recommended dose regimen of docetaxel is 75 mg/m2 immediately followed by cisplatin 75 mg/ m2 over 30-60 minutes or carboplatin (AUC 6 mg/ml/min) over 30-60 minutes. For treatment after failure of prior platinum-based chemotherapy, the recommended dosage is 75 mg/m^2 as a single agent.

Premedication regimen
In order to reduce the incidence and severity of fluid retention, all patients should be pretreated with oral corticosteroids. A premedication consisting only of oral corticosteroids, such as dexamethasone 16 mg/day (e.g., 8 mg BID) for 3 days starting one day prior to each docetaxel administration unless contraindicated, can be used.

Dosage adjustments
Monotherapy for breast cancer:
Patients with neutropenia, cutaneous reactions or neurosensory signs: like many others chemotherapeutic agents, careful monitoring of neutrophils counts is an essential part of docetaxel therapy. Docetaxel should not be administered until the neutrophil count is at least > 1,500 cells/mm3. Patients who experienced either febrile neutropenia, (neutrophil < 500 cells/mm3 for more than one week) severe or cumulative cutaneous reactions or severe neurosensory signs during docetaxel therapy should have the dosage of docetaxel reduced from 100 mg/m2 to 75 mg/m2 . If these reactions persist, the dosage should be decreased from 75 mg/m2 to 60 mg/m^2, the treatment should be discontinued.
Combination therapy with capecitabine for breast cancer
For capecitabine dose modifications, when combined with docetaxel, see local package insert.
For patients developing the first appearance of a Grade 2 toxicity, which persists at the time of the next DOCETAXEL KEMEX / 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 a Grade 2 toxicity, or the first appearance of a Grade 3 toxicity, at any time during the treatment cycle, delay treatment until resolved to Grade 0- 1, then resume treatment with DOCETAXEL KEMEX 55 mg/m^2. For any subsequent appearances of toxicities, or any Grade 4 toxicities, discontinue the DOCETAXEL KEMEX dose.
For docetaxel dose modifications due to hepatic impairment, see precaution sections.
Combination therapy with cisplatin/carboplatin for NSCLC
For patients who are dosed initially at docetaxel 75 mg/m2 in combination with cisplatin or carboplatin and whose nadir of platelet count during the previous course of therapy is <25000 cells/mm3 (with cisplatin) and <75000 cells/mm3 (with carboplatin) or in patients who experience febrile neutropenia, or in patients with severe non-hematologic toxicities, the docetaxel dosage in subsequent cycles should be reduced to 65 mg/m2. For cisplatin dosage adjustments, see local package insert.
Alternatively, prophylactic G-CSF may be used in patients who experience febrile neutropenia or severe infection during last cycle to be able to maintain dose intensity as clinically indicated. Patients with liver impairment: Based on pharmacokinetic data with docetaxel at 100 mg/m^2 as single agent, patients who have both elevations of transaminase values (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/m2 (see sections "Warnings and precautions"). For those patients with serum bilirubin grater than the ULN and/or ALT and AST grater than 3.5 times the ULN associated with alkaline phosphatase grater than 6 times the ULN, no dose-reduction 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.
Children: The safety and effectiveness of docetaxel in children have not been established.
Elderly: Based on a population pharmacokinetic analysis, there are no special instructions for use in the elderly. Fro capecitabine dosage reduction when combined with docetaxel, see local package insert.

Administration precautions
DOCETAXEL KEMEX must be administered intravenously. It is extremely important that the intravenous catheter by properly positioned before any DOCETAXEL KEMEX is injected. Leackage into surrounding tissue during intravenous administration of DOCETAXEL KEMEX may cause considerable irritation, local tissue necrosis and/or thrombophlebitis. If extravasation occurs, the injection should be discontinued immediately, and any remaining portion of the dose should be introduced into another vein.
When should this drug not be used (contraindications)
Docetaxel is contraindicated in patients
•who have a history of severe hypersensitivity reactions to docetaxel or to other drugs formulated with polysorbate 80.
•with baseline neutrophil counts of < 1500 cells/mm3.
•In pregnant or breast feeding women
•With severe liver impairment since there is no data available (see "Warnings and Precautions" and "How should this drug be used")
Contraindications for other drugs also apply when combined with docetaxel.

Warnings and precautions
The use of docetaxel should be confined to units specialized in the administration of cytotoxic chemotherapy and it should only be administered under supervision of a physician qualified in the use of anticancer chemotherapy. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.
Hematology: 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/mm3 (See "How should this drug be used"). In the case of severe neutropenia (<500 cells/mm3 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 (see How should this drug be used").
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. Severe reactions, characterized by hypotension, bronchospasm or generalized rash/erythema require immediate discontinuation of docetaxel. Severe symptoms resolve after discontinuation of the infusion and administration of appropriate therapy.
Cutaneous: localized erythema of the extremities (palms of the hands and soles of the feet) with edema followed by desquamation has been observed. In case of severe skin toxicity during a course of docetaxel therapy, a reduction in dose for subsequent courses of therapy is recommended (see "How should this drug be used").
Fluid retention: Patients with severe fluid retention such as pleural effusion, pericardial effusion and ascites should be monitored closely.
Patients with liver impairment: In patients treated with docetaxel at 100 mg/m2 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. The recommended dose of docetaxel in patients with elevated liver function test (LFTs) is 75 mg/m2 and LFTs should be measured at baseline and before each cycle (see "How should this drug be used"). For patients with serum bilirrubin 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.
No data are available in patients with hepatic impairment treated by docetaxel in combination.
Nervous system: The development of severe peripheral neurosensory signs requires a reduction of dose (see "How should this drug be used").
Elderly: an analysis of safety data in patients equal to or grater than 60 years of age treated with docetaxel plus capecitabine combination therapy showed an increased in the incidence of treatment related Grade3-4 adverse events, treatment related serious adverse events and early withdrawals from treatment due to the adverse events compared to patients less than 60 years of age. See local package insert for additional precautions related to the administration of capecitabine.
In the study conducted in chemotherapy-naïve patients with non-small cell lung cancer, 148 patients in the docetaxel plus cisplatin group were 65 years of age or grater, and 15 patients were 75 years of age and grater; in these patients, no overall difference in effectiveness were observed compared to younger patients. In elderly p0atients in the docetaxel plus cisplatin group, there was a trend toward more diarrhea and grade 3-4 events of neurotoxicity with respect to frequency and severity in comparison to the vinorelvine plus cisplatin group. In the docetaxel plus carboplatin group, 114 patients were 65 years of age or grater, and 15 patients were 75 years of age or grater; in this group there was a trend toward more diarrhea and grade 3-4 infections, and a trend toward less nausea/vomiting, neurotocicity and neurosensory events in comparison to the vinorelvine plus cisplatin group.
Carcinogenicity, Mutagenicity, Impairment of Fertility: the carcinogenic potential of Docetaxel has not been studied. Docetaxel has been shown to be mutagenic in the in vitro chromosome aberration test in CHO-K cells and in vivo micronucleus test in the mouse. However, it did not induce mutagenicity in the Ames test or the CHO-HGPRT gene mutation assays. These results are consistent with the pharmacological activity of docetaxel. Docetaxel has been shown to be both embryotoxic and fetotoxic in rabbits and rats, and to reduce fertility in rats.
Others: Contraceptive measures must be taken during and for at least three months after cessation of therapy.

Overdosage
There were a few reports of overdose. In case of overdose, the patient should be kept in a specialized unit where vital functions can be closely monitored and supportive treatment administered as necessary. There is no known antidote for docetaxel overdose. Anticipated complications of overdose include: bone marrow suppression, peripheral neurotoxicity and mucositis. Patients should receive therapeutic G-CSF as soon as possible after discovery of overdose. Other appropriate symptomatic measures should be taken, as needed.
Interactions
In vitro studies have shown that the metabolism of docetaxel may be modified by the concomitant administration of compounds which induce, inhibit or are metabolized by (and thus may inhibit the enzyme competitively) cytochrome P450-3A such as ciclosporine, terfenadine, ketoconazole, erythromycin and troleandomycin. As a result, caution should be exercised when treating patients with these drugs as concomitant therapy since there is a potential for a significant interaction. Although the possible in vivo interaction of docetaxel with concomitantly administered medication has not been investigated formally, in vitro interactions with tightly protein-bound drugs 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. In the doxorubicin/-docetaxel combination, the clearence of docetaxel was increased.
In the event of an overdose attend the nearest hospital or contact the Center for Toxicology.
Hospital de Niños Ricardo Gutiérrez.
Mark 011 if you live in the interior
(011) 4821-6666
Sánchez de Bustamante 1399 Capital Federal.
Specialty for adults:
Hospital Posadas.
Mark 011 if you live in the interior
(011) 4654-6648

Undesirable effect
The adverse reactions considered to be possibly or probably related to the administration of docetaxel have been obtained from patients treated by docetaxel as single agent or in combination, with normal LFT´s at baseline. Among the patients who received docetaxel in monotherapy, 1312 patients received 100 mg/m^2 and 121 patients received 75 mg/m^2 of docetaxel; furthermore 258 patients received 75 mg/m^2 of docetaxel with 50 mg/m^2 of doxorubicin. These reactions were described using NCI Common Toxicity Criteria and the COSTART terms.
Hematology: Bone marrow suppression and other hematologic adverse reactions to docetaxel included: Neutropenia, wich was the most frequent reaction (in patients who did not received G-CSF). And wich was reversible and not cumulative. The median day to nadir was 7 days and the median duration of severe neutropenia was 7 days. Febrile neutropenia, severe infections associated with neutrophil counts 500 cells/mm3 infectious episodes (including sepsis and pneumonia) that may be fatal, thrombocytopenia, leeding episodes and anemia were also reported.
Hypersensitivity reactions: Hypersensitivity reactions occurred generally within a few minutes following the start of the infusion of docetaxel and were usually mild to moderate. The most frequent manifestations were flushing, rash with or without pruritus, chest tightness, back pain, dyspnoea and drug fever or chills. Severe reactions, resolved after discontinuing the infusion and appropriate therapy.
Cutaneous: reversible cutaneous reactions were generally mild to moderate. Reactions were characterised by a rash including localized eruptions mainly on the feet and hands, 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. Nails disorders ware characterised by hypo- or hyperpigmentation pain and onycholysis. Very rare cases of bullous eruption such as erythema multiforme or Stevens-Johnson syndrome have been reported with docetaxel and other concomitant factors may have contributed to the development of these effects.
Fluid retention Events such as peripheral edema and less frequently pleural effusion, pericardial effusion, ascites and weight gain have been reported. The peripheral edema usually starts at the lower extremities and may become generalized with a weight gain of 3 kg or more. Fluid retention is cumulative in incidence and severity. In patients treated with docetaxel as a single agent at 100 mg/m2 the median cumulative dose to treatment discontinuation was more than 1,000 mg/m2 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/m2) in patients with premedication compared with patients without premedication (median cumulative dose: 489.7 mg/m2); however, it has been reported in some patients during the early courses of therapy. Fluid retention has not been accompanied by acute episodes of oliguria or hypotension. Dehydration and pulmonary oedema have rarely been reported.
Gastrointestinal the following gastrointestinal effects have been reported: nausea, vomiting, diarrhea, abdominal pain, anorexia, constipation, stomatitis, esophagitis, taste perversion, and gastrointestinal bleeding. Rare occurrences of dehydratation as a consequence of gastrointestinal events, gastrointestinal perforation, ischemic colitis, colitis and neutropenic enterocolitis have been reported. Very rare cases of ileous an dintestinal obstruction have been reported.
Neurologic Mild to moderate neurosensory signs and/or symptoms heve been reported.
Severe neurosensory symptoms characterized by paresthesia, dysesthesia or pain (including burning) were observed. Neuromotor events are mainly characterised by weakness. When these symptoms occur, dosage may be adjusted. If symptoms persist treatment should be discontinued. Rare cases of convulsion or transient loss of consciousness have been observed with docetaxel administration. These reactions sometimes appear during the infusion of the drug.
Cardiovascular the cardiovascular events consisted in: hypotension, dysrhytmia, hypertension and heart failure. Rare occurrences of venous thromboembolic events and myocardial infarction have been reported.
Hepatic in patients treated at 100 mg/m2 as single agent, increases in serum levels of ALT, AST, billirrubin, and alkaline phosphatase, wich where grater than2.5 times the ULN, were observed. Very rare case of hepatitis have been reported.
Others: alopecia, asthenia, arthralgia, myalgia, dyspnea, and generalized or localized pain, including chest pain without any cardiac or respiratory involvement have been reported. Rare cases of lacrimation with or without conjunctivitis have been reported and very rare cases of lacrimal duct obstruction resulting in excessive tearing have been reported primarly in patients receiving other anti-tumor agents concomitantly. Infusion site reactions were generally mild and consisted of hyperpigmentation, inflamation, redness or dryness syndrome, interstitial pneumonia, pulmonary fibrosis and radiation recall phenomena have rarely been reported.
Overall the adverse events pattern observed in the patients treated with docetaxel combination with doxorubicin is similar with that of those treated with docetaxel in monotherapy.

Sumary of adverse events in patients receiving decetaxel al 100 mg/m2 and at 75 mg/m2 and docetaxel in combination with doxorubicin 50 mg/m2

	% PATIENTS		
	Single agent		Combination with Doxorubicin 50 mg/m^2
	100 mg/ m^2	75 mg/ m^2	75 mg/ m^2
Hematologic			
Neutropenia			
All	96.6	89.8	99.2
Severe*	76.4	54.2	91.7
Febrile neutropenia	11.8	8.3	4.1
Thrombocytopenia			
All	7.8	10.0	28.1
Severe	0.2	1.7	0.8
Anemia			
All	90.4	93.3	96.1
Severe**	8.9	10.8	9.4
Infections			
All	20.0	10.7	35.3
Severe**	5.7	5.0	7.8
*NCI grade 4			
**NCI grade 3-4			
Hipersensitivity reactions			
All	25.9	2.5	4.7
Severe*	5.3	0	1.2
*NCI grade 3-4			
Cutaneous			
Cutaneous			
All	56.6	15.7	13.6
Severe*	5.9	0.8	0
Nail change			
All	27.9	9.9	20.2
Severe	2.6	0.8	0.4
* NCI grade 3-4			
Fluid retention			
All	64.1	24.8	35.7
Severe	6.5	0.8	1.2
Gastrointestinal			
Nausea			
All	40.5	28.9	64.0
Severe*	4	3.3	5.0
Vomiting			
All	24.5	16.5	45.0
Severe*	3	0.8	5.0
Diarrhea			
All	40.6	11.6	45.7
Severe*	4	1.7	6.2
Anorexia	16.8	19.0	8.5
Constipation	9.8	6.6	14.3
Stomatitis			
All	41.8	24.8	58.1
Severe*	5.3	1.7	7.8
*NCI grade 3-4			
Neurologic			
Neurosensory			
All	50.0	24.0	30.2
Severe*	4.1	0.8	0.4
Neuromotor			
All	13.8	9.9	2.3
Severe**	4.0	2.5	0.4
*NCI grade 3			
**NCI grade 3-4			
Cardiovascular			
Hypotension	3.8	1.7	0.4
Cardiac Dysrhythmia			0
All	4.1	2.5	1.2
Severe*	0.7	0	0
Heart failure	0.5	0	2.3
*NCI grade 3-4			
Hepatic			
AST increase: severe*	< 3.0	0	< 1.0
ALT increase: severe*	< 2.0	0	< 1.0
Bilirubin increase: severe *	< 5.0	< 2.0	< 2.5
Alkaline phosphatase increase: severe *	< 4.0	0	< 2.5
*NCI grade 3-4			

Combination therapy with docetaxel in Non-small cell lung cancer

The adverse reactions considered to be possibly or probably related to the administration of docetaxel in combination with cisplatin or carboplatin (except for the hematologic toxicities or as otherwise noted) have been obtained from 807 patients with unresectable stage IIIB or IV non-small cell lung cancer and no history of prior chemotherapy. These reactions were described using NCI common toxicity criteria and the COSTART terms.

ADVERSE EVENT	DOCETAXEL 75 MG/M2 + CISPLATIN 75 MG/M2 %	DOCETAXEL 75 MG/M2 + CARBOPLATIN (AUC 6 MG/ML/MIN) %
Hematology		
Neutropenia****		
Any	91.1	85.8
Grade 3/4	74.8	74.4
Anemia		
Any	88.6	89.5
Grade 3/4	6.9	10.5
Thrombocytopenia***		
Any	14.9	25.1
Grade 3/4	2.7	7.0
Infections		
Any	14.3	19.5
Grade 3/4	5.7	7.7
Fever in the absence of infection		
Any	17.2	16.5
Grade 3/4	1.2	0.5
Febrile Neutropenia***	4.9	3.7
Hypersensitivity reactions*		
Any	10.6	10.2
Grade 3/4	2.5	2.0
Cutaneous		
Nail disorder**		
Any	13.3	9.7
All severe	0.7	0.0
Skin		
Any	11.1	14.0
Grade 3/4	0.2	0.2
Fluid retention**		
Any	25.9	18.7
All severe	0.7	1.0
Gastrointestinal		
Nausea/Vomiting		
Any	73.9	55.6
Grade 3/4	12.1	7.0
Diarrhea		
Any	41.1	29.7
Grade 3/4	6.4	4.5
Anorexia**		
Any	28.8	19.7
All severe	4.9	2.5
Stomatitis		
Any	23.4	24.7
Grade 3/4	2.0	0.2
Constipation	9.4	6.5
Neurologic		
Neurosensory		
Any	40.4	22.9
Grade 3/4	3.7	0.7
Neuromotor		
Any	12.8	10.2
Grade 3/4	2.0	2.0
Others		
Alopecia		
Any	73.6	68.3
Grade 3/4 not is ISS	0.7	1.0
Asthenia**		
Any	51.5	45.9
All severe	9.9	6.7
Myalgia**		
Any	13.8	12.2
All severe	0.5	0.5
Infusion site reactions	6.2	6.7
Pain	5.4	6.2

* Repalces NCI term "Allergy"
** COSTART term and grading system
*** Incidences are presented as regardless of relationship
- Cycles where patients received G-CSF were considerer not evaluable for neutropenia, unless neutropenia was equal to Grade 4.

Combination therapy with capecitabine for breast cancer
For the docetaxel plus capecitabine therapy, the most frequent treatment related undesirable effects (≥5%) reported in a Phase III trial in breast cancer patients failing anthracycline treatment are presented in the following table:

Summary of at least remotely related adverse events reported in ≥ 5% of patients treated with docetaxel and capecitabine in combination

	Capecitabine 1250 mg/m2 twice daily with docetaxel 75 mg/m2/3 weeks (N=251)	
Body system	**Total**	**Grade 3 / 4**
Adverse event	%	%
Gastrointestinal		
Stomatitis	67	18
Diarrhea	64	14
Nausea	43	6
Vomiting	33	4
Constipation	14	1
Abdominal pain	14	2
Dyspepsia	12	-
Abdominal pain upper	9	-
Dry mouth	5	-
Skin and subcutaneous		
Hand-foot syndrome*	63	24
Alopecia	41	6
Nail disorder	14	2
Dermatitis	8	-
Rash erythematous	6	< 1
Nail discoloration	6	-
Onycholysis	5	1
General		
Asthenia	23	3
Pyrexia	21	1
Fatigue	21	4
Weakness	13	1
Pain in limb	9	< 1
Lethargy	6	-
Pain	6	-
Neurological		
Taste disturbance	15	< 1
Paresthesia	11	< 1
Dizziness	9	-
Headhache	7	< 1
Peripheral neuropathy	5	-
Metabolism		
Anorexia	12	1
Appetite decreased	10	-
Dehydration	8	2
Weight decreased	6	-
Eye		
Lacrimation increased	12	-
Musculoskeletal		
Myalgia	14	2
Arthralgia	11	1
Back pain	7	1
Cardiovascular		
Lower limb oedema	14	1
Respiratory		
Sore throat	11	2
Dyspnea	7	1
Cough	6	< 1
Epistaxis	5	< 1
Infection		
Oral candidiasis	6	< 1

-Not observed
* Grade 3 only

Frequent grade 3 and 4 laboratory abnormalities were:

Adverse Event	Capecitabine 1250 mg/m2/bid with docetaxel 75 mg/m2/3 weeks (n=251)
Laboratory Abnormalities (according to NCIC/CTC)	**Grade 3 / 4** %
Neutropenia	63
Anemia	10
Thrombocytopenia	3
Hyperbilirubinemia	9

Storage
Store refrigerated at a temperature between 2 and 8 °C. Protect from bright light.
The pre-mixed solution of docetaxel (10 mg of docetaxel/ml) and the fully prepared docetaxel infusion solution (in 0.9% sodium chloride solution or 5% dextrose solution) should be used as soon as possible.
However, the pre-mixed solution is stable for 8 hours when refrigerated between 2 and 8 °C.

How supplied
DOCETAXEL KEMEX for Injection Concentrate is supplied in a single-dose vial a sterile, pyrogen-free, non-aqueous, viscous solution with an accompanying sterile, non pyrogenic, solvent (13% ethanol in Water for Injection) vial.
The following strengths are available.
Unit dose vial of Docetaxel 20 mg/0.5ml. and 1.5 ml diluent vial.
Unit dose vial of Docetaxel 80 mg/2.0ml and 6.0 ml diluent vial.
Package containing 1 vial of docetaxel with 1 diluent vial.

"This medicine must be used exclusively under medical supervision and can not be repeated without any new medical prescription".

KEEP OUT OF REACH OF CHILDREN
MEDICAMENT AUTHORIZED BY THE MINISTRY OF HEALTH
CERTIFICATE N°. 50.599

Laboratorio Kemex S.A.–Nazarre 3446– Capital federal (C1417DXH)
Technical Director: Dr. Natalia Alonso – Pharmacist
Made in Argentina

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