

Docetaxel GP Pharm 75 mg/m ² in combination with doxorubicin			
System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	Rare adverse reactions ≤ 1% of the patients
Complementary exploration		↑ Blood bilirubin G3/4 (<2.5%) ↑ Blood alkaline phosphatase G3/4 (< 2.5%)	↑ GOT G3/4 (<1%) ↑ GPT G3/4 (<1%)
Cardiac disorders		Cardiac failure Arrhythmia (non-serious)	
Blood and lymphatic system disorders	Neutropenia (G4: 91.7%) Anemia (G3/4: 9.4%) Febrile neutropenia Thrombocytopenia (G4: 0.8%)		
Nervous system disorders	Peripheral sensory neuropathy (G3: 0.4%)	Peripheral motor neuropathy (G3/4: 0.4%)	
Gastrointestinal disorders	Nausea (G3/4: 5%) Stomatitis (G3/4: 7.8%) Diarrhea (G3/4: 6.2%) Vomiting (G3/4: 5%) Constipation		
Skin and subcutaneous tissue disorders	Alopecia Nails alterations (serious: 0.4%) Cutaneous reactions (non-serious)		
Musculoskeletal and connective tissue alterations		Myalgia	
Metabolism and nutrition disorders		Anorexia	
Infections and infestations	Infection (G3/4: 7.8%)		
Vascular disorders			Hypotension
General disorders and alterations in the administration site	Asthenia (serious: 8.1%) Fluid retention (serious: 1.2%) Pain		
Immunologic system disorders		Hypersensitivity (G3/4: 1.2%)	

Docetaxel GP Pharm 75 mg/m² in combination with cisplatin

System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	Rare adverse reactions ≤ 1% of the patients
Complementary exploration		↑ Blood bilirubin G3/4 (2.1%) ↑ GPT G3/4 (1.3%)	↑ GOT G3/4 (0.5%) ↑ Blood alkaline phosphatase G3/4 (0.3%)
Cardiac disorders		Arrythmia (G3/4: 0.7%)	Cardiac failure
Blood and lymphatic system disorders	Neutropenia (G4: 51.5%) Anemia (G3/4: 6.9%) Thrombocytopenia (G4: 0.5%)	Febrile neutropenia	
Nervous system disorders	Peripheral sensory neuropathy (G3: 3.7%) Peripheral motor neuropathy (G3/4: 2%)		
Gastrointestinal disorders	Nausea (G3/4: 9.6%) Vomiting (G3/4: 7.6%) Diarrhea (G3/4: 6.4%) Stomatitis (G3/4: 2%)		
Skin and subcutaneous tissue disorders	Alopecia Nails alteration (serious: 0.7%) Cutaneous reactions (G3/4: 0.2%)		
Musculoskeletal and connective tissue alterations	Myalgia (serious: 0.5%)		
Metabolism and the nutrition disorders	Anorexia		
Infections and infestations	Infection (G3/4: 5.7%)		
Vascular disorders		Hypotension (G3/4: 0.7%)	
General disorders and alterations in the administration site	Asthenia (serious: 9.9%) Fluid retention (serious: 0.7%) Fever (G3/4:1.2%) Hypersensitivity	Reaction in the infusion site Pain	
Immunologic system disorders			

(G3/4:2.5%)			
Docetaxel GP Pharm 100 mg/m ² in combination with trastuzumab			
System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	
Complementary exploration	Weight gaining		
Cardiac disorders			Cardiac failure
Blood and lymphatic system disorders	Neutropenia (G4: 32%) Febrile neutropenia (including neutropenia associated to fever and antibiotic administration) or neutropenic sepsis		
Nervous system disorders	Paresthesias. Headache. Dysgeusia. Hypoesthesia		
Ocular disorders	Lacrimation increase. Conjunctivitis		
Respiratory, thorax and mediastinal disorders	Epistaxis. Dolor pharyngolaringeo. Nasopharyngitis. Dyspnea. Cough. Rhinorrhea.		
Gastrointestinal disorders	Nausea. Diarrhea. Vomiting. Constipation. Stomatitis. Dyspepsia. Abdominal pain		
Skin and subcutaneous tissue disorders	Alopecia. Erythema. Rash. Nails alterations.		
Musculoskeletal and connective tissue alterations	Myalgia. Arthralgia. Extremities pain. Bone pain. Back pain.		
Metabolism and nutrition disorders	Anorexia		
Vascular disorders	Lymphoedema		
General disorders and alterations in the administration site	Asthenia. Peripheral edema. Pyrexia. Fatigue. Mucous inflammation. Pain. Similar disease to influenza. Thorax pain. Shivering.	Lethargy	
Psychiatric disorders	Insomnia		

Heart disorders

Symptomatic heart failure was observed in 2.2% of the patients receiving docetaxel with trastuzumab, compared to 0% of the patients administered docetaxel in monotherapy. In the group treated with docetaxel in association with trastuzumab, the 64% had received anthracycline as adjuvant therapy, compared to 55% in the group treated with docetaxel in monotherapy.
Blood and lymphatic system disorders
Frequent: the hematologic toxicity increased in patients who received trastuzumab and docetaxel, compared with docetaxel in monotherapy (neutropenia grade 3/4, 32% as against 22%, according to the criterion NCI-CTC). It should be taken into account that this is probably subestimated, since it is known that 100 mg/m² docetaxel dose in monotherapy produces neutropenia in 97% of the patients, 76% grade 4, according to blood count in the lowest point. The incidence of febrile neutropenia/sepsis associated to neutropenia increased in patients administered trastuzumab and docetaxel (23% as against 17% in patients treated only with docetaxel).

Docetaxel GP Pharm 75 mg/m² in combination with capecitabine

System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	
Complementary exploration		Weight lost ↑ Blood bilirubin G3/4 (9%)	
Blood and lymphatic system disorders	Neutropenia (G3/4: 63%); Anemia (G3/4: 10%)	Thrombocytopenia (G3/4: 3%)	
Nervous system disorders	Dysgeusia (G3/4: < 1%) Paresthesias (G3/4: < 1%)	Sickness Headache (G3/4: < 1%) Neuropathy peripheral	
Ocular disorders	Lacrimation increase		
Respiratory, thorax and mediastinal disorders	Pharyngolaringeo pain (G3/4: 2%)	Dyspnea (G3/4: 1%) Cough (G3/4: < 1%) Epistaxis (G3/4: < 1%)	
Gastrointestinal disorders	Stomatitis (G3/4: 18%) Diarrhea (G3/4: 14%) Nausea (G3/4: 6%) Vomiting (G3/4: 4%) Constipation (G3/4: 1%) Abdominal pain (G3/4: 2%) Dyspepsia	Upper abdominal pain. Mouth dryness.	
Skin and subcutaneous tissue disorders	Hand—foot syndrome (G3/4: 24%) Alopecia (G3/4: 6%) Nails alterations (G3/4: 2%)	Dermatitis Erythematous rash (G3/4: <1%) Nail bleach Onycholysis (G3/4: 1%)	

Musculoskeletal and connective tissue disorders	Myalgia (G3/4: 2%) Arthralgia (G3/4: 1%)	Extremities pain (G3/4: <1%) Backache (G3/4: 1%)
Metabolism and nutrition disorders	Anorexia (G3/4: 1%) Appetite lost	Dehydration (G3/4: 2%)
Infections and infestations		Oral candidiasis (G3/4: < 1%)
General disorders and alterations in the administration site	Asthenia (G3/4: 3%) Pyrexia (G3/4: 1%) Fatigue/weakness (G3/4: 5%) Peripheral edema (G3/4: 1%)	Lethargy. Pain.

Docetaxel GP Pharm 75 mg/m² in combination with prednisone or prednisolone

System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	
Heart disorders		Reduction of the cardiac function of the left ventricle (G3/4: 0.3%)	
Blood and lymphatic system disorders	Neutropenia (G3/4: 32%) Anemia (G3/4:4.9%)	Thrombocytopenia (G3/4: 0.6%) Febrile neutropenia	
Nervous system disorders	Neuropathy sensory peripheral (G3/4: 1.2%) Dysgeusia (G3/4: 0%)	Peripheral motor neuropathy (G3/4: 0%)	
Ocular disorders		Lacrimation increase (G3/4: 0.6%)	
Respiratory, thorax and mediastinal disorders		Epistaxis (G3/4: 0%) Dyspnea (G3/4: 0.4%) Cough (G3/4: 0%)	
Gastrointestinal disorders	Nausea (G3/4: 2.4%) Diarrhea (G3/4: 1.2%) Stomatitis/ Pharyngitis 0.9%) Vomiting (G3/4: 1.2%)		
Skin and subcutaneous tissue disorders	Alopecia Nail alteration (non-serious)	Exfoliative rash (G3/4: 0.3%)	
Musculoskeletal and connective tissue disorders		Arthralgia (G3/4: 0.3%) Myalgia (G3/4: 0.3%)	
Metabolism and nutrition disorders	Anorexia (G3/4: 0.6%)		
Infections and infestations	Infection (G3/4: 3.3%)		
General disorders and alterations in the administration site	Fatigue (G3/4: 3.9%) Fluid retention (serious 0.6%)		
Immunologic system disorders		Hypersensitivity (G3/4: 0.6%)	

Docetaxel GP Pharm 75 mg/m² in combination with doxorubicin and cyclophosphamide

System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	Rare adverse reactions ≤ 1% of the patients
Complementary exploration	Weight gaining or loss (G3/4: 0.3 %)		
Heart disorders		Arrhythmia (G3/4: 0.1%) Congestive heart failure	
Blood and lymphatic system disorders	Anemia (G3/4: 4.3%) Neutropenia (G3/4: 65.5%) Thrombocytopenia (G3/4: 2.0%) Febrile neutropenia		
Nervous system disorders	Dysgeusia (G3/4: 0.7%) Peripheral sensory neutropenia (G3/4: 0%)	Peripheral motor neuropathy (G3/4: 0%) Neurocardial (G3/4: 0.3%) Neurocerebellar (G3/4: 0.1%)	Syncope (G3/4: 0%)
Ocular disorders		Lacrimation alteration G3/4: 0.1%) Conjunctivitis (G3/4: 0.3%)	
Respiratory, thorax and mediastinal disorders		Cough (G3/4: 0%)	
Gastrointestinal disorders	Nausea (G3/4: 5.1%) Stomatitis (G3/4: 7.1%) Vomiting (G3/4: 4.3%) Diarrhea (G3/4: 3.2%) Constipation (G3/4: 0.4%)	Abdominal pain (G3/4: 0.5%)	Colitis/enteritis/ Large intestine perforation
Skin and subcutaneous tissue disorders	Alopecia Skin toxicity (G3/4: 0.7%) Nail alterations (G3/4: 0.4%)		

Musculoskeletal and connective tissue alterations	Myalgia (G3/4: 0.8%) Arthralgia (G3/4: 0.4%)		
Metabolism and nutrition disorders	Anorexia (G3/4: 2.2%)		
Infections and infestations	Infection (G3/4: 3.2%) Neutropenic infection There were no deaths due to sepsis		
Vascular disorders	Vasodilatation (G3/4: 0.9%)	Hypotension (G3/4: 0%)	Phlebitis (G3/4: 0%) Lymphoedema (G3/4: 0%)
General disorders and alterations in the administration site	Asthenia (G3/4: 11%) Fever (G3/4: 1.2%) Peripheral edema (G3/4: 0.4%)		
Immunologic system disorders	Hypersensitivity (G3/4: 1.1%)		
Breast and reproduction system disorders	Amenorrhea		

Heart disorders

Congestive heart failure was reported, too (2.3% with a follow-up median time of 70 months). In each therapy group, a patient died due to heart failure.
Nervous system disorders
It was observed that peripheral sensory neuropathy continued in the follow-up median time of 55 months in 9 of the patients out of 73 patients with peripheral sensory neuropathy at the end of chemotherapy.
Skin and subcutaneous disorders
It was observed that alopecia continued in the follow-up median time of 55 months in 22 patients out of 687 patients with alopecia at the end of chemotherapy.
General disorders and alterations in the administration site
It was observed that peripheral edema continued in the follow-up median time of 55 months in 18 patients out of 112 patients who had peripheral edema at the end of the chemotherapy.
Breast and reproduction system disorders
It was observed that amenorrhea continued in the follow-up median time of 55 months in 133 patients out of 233 patients with amenorrhea at the end of the chemotherapy.

Docetaxel GP Pharm 75 mg/m² in combination with cisplatin and 5-fluorouracil (for gastric adenocarcinoma)

System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	
Heart disorders		Arrhythmia (G3/4: 1.0%)	
Blood and lymphatic system disorders	Anemia (G3/4: 20.9%) Neutropenia (G3/4: 83.2%) Thrombocytopenia (G3/4: 8.8%) Febrile neutropenia		
Nervous system disorders	Peripheral sensory neuropathy (G3/4: 8.7%)	Sickness (G3/4: 2.3%) Peripheral motor neuropathy (G3/4: 1.3%)	
Ocular disorders		Lacrimation increase (G3/4: 0%)	
Ear and labyrinth disorders		Altered hearing (G3/4: 0%)	
Gastrointestinal disorders	Diarrhea (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%) Esophagitis/dysphagia/odynophagia (G3/4: 0.7%)	
Skin and subcutaneous tissue disorders	Alopecia (G3/4: 4.0%)	Rash/pruritus (G3/4: 0.7%) Nail alterations (G3/4: 0.7%) Cutaneous desquamation (G3/4: 0%)	
Metabolism and nutrition disorders	Anorexia (G3/4: 11.7%)		
Infections and infestations	Neutropenic infection Infection (G3/4: 11.7%)		
General disorders and alterations in the administration site	Lethargy (G3/4: 19%) Fever (G3/4: 2.3%) Fluid retention (serious/death threat: 1%)		
Immunologic system disorders	Hypersensitivity (G3/4: 1.7%)		

Blood and lymphatic system disorders

Febrile neutropenia and neutropenic infection appeared, respectively, in 17.2% and the 13.5% of the patients, regardless of using G-CSF. G-CSF was used as secondary prophylaxis in 19.3% of the patients (10.7% of the courses). Febrile neutropenia and the infection associated with neutropenia appeared, respectively, in 12.1% and 3.4% of the patients when they were administered G-CSF in prophylaxis and in 15.6% and 12.9% of the patients without G-CSF in prophylaxis.

Docetaxel GP Pharm 75 mg/m² in combination with cisplatin and 5-fluorouracil (for head and neck cancer)

- Induction therapy followed by radiotherapy (TAX 323)

System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	Rare adverse reactions ≤ 1% of the patients
Complementary explorations		Weight gaining	
Heart disorders		Myocardial ischemia (G3/4: 1.7%)	Arrhythmia (G3/4: 0.6%)

Blood and lymphatic system disorders	Neutropenia (G3/4: 76.3%) Anemia (G3/4: 9.2%) Thrombocytopenia (G3/4: 5.2%)	Febrile neutropenia	
Nervous system disorders	Dysgeusia/Parosmia Peripheral sensory neuropathy (G3/4: 0.6%)	Sickness	
Ocular disorders		Lacrimation increase Conjunctivitis	
Ear and labyrinth disorders		Hearing failure	
Gastrointestinal disorders	Nausea (G3/4: 0.6%) Stomatitis (G3/4: 4.0%) Diarrhea (G3/4: 2.9%) Vomiting (G3/4: 0.6%)	Constipation Esophagitis/dysphagia/odynophagia (G3/4: 0.6%) Abdominal pain Dyspepsia - Gastrointestinal hemorrhage (G3/4: 0.6%)	
Skin and subcutaneous tissue disorders	Alopecia (G3/4: 10.9%)	Rash/pruritus Skin dryness Cutaneous desquamation (G3/4: 0.6%)	
Musculoskeletal and connective tissue alterations		Myalgia (G3/4: 0.6 %)	
Metabolism and nutrition disorders	Anorexia (G3/4: 0.6%)		
Infections and infestations	Infection (G3/4: 6.3%) Neutropenic infection		
Benign, malignant and no specified neoplasias (including cysts and polyps)		Neoplastic pain (G3/4: 0.6%)	
Vascular disorders		Venous disorders (G3/4: 0.6%)	
General disorders and alterations in the administration site	Lethargy (G3/4: 3.4%) Pyrexia (G3/4: 0.6%) Fluid retention Edema		
Immunologic system disorders		Hypersensitivity (non serious)	

- Induction therapy followed by chemoradiotherapy (TAX 324)

System of organ classification MedDRA	Frequent adverse reactions ≥ 10% of the patients	Occasional adverse reactions 1% - 10% of the patients	Rare adverse reactions ≤ 1% of the patients
Complementary explorations	Weight loss		Weight gaining
Heart disorders		Arrhythmia (G3/4: 2.0%)	Myocardial ischemia
Blood and lymphatic system disorders	Neutropenia (G3/4: 83.5%) Anemia (G3/4: 12.4%) Thrombocytopenia (G3/4: 4.0%) Febrile neutropenia		
Nervous system disorders	Dysgeusia/parosmia (G3/4: 0.4%) Peripheral sensory neuropathy (G3/4: 1.2%)	Sickness (G3/4: 2.0%) Peripheral motor neuropathy (G3/4: 0.4%)	
Ocular disorders		Lacrimation increase	Conjunctivitis
Ear and labyrinth disorders	Hearing failure (G3/4: 1.2%)		
Gastrointestinal disorders	Nausea (G3/4: 13.9%) Stomatitis (G3/4: 20.7%) Vomiting (G3/4: 8.4%) Diarrhea (G3/4: 6.8%) Esophagitis/dysphagia/odynophagia (G3/4: 12.0%) Constipation (G3/4: 0.4%)	Dyspepsia G3/4: 0.8%) Gastrointestinal pain G3/4: 1.2%) Gastrointestinal hemorrhagia (G3/4: 0.4%)	
Skin and subcutaneous tissue disorders	Alopecia (G3/4: 4%) Rash/pruritus	Skin dryness Cutaneous desquamation	
Musculoskeletal and connective tissue alterations		Myalgia (G3/4: 0.4 %)	
Metabolism and nutrition disorders	Anorexia (G3/4: 12.0%)		
Infections and infestations	Infection (G3/4: 3.6%)	Neutropenic infection	
Benign, malignant and non specified neoplasia (including cysts and polyps)		Neoplastic pain (G3/4: 1.2%)	
Vascular disorders			Venous disorders

General disorders and alterations in the administration site	Lethargy (G3/4: 4.0%) Pyrexia (G3/4: 3.6%) Fluid retention (G3/4: 1.2%) Edema (G3/4: 1.2%)		
Immunologic system disorders			Hypersensitivity

Post-marketing experience

Heart disorders

Rare cases of myocardial infarction were reported.
Blood and lymphatic system disorders
Bone marrow suppression and other hematological adverse reactions were informed. Disseminated intravascular coagulation, frequently associated to sepsis or multiorgan failure, was reported.
Nervous system disorders
Rare episodes of seizures or temporary consciousness loss were observed. These reactions sometimes occur while administering the drug.
Ocular disorders
Rare episodes of temporary visual disorders were informed (sparkles, blinding lights, scotoma) which appear during the drug administration and associated with hypersensitivity reactions. They were reversible when interrupting the infusion. Rare episodes of lacrimation with or without conjunctivitis, as the lacrimal canal occlusion which causes excessive lacrimation were reported.

Ear and labyrinth disorders

Rare episodes of ototoxicity, disorders and/or hearing loss were informed.
Respiratory, thorax and mediastinal disorders
Acute respiratory distress syndrome, interstitial pneumonia and fibrosis of the lungs were rarely reported. Rare cases of pneumonitis due to radiation in patients who had already received radiotherapy concomitantly were informed.
Gastrointestinal disorders
Rare episodes of dehydration as a consequence of gastrointestinal episodes, gastrointestinal perforation, ischemic colitis and neutropenic enterocolitis were reported. There were rare cases of paralytic ileus and intestinal obstruction.

Very rare cases of cutaneous erythematous lupus and bullous eruptions, like multiform erythema, Stevens-Johnson syndrome, toxic epidermal necrolysis were informed with docetaxel. In some episodes, other concomitant factors may have contributed in the development of these effects. Scleroderma-kind modifications generally preceded by peripheral lymphoedema were informed.
Benign and malignant and non-specified neoplasia (including cysts and polyps)
Very rare cases of acute myeloid leukemia and myelodysplastic syndrome related to docetaxel when it was used in combination with other chemotherapeutic agents and/or radiotherapy were reported.

Vascular disorders

Rarely venous thromboembolic events were reported.
General disorders and alterations in the administration site
Rarely radiation recollection events were informed.
Fluid retention was not accompanied by acute episodes of oliguria or hypotension.
Rarely dehydration or pulmonary edema was reported.
Immunologic system disorders
Some anaphilactic shock events, sometimes fatal, were informed.
Hepatobiliary disorders
Very rare cases of hepatitis, sometime fatal, mainly in patients with prior hepatic alterations were reported.

OVERDOSE

Few cases of overdose have been reported. It is not known whether there exist antidotes for docetaxel overdose. In this case, the patient must be admitted to a specialized unit where vital signs can be monitored and support therapy can be administered as needed. In case of overdose, adverse reactions are expected to worsen. The earliest and the most important complications of overdose may include bone marrow suppression, peripheral neurotoxicity and mucositis. The patient should receive therapy with G-CSF as soon as possible when the overdose is known. When necessary, appropriate symptomatic measures shall be adopted.

STORING CONDITIONS

Store at temperature at 2 to 8°C and protected from light.

HOW SUPPLIED

Docetaxel GP Pharm 20 mg/0.5 ml x 1 concentrate vial and 1 solvent vial.
Docetaxel GP Pharm 80 mg/2 ml x 1 concentrate vial and 1 solvent vial.

KEEP AWAY FROM CHILDREN

Medicine Authorized by the Ministry of Health of Argentina.
Certificate N° 47.910.

Manufacturers:

GP Pharm S.A.

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