

## Docetaxel: Drug information

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(For additional information [see "Docetaxel: Patient drug information"](#) and [see "Docetaxel: Pediatric drug information"](#))

For abbreviations and symbols that may be used in Lexicomp ([show table](#))

### ALERT: US Boxed Warning

#### Increased mortality:

The incidence of treatment-related mortality associated with docetaxel is increased in patients with abnormal liver function, patients receiving higher doses, and patients with non–small cell lung cancer and a history of prior treatment with platinum-based chemotherapy who receive docetaxel as a single agent at a dose of 100 mg/m<sup>2</sup>.

#### Hepatic function impairment:

Do not give docetaxel to patients with bilirubin above the upper limit of normal (ULN), or patients with AST and/or ALT above 1.5 times the ULN concomitant with alkaline phosphatase above 2.5 times the ULN. Patients with elevations of bilirubin or abnormalities of transaminase concurrent with alkaline phosphatase are at increased risk for the development of grade 4 neutropenia, febrile neutropenia, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity, and toxic death. Patients with isolated elevations of transaminase above 1.5 times the ULN also had a higher rate of febrile grade 4 neutropenia but did not have an increased incidence of toxic death. Obtain bilirubin, AST or ALT, and alkaline phosphatase values prior to each cycle of docetaxel therapy.

#### Neutropenia:

Do not give docetaxel therapy to patients with neutrophil counts below 1,500 cells/mm<sup>3</sup>. In order to monitor the occurrence of neutropenia, which may be severe and result in infection, perform frequent blood cell counts on all patients receiving docetaxel.

#### Hypersensitivity:

Severe hypersensitivity reactions, characterized by general rash/erythema, hypotension, and/or bronchospasm, or, very rarely, fatal anaphylaxis, have been reported in patients who received a 3-day dexamethasone premedication. Hypersensitivity reactions require immediate discontinuation of the docetaxel infusion and administration of appropriate therapy. Do not give docetaxel to patients who have a history of severe hypersensitivity reactions to docetaxel or to other drugs formulated with polysorbate 80.

## Fluid retention:

Severe fluid retention occurred in 6.5% of patients despite the use of a 3-day dexamethasone premedication regimen. It was characterized by 1 or more of the following events: poorly tolerated peripheral edema, generalized edema, pleural effusion requiring urgent drainage, dyspnea at rest, cardiac tamponade, or pronounced abdominal distention (due to ascites).

**Brand Names: US** Docefrez [DSC]; Taxotere

**Brand Names: Canada** Docetaxel for Injection; Docetaxel Injection; Taxotere

**Pharmacologic Category** Antineoplastic Agent, Antimicrotubular; Antineoplastic Agent, Taxane Derivative

**Dosing: Adult** **Note:** Premedicate with corticosteroids for 3 days, beginning one day prior to docetaxel administration, to reduce the severity of hypersensitivity reactions and fluid retention. Patients being treated for prostate cancer with concurrent prednisone should be premedicated with oral dexamethasone at 12 hours, 3 hours, and 1 hour prior to docetaxel administration.

### **Breast cancer: IV:**

*Locally advanced or metastatic:* 60 to 100 mg/m<sup>2</sup> every 3 weeks (as a single agent)

*Operable, node-positive (adjuvant treatment):* TAC regimen: 75 mg/m<sup>2</sup> every 3 weeks for 6 courses (in combination with doxorubicin and cyclophosphamide) (Mackey 2013; Martin 2005)

*Adjuvant treatment (off-label dosing):* 75 mg/m<sup>2</sup> every 21 days (in combination with cyclophosphamide) for 4 cycles (Jones 2006) **or** 75 mg/m<sup>2</sup> every 21 days (in combination with carboplatin and trastuzumab) for 6 cycles (Slamon 2011)

*Neoadjuvant treatment (off-label dosing):* 75 mg/m<sup>2</sup> (cycle 1; if tolerated, may increase to 100 mg/m<sup>2</sup> in subsequent cycles) every 21 days for a total of 4 cycles (in combination with trastuzumab and pertuzumab) (Gianni 2012)

### *Metastatic treatment (off-label dosing):*

Every-3-week administration: 75 mg/m<sup>2</sup> (cycle 1; may increase to 100 mg/m<sup>2</sup> in subsequent cycles) every 21 days for at least 6 cycles (in combination with trastuzumab and pertuzumab) (Baselga 2012; Swain 2013) **or** 100 mg/m<sup>2</sup> every 21 days (in combination with trastuzumab) for at least 6 cycles (Marty 2005) **or** 75 mg/m<sup>2</sup> every 21 days (in combination with capecitabine) until disease progression or unacceptable toxicity (O'Shaughnessy 2002) **or** 60 mg/m<sup>2</sup>, 75 mg/m<sup>2</sup>, or 100 mg/m<sup>2</sup> every 21 days for at least 6 cycles until disease progression, unacceptable toxicity, or discontinuation (Harvey 2006)

Weekly administration: 40 mg/m<sup>2</sup>/dose once a week (as a single agent) for 6 weeks followed by a 2-week rest, repeat until disease progression or unacceptable toxicity (Burstein 2000) **or** 35 mg/m<sup>2</sup>/dose once weekly for 3 weeks, followed by a 1-week rest, may increase to 40 mg/m<sup>2</sup> once weekly for 3 weeks followed by a 1-week rest with cycle 2 (Rivera 2008) **or** 35 mg/m<sup>2</sup>/dose once weekly (in combination with trastuzumab) for 3 weeks followed by a 1-week rest; repeat until disease progression or unacceptable toxicity (Esteva 2002)

**Gastric adenocarcinoma :** IV: 75 mg/m<sup>2</sup> every 3 weeks (in combination with cisplatin and fluorouracil)

*Sequential chemotherapy and chemoradiation (off-label dosing):* Induction: 75 mg/m<sup>2</sup> on days 1 and 22 (in combination with cisplatin) for 2 cycles, followed by chemoradiation: 20 mg/m<sup>2</sup> weekly for 5 weeks (in combination with cisplatin and radiation) (Ruhstaller 2009)

*Locally advanced or metastatic disease (off-label dosing):* 50 mg/m<sup>2</sup> on day 1 every 2 weeks (in combination with fluorouracil, leucovorin, and oxaliplatin) until disease progression or unacceptable toxicity up to a maximum of 8 cycles (Al-Batran 2008)

**Head and neck cancer:** IV: 75 mg/m<sup>2</sup> every 3 weeks (in combination with cisplatin and fluorouracil) for 3 or 4 cycles, followed by radiation therapy

**Non-small cell lung cancer:** IV: 75 mg/m<sup>2</sup> every 3 weeks (as a single agent or in combination with cisplatin)

**Prostate cancer:** IV: 75 mg/m<sup>2</sup> every 3 weeks (in combination with prednisone)

**Bladder cancer, metastatic (off-label use):** IV: 100 mg/m<sup>2</sup> every 3 weeks (as a single agent) (McCaffrey 1997) **or** 35 mg/m<sup>2</sup> on days 1 and 8 of a 21-day cycle (in combination with gemcitabine and cisplatin) for at least 6 cycles or until disease progression or unacceptable toxicity (Pectasides 2002)

**Esophageal cancer (off-label use):** IV:

*Sequential chemotherapy and chemoradiation:* Induction: 75 mg/m<sup>2</sup> on days 1 and 22 (in combination with cisplatin) for 2 cycles, followed by chemoradiation: 20 mg/m<sup>2</sup> weekly for 5 weeks (in combination with cisplatin and radiation) (Ruhstaller 2009)

*Definitive chemoradiation:* 60 mg/m<sup>2</sup> on days 1 and 22 (in combination with cisplatin and radiation) for 1 cycle (Li 2010)

*Locally advanced or metastatic disease:* 75 mg/m<sup>2</sup> on day 1 every 3 weeks (in combination with cisplatin and fluorouracil) (Ajani 2007; Van Cutsem 2006) **or** 50 mg/m<sup>2</sup> on day 1 every 2 weeks (in combination with fluorouracil, leucovorin, and oxaliplatin) until disease progression or unacceptable toxicity up to a maximum of 8 cycles (Al-Batran 2008) **or** 35 mg/m<sup>2</sup> on days 1, 8, 15, 29, 36, 43, 50, and 57 (in combination with cisplatin, fluorouracil, and radiotherapy; neoadjuvant setting) (Pasini 2013)

**Ewing sarcoma or osteosarcoma (recurrent or progressive; off-label uses):** IV: 100 mg/m<sup>2</sup> on day 8 of a 21-day cycle (in combination with gemcitabine) (Navid 2008)

**Ovarian cancer (off-label use):** IV: 60 mg/m<sup>2</sup> every 3 weeks (in combination with carboplatin) for up to 6 cycles (Markman 2001) **or** 75 mg/m<sup>2</sup> every 3 weeks (in combination with carboplatin) for 6 cycles (Vasey 2004) **or** 35 mg/m<sup>2</sup> (maximum dose: 70 mg) weekly for 3 weeks followed by a 1-week rest (in combination with carboplatin) (Kushner 2007)

**Prostate cancer, metastatic, hormone-sensitive (off-label use):** 75 mg/m<sup>2</sup> on day 1 every 3 weeks (in combination with androgen deprivation therapy and prednisolone) for 6 cycles (James 2016) **or** 75 mg/m<sup>2</sup> on day 1 every 3 weeks (in combination with androgen deprivation therapy; daily prednisone not required) for 6 cycles (Sweeney 2015).

**Small cell lung cancer, relapsed (off-label use):** IV: 100 mg/m<sup>2</sup> every 3 weeks (Smyth 1994)

**Soft tissue sarcoma (off-label use):** IV: 100 mg/m<sup>2</sup> on day 8 of a 3-week treatment cycle (in combination with gemcitabine and filgrastim or pegfilgrastim) (Leu 2004; Maki 2007)

**Unknown-primary, adenocarcinoma (off-label use):** IV: 65 mg/m<sup>2</sup> every 3 weeks (in combination with carboplatin) (Greco 2000) **or** 75 mg/m<sup>2</sup> on day 8 of a 3-week treatment cycle (in combination with gemcitabine) for up to 6 cycles (Pouessel 2004) **or** 60 mg/m<sup>2</sup> on day 1 of a 3-week treatment cycle (in combination with cisplatin) (Mukai 2010)

*Dosing adjustment for concomitant CYP3A4 inhibitors:* Avoid the concomitant use of strong CYP3A4 inhibitors with docetaxel. If concomitant use of a strong CYP3A4 inhibitor cannot be avoided, consider reducing the docetaxel dose by 50% (based on limited pharmacokinetic data).

## Dosing: Pediatric

(For additional information [see "Docetaxel: Pediatric drug information"](#))

**Note:** Premedicate with corticosteroids for 3 days, beginning one day prior to docetaxel administration, to reduce the severity of hypersensitivity reactions and fluid retention. Dexamethasone (dose not specified) was administered for 3 to 4 days, starting the day before or the day of docetaxel administration and continuing for 2 days afterward in the bone sarcoma study (Navid 2008).

**Ewing sarcoma or osteosarcoma (recurrent or progressive; off-label uses):** Children ≥8 years and Adolescents: IV: 100 mg/m<sup>2</sup> on day 8 of a 21-day cycle (in combination with gemcitabine) (Navid 2008)

**Dosing: Geriatric** Refer to adult dosing.

**Dosing: Renal Impairment** Renal excretion is minimal (~6%), therefore, the need for dosage adjustments for renal dysfunction is unlikely (Janus 2010; Li 2007). Not removed by hemodialysis, may be administered before or after hemodialysis (Janus 2010).

## Dosing: Hepatic Impairment

Total bilirubin greater than the ULN, or AST and/or ALT >1.5 times ULN concomitant with alkaline phosphatase >2.5 times ULN: Use is not recommended.

Hepatic impairment dosing adjustment specific for gastric or head and neck cancer:

AST/ALT >2.5 to ≤5 times ULN and alkaline phosphatase ≤2.5 times ULN: Administer 80% of dose

AST/ALT >1.5 to ≤5 times ULN and alkaline phosphatase >2.5 to ≤5 times ULN: Administer 80% of dose

AST/ALT >5 times ULN and /or alkaline phosphatase >5 times ULN: Discontinue docetaxel

**The following adjustments have also been used (Floyd 2006):**

Transaminases 1.6 to 6 times ULN: Administer 75% of dose.

Transaminases >6 times ULN: Use clinical judgment.

**Dosing: Obesity** *ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer:* Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based

dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs 2012).

**Dosing: Adjustment for Toxicity** **Note:** Toxicity includes febrile neutropenia, neutrophils  $<500/\text{mm}^3$  for  $>1$  week, severe or cumulative cutaneous reactions; in non–small cell lung cancer, this may also include platelet nadir  $<25,000/\text{mm}^3$  and other grade 3/4 nonhematologic toxicities. Refer to specific reference/protocol for dosage adjustments for off-label uses or combinations.

**Breast cancer (single agent):** Patients dosed initially at  $100 \text{ mg}/\text{m}^2$ ; reduce dose to  $75 \text{ mg}/\text{m}^2$ ; **Note:** If the patient continues to experience these adverse reactions, the dosage should be reduced to  $55 \text{ mg}/\text{m}^2$  or therapy should be discontinued; discontinue for peripheral neuropathy  $\geq$  grade 3. Patients initiated at  $60 \text{ mg}/\text{m}^2$  who do not develop toxicity may tolerate higher doses.

**Breast cancer, adjuvant treatment (combination chemotherapy):** TAC regimen should be administered when neutrophils are  $\geq 1,500/\text{mm}^3$ . Patients experiencing febrile neutropenia should receive G-CSF in all subsequent cycles. Patients with persistent febrile neutropenia (while on G-CSF), patients experiencing severe/cumulative cutaneous reactions, moderate neurosensory effects (signs/symptoms) or grade 3 or 4 stomatitis should receive a reduced dose ( $60 \text{ mg}/\text{m}^2$ ) of docetaxel. Discontinue therapy with persistent toxicities after dosage reduction.

#### **Non-small cell lung cancer:**

Monotherapy: Patients dosed initially at  $75 \text{ mg}/\text{m}^2$  should have dose held until toxicity is resolved, then resume at  $55 \text{ mg}/\text{m}^2$ ; discontinue for peripheral neuropathy  $\geq$  grade 3.

Combination therapy (with cisplatin): Patients dosed initially at  $75 \text{ mg}/\text{m}^2$  should have the docetaxel dosage reduced to  $65 \text{ mg}/\text{m}^2$  in subsequent cycles; if further adjustment is required, dosage may be reduced to  $50 \text{ mg}/\text{m}^2$ .

**Prostate cancer:** Reduce dose to  $60 \text{ mg}/\text{m}^2$ ; discontinue therapy if toxicities persist at lower dose.

**Gastric cancer, head and neck cancer: Note:** Cisplatin may require dose reductions/therapy delays for peripheral neuropathy, ototoxicity, and/or nephrotoxicity. Patients experiencing febrile neutropenia, documented infection with neutropenia or neutropenia  $>7$  days should receive G-CSF in all subsequent cycles. For neutropenic complications despite G-CSF use, further reduce dose to  $60 \text{ mg}/\text{m}^2$ . Dosing with neutropenic complications in subsequent cycles should be further reduced to  $45 \text{ mg}/\text{m}^2$ . Patients who experience grade 4 thrombocytopenia should receive a dose reduction from  $75 \text{ mg}/\text{m}^2$  to  $60 \text{ mg}/\text{m}^2$ . Discontinue therapy for persistent toxicities.

*Gastrointestinal toxicity for docetaxel in combination with cisplatin and fluorouracil for treatment of gastric cancer or head and neck cancer:*

Diarrhea, grade 3:

First episode: Reduce fluorouracil dose by 20%

Second episode: Reduce docetaxel dose by 20%

Diarrhea, grade 4:

First episode: Reduce fluorouracil and docetaxel doses by 20%

Second episode: Discontinue treatment

Stomatitis, grade 3:

First episode: Reduce fluorouracil dose by 20%

Second episode: Discontinue fluorouracil for all subsequent cycles

Third episode: Reduce docetaxel dose by 20%

Stomatitis, grade 4:

First episode: Discontinue fluorouracil for all subsequent cycles

Second episode: Reduce docetaxel dose by 20%

**Dosage Forms** Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

Concentrate, Intravenous:

Taxotere: 20 mg/mL (1 mL); 80 mg/4 mL (4 mL) [contains alcohol, usp, polysorbate 80]

Generic: 20 mg/mL (1 mL); 80 mg/4 mL (4 mL); 160 mg/8 mL (8 mL); 200 mg/10 mL (10 mL); 20 mg/0.5 mL (0.5 mL); 80 mg/2 mL (2 mL)

Concentrate, Intravenous [preservative free]:

Generic: 20 mg/mL (1 mL); 80 mg/4 mL (4 mL); 140 mg/7 mL (7 mL [DSC]); 160 mg/8 mL (8 mL)

Solution, Intravenous:

Generic: 20 mg/2 mL (2 mL); 80 mg/8 mL (8 mL); 160 mg/16 mL (16 mL); 200 mg/20 mL (20 mL [DSC]); 20 mg/mL (1 mL); 80 mg/4 mL (4 mL); 160 mg/8 mL (8 mL)

Solution Reconstituted, Intravenous:

Docefrez: 20 mg (1 ea [DSC]); 80 mg (1 ea [DSC]) [contains alcohol, usp, polysorbate 80]

**Generic Equivalent Available (US)** May be product dependent

## Dosage Forms Considerations

Non-alcohol formulation (Eagle/Teikoku pharmaceuticals): Solution, Intravenous [alcohol-free]: Generic: 20 mg/mL (1 mL; single-dose vial); 80 mg/4 mL (4 mL multi-dose vial); 160 mg/8 mL (8 mL; multi-dose vial)

**Administration** Administer IV infusion over 1-hour through nonsorbing polyethylene lined (non-DEHP) tubing. **Note:** Premedication with corticosteroids for 3 days, beginning the day before docetaxel administration, is recommended to reduce the incidence and severity of hypersensitivity reactions and fluid retention. Some docetaxel formulations contain alcohol (content varies by formulation); use with caution in patients for whom alcohol intake should be avoided or minimized (a non-alcohol generic formulation [20 mg/mL] is also available).

The use of an in-line filter is not necessary during Taxotere administration; according to the manufacturer, studies have not been performed to determine the compatibility of IV filters for administration and filters are

not recommended for use with docetaxel (data on file [Sanofi Aventis 2016]). The use of an inline filter is also not recommended for administration of the non-alcohol docetaxel formulation (data on file [Eagle Pharmaceuticals 2016]).

Irritant with vesicant-like properties; avoid extravasation. Assure proper needle or catheter position prior to administration.

**Extravasation management:** If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); remove needle/cannula; elevate extremity. Information conflicts regarding the use of warm or cold compresses (Perez Fidalgo 2012; Polovich 2009).

## Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

## Use

Docefrez:

**Breast cancer:** Treatment of breast cancer (locally advanced/metastatic) after prior chemotherapy failure

**Non-small cell lung cancer:** Treatment of locally advanced or metastatic non–small cell lung cancer (NSCLC) after prior platinum-based chemotherapy failure; treatment of previously untreated unresectable locally advanced or metastatic NSCLC (in combination with cisplatin)

**Prostate cancer:** Treatment of hormone-refractory metastatic prostate cancer (in combination with prednisone)

Taxotere (and various generic brands):

**Breast cancer:** Treatment of breast cancer (locally advanced/metastatic) after prior chemotherapy failure; adjuvant treatment (in combination with doxorubicin and cyclophosphamide) of operable node-positive breast cancer

**Gastric cancer:** Treatment of advanced gastric adenocarcinoma, including gastroesophageal junction adenocarcinoma (in combination with cisplatin and fluorouracil) in patients who have not received prior chemotherapy for advanced disease

**Head and neck cancer:** Treatment (induction) of locally advanced squamous cell head and neck

cancer (in combination with cisplatin and fluorouracil)

**NSCLC:** Treatment of locally advanced or metastatic NSCLC after failure of prior platinum-based chemotherapy; treatment of previously untreated unresectable locally advanced or metastatic NSCLC (in combination with cisplatin)

**Prostate cancer:** Treatment of androgen-independent (hormone refractory) metastatic prostate cancer (in combination with prednisone)

## Use: Off-Label

Bladder cancer, metastatic (single-agent); Esophageal cancer, chemoradiation; Esophageal cancer, locally-advanced or metastatic disease; Ewing sarcoma, osteosarcoma (recurrent or progressive); Ovarian cancer; Prostate cancer, metastatic, hormone-sensitive; Small cell lung cancer, relapsed; Soft tissue sarcoma; Unknown-primary, adenocarcinoma

## Medication Safety Issues

### Sound-alike/look-alike issues:

DOCEtaxel may be confused with cabazitaxel, PACLitaxel

Taxotere may be confused with Taxol

### High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

### Administration issues:

Multiple concentrations: Docetaxel is available as a one-vial formulation at concentrations of 10 mg/mL (generic formulation) and 20 mg/mL (concentrate/solution; Taxotere or non-alcohol generic formulation), and as a lyophilized powder (Docefrez) which is reconstituted (with provided diluent) to 20 mg/0.8 mL (20 mg vial) or 24 mg/mL (80 mg vial). Docetaxel was previously available as a two-vial formulation (a concentrated docetaxel solution vial and a diluent vial) resulting in a reconstituted concentration of 10 mg/mL. The two-vial formulation has been discontinued by the Taxotere manufacturer (available generically). Admixture errors have occurred due to the availability of various docetaxel concentrations.

**Adverse Reactions** Percentages reported for docetaxel monotherapy; frequency may vary depending on diagnosis, dose, liver function, prior treatment, and premedication.

>10%:

Central nervous system: Central nervous system toxicity (20% to 58%; severe: ≤6%; including neuropathy)



Dermatologic: Alopecia (56% to 76%), dermatological reaction (20% to 48%; severe: ≤5%), nail disease (11% to 41%)

Endocrine & metabolic: Fluid retention (includes edema and effusion; 13% to 60%; severe: 7% to 9%; dose dependent)

Gastrointestinal: Stomatitis (19% to 53%; severe 1% to 8%), diarrhea (23% to 43%; severe: 5% to 6%), nausea (34% to 42%), vomiting (22% to 23%)

Hematologic & oncologic: Neutropenia (84% to 99%; grade 4: 75% to 86%; nadir [median]: 7 days, duration [severe neutropenia]: 7 days; dose dependent), leukopenia (84% to 99%; grade 4: 32% to 44%), anemia (65% to 97%; dose dependent; grades 3/4: 8% to 9%), thrombocytopenia (8% to 14%; grade 4: 1%; dose dependent), febrile neutropenia (≤14%; dose dependent)

Hepatic: Increased serum transaminases (4% to 19%)

Hypersensitivity: Hypersensitivity (1% to 21%; with premedication 15%)

Infection: Infection (1% to 34%; dose dependent)

Neuromuscular & skeletal: Weakness (53% to 66%; severe: ≤18%), myalgia (3% to 23%), neuromuscular reaction (16%)

Respiratory: Pulmonary reaction (41%)

Miscellaneous: Fever (31% to 35%)

1% to 10%:

Cardiovascular: Decreased left ventricular ejection fraction (8%), hypotension (3%)

Central nervous system: Peripheral motor neuropathy (4%; severe; mainly distal extremity weakness)

Gastrointestinal: Dysgeusia (6%)

Hepatic: Increased serum bilirubin (9%), increased serum alkaline phosphatase (4% to 7%)

Infection: Severe infection (6%)

Local: Infusion site reactions (4%, including hyperpigmentation, inflammation, redness, dryness, phlebitis, extravasation, swelling of the vein)

Neuromuscular and skeletal: Arthralgia (3% to 9%)

<1%, postmarketing, and/or case reports: Abdominal pain, acute myelocytic leukemia, acute respiratory distress, alopecia (permanent), anaphylactic shock, anorexia, ascites, atrial fibrillation, atrial flutter, back pain, bronchospasm, cardiac arrhythmia, cardiac tamponade, chest pain, chest tightness, chills, colitis, confusion, conjunctivitis, constipation, cystoid macular edema, deep vein thrombosis, dehydration, disease of the lacrimal apparatus (duct obstruction), disseminated intravascular coagulation, drug fever, duodenal ulcer, dyspnea, ECG abnormality, epiphora (more common with weekly administration [Kintzel 2006]), erythema multiforme, esophagitis, flushing, gastrointestinal hemorrhage, gastrointestinal obstruction, gastrointestinal perforation, hearing loss, hemorrhagic diathesis, hepatitis, hypertension, hyponatremia, intestinal obstruction, interstitial pulmonary disease, ischemic colitis, lacrimation, localized erythema of the extremities, loss of consciousness (transient), lymphedema (peripheral), multiorgan

failure, myelodysplastic syndrome, myocardial infarction, neutropenic enterocolitis, ototoxicity, pain, palmar-plantar erythrodysesthesia, pneumonia, pneumonitis, pruritus, pulmonary edema, pulmonary embolism, pulmonary fibrosis, radiation pneumonitis, radiation recall phenomenon, renal failure, renal insufficiency, respiratory failure, skin changes (scleroderma-like), seizure, sepsis, sinus tachycardia, skin rash, Stevens-Johnson syndrome, subacute cutaneous lupus erythematosus, syncope, tachycardia, thrombophlebitis, toxic epidermal necrolysis, unstable angina pectoris, visual disturbance (transient)

## Contraindications

Severe hypersensitivity to docetaxel or any component of the formulation; severe hypersensitivity to other medications containing polysorbate 80; neutrophil count  $<1,500/\text{mm}^3$

*Canadian labeling:* Additional contraindications (not in the US labeling): Severe hepatic impairment; pregnancy; breastfeeding

## Warnings/Precautions

### **Concerns related to adverse effects:**

- Bone marrow suppression: **[US Boxed Warning]: Patients with an absolute neutrophil count  $<1,500/\text{mm}^3$  should not receive docetaxel. Monitor blood counts frequently to monitor for neutropenia (which may be severe and result in infection).** The dose-limiting toxicity is neutropenia. Platelets should recover to  $>100,000/\text{mm}^3$  prior to treatment. Patients with increased liver function tests experienced more episodes of neutropenia with a greater number of severe infections; monitor liver function tests frequently. Hematologic toxicity may require dose reduction or therapy discontinuation.
- Cutaneous reactions: Cutaneous reactions, including erythema (with edema) and desquamation, have been reported; may require dose reduction.
- Extravasation: Docetaxel is an irritant with vesicant-like properties; ensure proper needle or catheter placement prior to and during infusion; avoid extravasation.
- Fluid retention: **[US Boxed Warning]: Severe fluid retention, characterized by pleural effusion (requiring immediate drainage), ascites with pronounced abdominal distention, peripheral edema (poorly tolerated), dyspnea at rest, cardiac tamponade, generalized edema, and weight gain, has been reported (despite the use of premedication with 3 days of dexamethasone).** Fluid retention may begin as lower extremity peripheral edema and become generalized with a median weight gain of 2 kg. In patients with breast cancer, the median cumulative dose to onset of moderate or severe fluid retention was  $819 \text{ mg}/\text{m}^2$ ; fluid retention resolves in a median of 16 weeks after discontinuation. Patients should be premedicated with a corticosteroid (starting 1 day prior to administration) to reduce the incidence and severity of fluid retention. Closely monitor patients with existing effusions.
- Hypersensitivity reactions: **[US Boxed Warning]: Severe hypersensitivity reactions, characterized by generalized rash/erythema, hypotension, bronchospasms, or rare anaphylaxis may occur (may be fatal; has occurred in patients receiving a 3-day corticosteroid premedication). Hypersensitivity reactions require immediate discontinuation of the docetaxel infusion and administration of appropriate therapy. Do not administer to patients with a history of severe hypersensitivity to docetaxel or polysorbate 80.** Minor

reactions including flushing or localized skin reactions may also occur. Observe for hypersensitivity, especially with the first 2 infusions. Discontinue for severe reactions; do not rechallenge if severe. Patients should be premedicated with a corticosteroid (starting 1 day prior to administration) to prevent or reduce the severity of hypersensitivity reactions.

- Neurosensory symptoms: Dosage adjustment is recommended with severe neurosensory symptoms (paresthesia, dysesthesia, pain); persistent symptoms may require discontinuation. Reversal of symptoms may be delayed after discontinuation.
- Ocular adverse effects: Cystoid macular edema (CME) has been reported; if vision impairment occurs, a prompt comprehensive ophthalmic exam is recommended. If CME is diagnosed, initiate appropriate CME management and discontinue docetaxel (consider non-taxane treatments). In a study of patients receiving docetaxel for the adjuvant treatment of breast cancer, a majority of patients experienced tearing, which occurred in patients with and without lacrimal duct obstruction at baseline. Onset was generally after cycle 1, but subsided in most patients within 4 months after therapy completion (Chan 2013).
- Secondary malignancies: Treatment-related acute myeloid leukemia or myelodysplasia occurred in patients receiving docetaxel in combination with anthracyclines and/or cyclophosphamide.
- Treatment-related mortality: **[US Boxed Warning]: Patients with abnormal liver function, those receiving higher doses, and patients with non–small cell lung cancer and a history of prior treatment with platinum derivatives who receive single-agent docetaxel at a dose of 100 mg/m<sup>2</sup> are at higher risk for treatment-related mortality.**
- Weakness: Fatigue and weakness (may be severe) have been reported; symptoms may last a few days up to several weeks. In patients with progressive disease, weakness may be associated with a decrease in performance status.

#### ***Disease-related concerns:***

- Heart failure: In a scientific statement from the American Heart Association, docetaxel has been determined to be an agent that may either cause direct myocardial toxicity or exacerbate underlying myocardial dysfunction (magnitude: moderate) (AHA [Page 2016]).
- Hepatic impairment: **[US Boxed Warning]: Avoid use in patients with bilirubin exceeding upper limit of normal (ULN) or AST and/or ALT >1.5 times ULN in conjunction with alkaline phosphatase >2.5 times ULN. Patients with bilirubin elevations or abnormal transaminases (with concurrent abnormal alkaline phosphatase) are at increased risk for grade 4 neutropenia, neutropenic fever, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity, and toxic death. Patients with isolated transaminase elevations >1.5 times ULN also had a higher rate of grade 4 neutropenic fever, although no increased incidence of toxic death. Monitor bilirubin, AST or ALT, and alkaline phosphatase prior to each docetaxel cycle.** The alcohol content of the docetaxel formulation should be taken into account when administering to patients with hepatic impairment.

#### ***Concurrent drug therapy issues:***

- Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

### **Dosage form specific issues:**

- Alcohol content: Some docetaxel formulations contain alcohol (content varies by formulation), which may affect the central nervous system and cause symptoms of alcohol intoxication. Consider alcohol content and use with caution in patients for whom alcohol intake should be avoided or minimized. Patients should avoid driving or operating machinery immediately after the infusion. An FDA-approved non-alcohol generic formulation (20 mg/mL) is available.
- Polysorbate 80: Some dosage forms may contain polysorbate 80 (also known as Tweens). Hypersensitivity reactions, usually a delayed reaction, have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals (Isaksson 2002; Lucente 2000; Shelley 1995). Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure have been reported in premature neonates after receiving parenteral products containing polysorbate 80 (Alade 1986; CDC 1984). See manufacturer's labeling.

### **Other warnings/precautions:**

- Premedication: Premedication with oral corticosteroids is recommended to decrease the incidence and severity of fluid retention and severity of hypersensitivity reactions. The manufacturer recommends dexamethasone 16 mg/day (8 mg twice daily) orally for 3 days, starting the day before docetaxel administration; for prostate cancer, when prednisone is part of the antineoplastic regimen, dexamethasone 8 mg orally is administered at 12 hours, 3 hours, and 1 hour prior to docetaxel.

**Metabolism/Transport Effects** **Substrate** of CYP3A4 (major), P-glycoprotein; **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

## **Drug Interactions**

(For additional information: [Launch drug interactions program](#)) Lexicomp<sup>®</sup>

Antineoplastic Agents (Anthracycline, Systemic): Taxane Derivatives may enhance the adverse/toxic effect of Antineoplastic Agents (Anthracycline, Systemic). Taxane Derivatives may increase the serum concentration of Antineoplastic Agents (Anthracycline, Systemic). Taxane Derivatives may also increase the formation of toxic anthracycline metabolites in heart tissue. *Risk D: Consider therapy modification*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Bosentan: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of CYP3A4 Substrates. *Risk C:*

## *Monitor therapy*

CYP3A4 Inducers (Strong): May increase the metabolism of CYP3A4 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

CYP3A4 Inhibitors (Moderate): May decrease the metabolism of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inhibitors (Strong): May increase the serum concentration of DOCEtaxel. Management: Avoid the concomitant use of docetaxel and strong CYP3A4 inhibitors when possible. If combined use is unavoidable, consider a 50% docetaxel dose reduction and monitor for increased docetaxel toxicities. *Risk D: Consider therapy modification*

Dabrafenib: May decrease the serum concentration of CYP3A4 Substrates. Management: Seek alternatives to the CYP3A4 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyron: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Dronedarone: May increase the serum concentration of DOCEtaxel. Management: Avoid this combination whenever possible. If this combination must be used, consider using a reduced docetaxel dose, and/or increase monitoring for evidence of serious docetaxel toxicity (e.g., neutropenia, mucositis, etc.). *Risk D: Consider therapy modification*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Enzalutamide: May decrease the serum concentration of CYP3A4 Substrates. Management: Concurrent use of enzalutamide with CYP3A4 substrates that have a narrow therapeutic index should be avoided. Use of enzalutamide and any other CYP3A4 substrate should be performed with caution and close monitoring. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Idelalisib: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

MiFEPRIStone: May increase the serum concentration of CYP3A4 Substrates. Management: Minimize doses of CYP3A4 substrates, and monitor for increased concentrations/toxicity, during and 2 weeks following treatment with mifepristone. Avoid cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus. *Risk D: Consider therapy modification*

Mitotane: May decrease the serum concentration of CYP3A4 Substrates. Management: Doses of CYP3A4 substrates may need to be adjusted substantially when used in patients being treated with mitotane. *Risk D: Consider therapy modification*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Netupitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

P-glycoprotein/ABCB1 Inhibitors: May increase the serum concentration of P-glycoprotein/ABCB1 Substrates. P-glycoprotein inhibitors may also enhance the distribution of p-glycoprotein substrates to specific cells/tissues/organs where p-glycoprotein is present in large amounts (e.g., brain, T-lymphocytes, testes, etc.). *Risk C: Monitor therapy*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Platinum Derivatives: May enhance the myelosuppressive effect of Taxane Derivatives. Administer Taxane derivative before Platinum derivative when given as sequential infusions to limit toxicity. *Risk D: Consider therapy modification*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Ranolazine: May increase the serum concentration of P-glycoprotein/ABCB1 Substrates. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider*

### *therapy modification*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

SORafenib: May increase the serum concentration of DOCEtaxel. *Risk C: Monitor therapy*

St John's Wort: May decrease the serum concentration of CYP3A4 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates. Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

## **Pregnancy Risk Factor** D ([show table](#))

**Pregnancy Implications** Adverse events have been observed in animal reproduction studies. An *ex vivo* human placenta perfusion model illustrated that docetaxel crossed the placenta at term. Placental transfer was low and affected by the presence of albumin; higher albumin concentrations resulted in lower docetaxel placental transfer (Berveiller, 2012). Some pharmacokinetic properties of docetaxel may be altered in pregnant women (van Hasselt 2014). Women of childbearing potential should avoid becoming pregnant during therapy. A pregnancy registry is available for all cancers diagnosed during pregnancy at Cooper

Health (877-635-4499).

**Breast-Feeding Considerations** It is not known if docetaxel is excreted into breast milk. Due to the potential for serious adverse reactions in breastfeeding the infant, the US labeling recommends a decision be made to discontinue breastfeeding or the drug, taking into account the importance of treatment to the mother.

**Monitoring Parameters** CBC with differential, liver function tests, bilirubin, alkaline phosphatase, renal function; monitor for hypersensitivity reactions, neurosensory symptoms, gastrointestinal toxicity (eg, diarrhea, stomatitis), cutaneous reactions, visual impairment, fluid retention, epiphora, and canalicular stenosis

**Mechanism of Action** Docetaxel promotes the assembly of microtubules from tubulin dimers, and inhibits the depolymerization of tubulin which stabilizes microtubules in the cell. This results in inhibition of DNA, RNA, and protein synthesis. Most activity occurs during the M phase of the cell cycle.

**Pharmacodynamics/Kinetics** Exhibits linear pharmacokinetics at the recommended dosage range

Distribution: Extensive extravascular distribution and/or tissue binding;  $V_{dss}$ : 113 L (mean steady state)

Protein binding: ~94% to 97%, primarily to  $\alpha_1$ -acid glycoprotein, albumin, and lipoproteins

Metabolism: Hepatic; oxidation via CYP3A4 to metabolites

Half-life elimination: Terminal: ~11 hours

Excretion: Feces (~75%, <8% as unchanged drug); urine (~6%)

## Pricing: US

### Concentrate (DOCEtaxel Intravenous)

20 mg/0.5 mL (0.5 mL): \$365.15

20 mg/mL (1 mL): \$240.00

80 mg/2 mL (2 mL): \$1460.60

80 mg/4 mL (4 mL): \$960.00

160 mg/8 mL (8 mL): \$1920.00

200 mg/10 mL (10 mL): \$840.00

### Concentrate (Taxotere Intravenous)

20 mg/mL (1 mL): \$690.72

80 mg/4 mL (4 mL): \$2762.81

### Solution (DOCEtaxel (Non-Alcohol) Intravenous)

20 mg/mL (1 mL): \$258.00



80 mg/4 mL (4 mL): \$1032.00

160 mg/8 mL (8 mL): \$2064.00

### **Solution (DOCEtaxel Intravenous)**

20 mg/2 mL (2 mL): \$199.84

80 mg/8 mL (8 mL): \$799.48

160 mg/16 mL (16 mL): \$3036.35

**Disclaimer:** The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

**International Brand Names** Asodoc (CR, DO, GT, HN, MX, NI, PA, SV); Belotaxel (KR); Bestdocel (VN); Brexel (ID); Camitotic (LV); Celtere (LK); Daxotel (PH, SG, TH, VE, ZW); Decexan (LK); Dexotel (IN); Docefere (LK); Docetax (BD, IN, PH); Docetere (ID); Docexan (BD); Dolectran (EC); Doletran (PY); Donataxel (EC); Dotaxel (KR); Dotsetaks (UA); Doxecal (PH); Doxestad (PH); Doxetal (JO); Doxetasan (ID, LK); Hentaxel (PH); Isotera (TW); Monotaxel (KR); Newtaxel-A (PH); Newtaxell (VN); Oncodocel (BR, CO); Oncotaxel (AU, SG, TH); Pacancer (KR); Qvidadotax (ES); Taceedo (ET, PH); Taxanit (CR, DO, GT, HN, MX, NI, PA, SV); Taxanit RTU (CR, DO, GT, HN, NI, PA, SV); Taxelo (KR); Taxomed (PE); Taxotere (AE, AR, AT, AU, BD, BE, BF, BG, BH, BJ, BO, BR, CH, CI, CL, CN, CO, CR, CY, CZ, DE, DK, DO, EE, EG, ES, ET, FI, FR, GB, GH, GM, GN, GR, GT, HK, HN, HR, HU, ID, IE, IL, IS, IT, JO, JP, KE, KR, KW, LB, LR, LT, LU, LV, MA, ML, MR, MT, MU, MW, MX, MY, NE, NG, NI, NL, NZ, PA, PE, PH, PK, PL, PR, PT, PY, QA, RO, RU, SA, SC, SD, SE, SG, SI, SK, SL, SN, SV, TH, TN, TR, TW, TZ, UA, UG, UY, VE, VN, ZA, ZM, ZW); Taxozen (KR); Tedocad (BG); Texot (AR, LB, UY); Tyxan (TW); Vexdo (PH)

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