Docetaxel

Class:
Antineoplastic agent, Antimicrotubular, Taxane derivative.

Indications:
-Breast cancer:
-Non small cell lung cancer
-Prostate cancer
-Gastric adenocarcinoma
_Head and neck cancer
Unlabeled uses:
_Bladder cancer, metastatic
_Esophageal cancer
_Ewing sarcoma, osteosarcoma
_Ovarian cancer
_Small cell lung cancer, relapsed
_Soft tissue sarcoma
_Unknown-primary, adenocarcinoma

Available dosage form in the hospital:
20mg VIAL, 80mg VIAL

Trade Names:
Docefrez
Taxotere

Doses: Note: Premedicate with corticosteroids, beginning the day before docetaxel administration, (administer corticosteroids for 3 days) to reduce the severity of hypersensitivity reactions and fluid retention. Details concerning dosing in combination regimens should also be consulted.

-U.S. labeling:
-Breast cancer:I.V. infusion
-Locally-advanced or metastatic: 60-100 mg/m^2 every 3 weeks (as a single agent)
-Operable, node-positive (adjuvant treatment): 75 mg/m^2 every 3 weeks for 6 courses (in combination with doxorubicin and cyclophosphamide)
-Adjuvant treatment (unlabeled dosing): 75 mg/m^2 every 21 days (in combination with cyclophosphamide) for 4 cycles **or** 75 mg/m^2 every 21 days (in combination with carboplatin and trastuzumab) for 6 cycles
-Metastatic treatment (unlabeled dosing):
-Every-3-week administration: 75 mg/m^2 every 21 days (in combination with trastuzumab and pertuzumab) until disease progression or unacceptable toxicity **or** 100 mg/m^2 every 21 days (in combination with trastuzumab) for 6 cycles **or** 75 mg/m^2 every 21 days (in combination with capecitabine) until disease progression or unacceptable toxicity.
-Weekly administration: 40 mg/m^2/dose once a week (as a single agent) for 6 weeks followed by a 2-week rest, repeat until disease progression or unacceptable toxicity **or** 35 mg/m^2/dose once weekly for 3 weeks, followed by a 1-week rest, may increase to 40 mg/m^2 once weekly for 3 weeks followed by a 1-week rest with cycle 2 **or** 35 mg/m^2/dose once weekly (in combination with trastuzumab) for 3 weeks followed by a 1-week rest; repeat until disease progression or unacceptable toxicity

-Non small cell lung cancer:
I.V. infusion: 75 mg/m^2 every 3 weeks (as a single agent or in combination with cisplatin)
-Prostate cancer:
I.V. infusion: 75 mg/m^2 every 3 weeks (in combination with prednisone)

-Gastric adenocarcinoma:

-I.V. infusion: 75 mg/m^2 every 3 weeks (in combination with cisplatin and fluorouracil).

-Sequential chemotherapy and chemoradiation (unlabeled dosing): Induction: 75 mg/m^2 on days 1 and 22 (in combination with cisplatin) for 2 cycles, followed by chemoradiation: 20 mg/m^2 weekly for 5 weeks (in combination with cisplatin and radiation)

-Locally-advanced or metastatic disease (unlabeled dosing): 50 mg/m^2 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.

-Head and neck cancer: I.V. infusion: 75 mg/m^2 every 3 weeks (in combination with cisplatin and fluorouracil) for 3 or 4 cycles, followed by radiation therapy.

Canadian labeling:

-Breast cancer: I.V. infusion:

-*Locally-advanced or metastatic:* 75 mg/m^2 (as combination therapy) **or** 100 mg/m^2 (as a single agent) every 3 weeks

-*Operable, node-positive (adjuvant treatment):* 75 mg/m^2 every 3 weeks for 6 courses (in combination with doxorubicin and cyclophosphamide)

-Nonsmall cell lung cancer (locally-advanced or metastatic), ovarian cancer (metastatic), head and neck cancer (recurrent and/or metastatic): I.V. infusion: 75 mg/m^2 (as combination therapy) **or** 100 mg/m^2 (as a single agent) every 3 weeks

-Prostate cancer (hormone-refractory, metastatic): I.V. infusion: 75 mg/m^2 every 3 weeks (in combination with prednisone or prednisolone)

Unlabeled uses:

-Bladder cancer, metastatic (unlabeled use)): I.V. infusion: 100 mg/m^2 every 3 weeks (as a single agent) **or** 35 mg/m^2 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.

-Esophagealcancer(unlabeleduse):I.V.infusion:

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

- *Definitive chemoradiation*: 60 mg/m^2 on days 1 and 22 (in combination with cisplatin and radiation) for 1 cycle (Li, 2010).

- *Locally-advanced or metastatic disease*: 75 mg/m^2 on day 1 every 3 weeks (in combination with cisplatin and fluorouracil) **or** 50 mg/m^2 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 **or** 35 mg/m^2 weekly for 8 weeks (in combination with cisplatin, fluorouracil, and radiotherapy; neoadjuvant setting).

-Ewing sarcoma, osteosarcoma (recurrent or progressive; unlabeled uses): 100 mg/m^2 on day 8 of a 21-day cycle (in combination with gemcitabine)

-Ovarian cancer (unlabeled use in U.S.) I.V. infusion: 60 mg/m^2 every 3 weeks (in combination with carboplatin) **or** 75 mg/m^2 every 3 weeks (in combination with carboplatin) **or** 35 mg/m^2 (maximum dose: 70 mg) weekly for 3 weeks followed by a 1-week rest (in combination with carboplatin)

-Small cell lung cancer, relapsed (unlabeled use): I.V. infusion: 100 mg/m^2 every 3 weeks

-Soft tissue sarcoma (unlabeled use): I.V. infusion: 100 mg/m^2 on day 8 of a 3-week treatment cycle (in combination with gemcitabine and filgrastim or pegfilgrastim)

-Unknown-primary, adenocarcinoma (unlabeled use):I.V. infusion: 65 mg/m^2 every 3 weeks (in combination with carboplatin) (Greco, 2000) **or** 75 mg/m^2 on day 8 of a 3-week treatment cycle (in combination with gemcitabine) for up to 6 cycles (Pouessel, 2004) **or** 60 mg/m^2 on day 1 of a 3-week treatment cycle (in combination with cisplatin) .

-*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).

Geriatric
Refer to adult 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).

Hepatic Impairment:

U.S. labeling:

-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/

Canadian labeling: **Note:** Dosing recommendations when used as a single agent; dosage adjustment when used as part of combination therapy not provided in manufacturer's labeling.

- AST and/or ALT >1.5 times ULN and alkaline phosphatase >2.5 times ULN: Reduce dose from 100 mg/m^2 to 75 mg/m^2
- Serum bilirubin >ULN and/or AST and ALT > 3.5 times ULN associated with alkaline phosphatase >6 times ULN: Avoid use unless strictly indicated.
- Severe hepatic impairment: Use is contraindicated.

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

- Transaminases 1.6-6 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/mm^3 for >1 week, severe or cumulative cutaneous reactions; in nonsmall cell lung cancer, this may also include platelet nadir <25,000/mm^3 and other grade 3/4 nonhematologic toxicities.

-Breast cancer (single agent): Patients dosed initially at 100 mg/m^2; reduce dose to 75 mg/m^2;**Note:** If the patient continues to experience these adverse reactions, the dosage should be reduced to 55 mg/m^2 or therapy should be discontinued; discontinue for peripheral neuropathy ≥ grade 3. Patients initiated at 60 mg/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 ≥1500/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 mg/m^2) of docetaxel. Discontinue therapy with persistent toxicities after dosage reduction.

-Nonsmall cell lung cancer:

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

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

-Prostate cancer: Reduce dose to 60 mg/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 mg/m^2. Dosing with neutropenic complications in subsequent cycles should be further reduced to 45 mg/m^2. Patients who experience grade 4 thrombocytopenia should receive a dose reduction from 75 mg/m^2 to 60 mg/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%

-Canadian labeling: **Note:** Toxicity includes febrile neutropenia, neutrophils ≤500/mm^3 for >1 week, severe or cumulative cutaneous reactions, or severe neurosensory symptoms.

Patients initially dosed at 100 mg/m^2: Reduce dose to 75 mg/m^2; Patients initially dosed at 75 mg/m^2: Reduce dose to 60 mg/m^2. Discontinue therapy for persistent toxicities after dosage reduction.

-Breast cancer, adjuvant treatment (combination chemotherapy): 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, severe neurosensory symptoms, or grade 3 or 4 stomatitis should receive a reduced dose (60 mg/m^2). Discontinue therapy with persistent toxicities after dosage reduction.

-Concomitant use with capecitabine (treatment of metastatic breast cancer):

-Grade 2 toxicities:

- First episode: Interrupt therapy until resolution to < grade 2, then resume docetaxel and capecitabine at previous dose; consider prophylactic measures if appropriate and/or possible
- Second episode of same toxicity: Interrupt therapy until resolution to < grade 2, then resume docetaxel at 55 mg/m^2; reduce capecitabine dose to 75% of original dose
- Further episodes of same toxicity: Discontinue docetaxel; interrupt capecitabine until resolution to < grade 2, then resume at 50% of original dose (third episode) or discontinue therapy altogether (fourth episode)

-Grade 3 toxicities:

- First episode: Occurring at time treatment is due: Interrupt docetaxel until resolution to < grade 2 (maximum delay ≤2 weeks), then resume docetaxel at 55 mg/m^2; reduce capecitabine dose to 75% of original dose (consider prophylactic measure if appropriate); if no resolution to < grade 2 within 2 weeks, discontinue docetaxel but may resume capecitabine at 75% of original dose after resolution to < grade 2. Occurring between cycles and resolves to < grade 2 by time of next treatment: Administer docetaxel at 55 mg/m^2 and reduce capecitabine dose to 75% of original dose; consider prophylactic measures if appropriate and/or possible.
- Further episodes of same toxicity: Discontinue docetaxel; interrupt capecitabine until resolution to < grade 2, then resume capecitabine at 50% of original dose (second episode) or discontinue therapy altogether (third episode)

-Grade 4 toxicities: First episode: Discontinue docetaxel and capecitabine therapy or if deemed clinically necessary, capecitabine may be continued at 50% of original dose

Common side effects:

Central nervous system: Central nervous system toxicity ; including neuropathy) Dermatologic: Alopecia (, dermatological reaction, nail disease.

Endocrine & metabolic: Fluid retention (13% to 60%; dose dependent)

Gastrointestinal: Stomatitis, diarrhea; severe, nausea, vomiting

Hematologic & oncologic: Neutropenia, leukopenia, anemia, thrombocytopenia, febrile neutropenia

Hepatic: Increased serum transaminases

Hypersensitivity: Hypersensitivity

Infection: Increased susceptibility to infection

Neuromuscular & skeletal: Weakness, myalgia, neuromuscular reaction

Respiratory: Pulmonary events

Miscellaneous: Fever

Pregnancy Risk Factor: D