Docetaxel (Breast)

Indication

Treatment of advanced breast cancer where initial chemotherapy (including an anthracycline) has failed or is inappropriate.

(NICE CG 81)

ICD-10 codes

Codes with a prefix C50

Regimen details

Day	Drug	Dose	Route
1	Docetaxel	*100mg/m^2	IV infusion

*consider starting dose of 75mg/m^2 if patients are heavily pre-treated, have extensive bone metastases, significant co-morbidities or impaired LFTs.

Cycle frequency

21 days

Number of cycles

6 cycles (if well tolerated and patient has ongoing response, further cycles may be administered – consultant decision)

Administration

Docetaxel is administered as an IV infusion in 250mL or 500mL (concentration dependent) PVC free sodium chloride 0.9% over 60 minutes.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions.

Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of docetaxel and therefore facilities for the treatment of hypotension and bronchospasm must be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve re-started at a slower infusion rate. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate therapy.

Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel.

Pre-medication

Dexamethasone 8 mg BD (morning and lunchtime) for 3 days starting 24 hours prior to chemotherapy. (Note: Patients must receive 3 doses of dexamethasone prior to treatment).
In the case where 3 doses have not been taken, dexamethasone 16-20mg IV should be administered 30-60 minutes prior to chemotherapy and the remaining 3 oral doses should be taken as normal.

Emetogenicity

This regimen has mild - moderate emetic potential

Additional supportive medication

Mouthwashes as per local policy
H_2 antagonist or proton-pump inhibitor if required
Loperamide if required.
Scalp cooling may be offered.

Extravasation

Docetaxel is an exfoliant (Group 4)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Bilirubin	≤ 1.5 ULN
AST/ALT	≤ 1.5 x ULN
Alkaline Phosphatase*	≤ 2.5 x ULN

*unless due to bone metastases only

Dose modifications

- **Haematological toxicity**

If neutrophils <1.0 x 10^9/L and/or platelets <100 x 10^9/L delay 1 week or until recovery.

If febrile neutropenia or neutrophils < 0.5 x 10^9/L for more than 1 week reduce dose to 75% for all subsequent cycles. If a second occurrence reduce dose to 60% for future cycles.

If nadir platelets <25 x 10^9/L consider dose reduction to 60mg/m^2 after recovery (discuss with consultant)

- **Renal impairment**

There is no data available on the use of docetaxel in severe renal impairment. No modifications required.

- **Hepatic impairment**

AST/ALT (x ULN)		**Alkaline phosphatase*** (x ULN)	**Docetaxel dose**
≤ 1.5	and	< 2.5	100%
> 1.5	or	≥ 2.5- ≥ 5	75%
> 3.5	or	≥ 5	60% or discontinue (discuss with consultant)

*unless due to bone metastases only. If bilirubin > 1.5 x ULN withhold dose (or consultant decision to treat)

- **Other toxicities**

Toxicity	**Definition**	**Docetaxel dose**
Peripheral neuropathy	Grade 2	75%
	Grade 3 or 4	Discuss with consultant
Diarrhoea	Grade 3 or 4	1st occurrence – 75%
		2nd occurrence – 60%
Stomatitis	Grade 3 or 4	1st occurrence – 75%
		2nd occurrence – 60%

Any other grade 3 or 4 toxicity- discuss with consultant.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Secondary malignancy
Myelosuppression
Infusion related reactions
Anaphylaxis
Interstitial pneumonitis
Teratogenicity
Infertility
Cardiotoxicity

- **Frequently occurring side effects**

Diarrhoea
Constipation
Fatigue
Nausea and vomiting
Myelosuppression
Stomatitis and mucositis
Peripheral neuropathy
Arthralgia and myalgia

- **Other side effects**

Alopecia
Fluid retention
Deranged liver function
Phlebitis
Skin toxicity
Nail changes

Significant drug interactions – for full details consult product literature/ reference texts

CYP3A4 Enzyme inducers/inhibitors: in vitro studies suggest that CYP3A inhibitors (such as ketoconazole, ritonavir, clarithromycin and erythromycin) may raise docetaxel levels, whereas CYP3A inducers (such as rifampicin and barbiturates) may reduce docetaxel levels.

Additional comments

Nil

References

- Chan, S., et al. Randomised trial of docetaxel v doxorubicin in patients with metastatic breast cancer. JCO. 1999. 17 (8) 2341.
- National Institute for Health and Clinical Excellence. Clinical Guideline 81 – Advanced breast Cancer accessed 2 July 2014 via www.nice.org.uk
- Summary of Product Characteristics Docetaxel (Sanofi Aventis) accessed on 2 July 2014 via www.medicines.org.uk

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