DOCEtaxel Monotherapy 100mg/m^2 – 21 day cycle

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement status
DOCEtaxel monotherapy is indicated for the treatment of patients with locally advanced or metastatic breast cancer.	C50	00202a	Hospital

**If the reimbursement status is not defined [i], the indication has yet to be assessed through the formal HSE reimbursement process.*

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

DOCEtaxel is administered once every 21 days until disease progression or unacceptable toxicity develops.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	DOCEtaxel	100mg/m^2	IV infusion	[a]250ml 0.9% sodium chloride over 60min	Repeat every 21 days
Primary prophylaxis with G-CSF should be considered to reduce the risk of neutropenic complications (See Adverse Effects/Regimen Specific Complications)					
[a]75-185 mg dose use 250mL infusion bag. For doses > 185mg use 500mL infusion bag. Use non-PVC equipment					

ELIGIBILTY:

- Indications as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to DOCEtaxel or to any of the excipients
- Severe liver impairment
- Baseline neutrophil count < 1.5x10^9 cells/L

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile

Regular tests:

- FBC, renal and liver profile*
  *See Adverse Effects/Regimen specific complications for guidelines regarding hepatic dysfunction

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Haematological:

Table 1: Dose modification of DOCEtaxel for haematological toxicity

ANC ($x10^9$/L)	Dose
≥ 1.5	100mg/m^2
0.5 to less than 1.5	Delay treatment until recovery
Febrile neutropenia or <0.5 for more than 1 week	Reduce dose from 100 mg/m^2 to 75mg/m^2 and/or from 75 to 60 mg/m^2

Renal and Hepatic Impairment:

Table 2. Dose modification of DOCEtaxel in renal and hepatic impairment

Renal Dose Modification	Hepatic Dose modification					
	Alkaline Phosphatase		**AST and/or ALT**		**Serum Bilirubin**	**Dose**
No data available in patients with severely impaired renal function	Starting dose					100 mg/m^2
	> 2.5 ULN	and	> 1.5 ULN			75 mg/m^2
	> 6 ULN	and/or	> 3.5 ULN (AST and ALT)	and	> ULN	Stop treatment unless strictly indicated and should be discussed with a Consultant.

Management of adverse events:

Table 3: Dose modification schedule based on adverse events

Adverse reactions	Recommended dose modification
Grade 3 skin reaction	Reduce dose from 100 mg/m^2 to 75 mg/m^2 and/or from 75 mg/m^2 to 60mg/m^2
Grade >2 peripheral neuropathy	
Grade 3 or 4 stomatitis	Decrease dose to 60 mg/m^2

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Low **(Refer to local policy).**

PREMEDICATIONS:

Dexamethasone 8 mg PO twice daily for 3 days, starting one day prior to each DOCEtaxel administration unless contraindicated. Patient must receive minimum of 3 doses pre-treatment.
Consideration may be given, at the discretion of the prescribing consultant, to the use of a single dose of dexamethasone 20mg IV immediately before chemotherapy where patients have missed taking the oral premedication dexamethasone as recommended by the manufacturer.(4,5)

OTHER SUPPORTIVE CARE:
Primary prophylaxis with G-CSF should be considered to reduce the risk of neutropenic complications

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia**: Most frequent adverse reaction. Fever or other evidence of infection must be assessed promptly and treated appropriately. Frequent blood count monitoring should be conducted in all patients treated with DOCEtaxel. DOCEtaxel should be administered when the neutrophil count is > 1.5 x 10^9cells/L.
- **Neutropenic Enterocolitis:** A number of cases of neutropenic enterocolitis have been reported in patients treated with DOCEtaxel in France.(6) This is a known and rare side effect of DOCEtaxel which may affect up to one in 1,000 people).
- **Fluid Retention**: Dexamethasone premedication must be given to reduce the incidence and severity of fluid retention. It can also reduce the severity of the hypersensitivity reaction.
- **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. If hypersensitivity reactions occur, minor symptoms such as flushing or localized cutaneous reactions do not require interruption of therapy. However, severe reactions, such as severe 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.
- **Extravasation**: DOCEtaxel causes pain and tissue necrosis if extravasated. (Refer to local extravasation guidelines).
- **Hepatic Dysfunction**: DOCEtaxel undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST) may lead to increased toxicity and usually requires a dose reduction.

DRUG INTERACTIONS:

- Risk of drug interactions causing increased concentrations of DOCEtaxel with CYP3A inhibitors. Patients should also be counselled with regard to consumption of grapefruit juice.
- Risk of drug interactions causing decreased concentrations of DOCEtaxel with CYP3A inducers.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

DOCEtaxel - L01CD02

REFERENCES:

1. Trudeau ME, Eisenhauer ES, Higgins BP, Letendre F et al. DOCEtaxel in patients with metastatic breast cancer: a phase II study of the National Cancer Institute of Canada – Clinical Trials Group. J. Clin Oncol 1996; 14:422-8.
2. Chan, S., K. Friedrichs, D. Noel, et al., Prospective randomized trial of DOCEtaxel versus doxorubicin in patients with metastatic breast cancer. J Clin Oncol 1999;17:2341-2354.
3. Alexandre J, Bleuzen P, Bonneterre J, Sutherland W et al. Factors predicting for efficacy and safety of DOCEtaxel in a compassionate-use cohort of 825 heavily pretreated advanced breast cancer patients. J Clin Oncol 2000; 18:562-573.
4. Chouhan et al. Single premedication dose of dexamethasone 20mg IV before DOCEtaxel administration. J Oncol Pharm Practice 2010;17(3): 155–159.
5. Rogers ES et al. Efficacy and safety of a single dose of dexamethasone pre DOCEtaxel treatment: The Auckland experience. Annals of Oncology (2014) 25 (suppl_4): iv517-iv541.
6. Fatal Neutropenic Enterocolitis With DOCEtaxel in France by Aude Lecrubier. Available at: https://www.medscape.com/viewarticle/876014
7. Taxotere ® Summary of Product Characteristics. EMA Last updated 27/03/2019. Accessed May 2019 Available at: https://www.ema.europa.eu/en/documents/product-information/taxotere-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	10/02/2014		Dr Maccon Keane
2	30/05/2015	Modification of premedication regimen	Dr Maccon Keane
3	23/05/2017	Updated with new NCCP regimen format	Prof Maccon Keane
4	21/07/2017	Clarified use of G-CSF and updated re neutropenic enterocolitis	Prof Maccon Keane
5	22/05/2019	Treatment table infusion fluid standardised. Supportive care updated.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/