DOXOrubicin 50mg/m^2/DOCEtaxel 75mg/m^2(AT 50/75) Therapy– 21 day cycle

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement status
Treatment of locally advanced or metastatic breast carcinoma	C50	00423a	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.

DOXOrubicin and DOCEtaxel are administered on day 1 of a 21 day cycle for 6 cycles or until disease progression or unacceptable toxicity develops.

Order of Admin	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	DOXOrubicin	50mg/ m^2	IV push	Slow IV push over 15min	Repeat every 21 days
2	1	DOCEtaxel	75mg/m^2	IV infusion	*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)						
Lifetime cumulative dose of DOXOrubicin is 450mg/m^2 In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors outlined below[ii] and to the age of the patient.						
*75-185mg dose use 250mL infusion bag. For doses> 185mg use 500mL infusion bag. **Use non-PVC equipment**						

ELIGIBILTY:

- Indications as above
- ECOG 0-1
- Adequate haematological parameters (ANC > 1.5 x 10^9/L, platelets > 100 x 10^9/L)

EXCLUSIONS:

- Hypersensitivity to DOXOrubicin, DOCEtaxel or to any of the excipients
- Congestive heart failure (LVEF < 50%) or other significant heart disease
- Severe liver impairment
- Baseline neutrophil count < 1.5 x 10^9 cells/L
- Pregnancy or breast feeding
- Grade ≥ 2 peripheral neuropathy

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- ECG
- MUGA or ECHO (LVEF > 50% to administer DOXOrubicin) if > 65 years or clinically indicated.

Regular tests:

- FBC, renal and liver profile*
- If clinically indicated MUGA scan or echocardiogram.

*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 for haematological toxicity

ANC (x10^9/L)		Platelets (x10^9/L)	Dose
≥ 1.5	and	≥ 100	100%
<1.5	or	<100	Delay for 1 week

Renal and Hepatic Impairment:

Table 2: Dose modification in renal and hepatic impairment

Drug	Renal Impairment	Hepatic Impairment	
DOXOrubicin	No dose reduction required. Clinical decision in severe impairment	**Serum Bilirubin (micromol/L)**	**Dose**
		20-51	50%
		51-85	25%
		>85	Omit
		If AST 2-3 x normal give 75% If AST > 3 x ULN give 50%	
DOCEtaxel	No dose reduction required	See Table3 below	

Table 3 : Dose modification of DOCEtaxel in hepatic impairment.

Alkaline Phosphatase		AST and/or ALT		Serum Bilirubin	Dose
> 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 4: Dose modification of DOCEtaxel for adverse events

Adverse reactions	Recommended dose modification
Grade 3 skin reaction	Decrease dose to 60mg/m^2 If the patient continues to experience these reactions at 60 mg/m^2, the treatment should be discontinued
Grade >2 peripheral neuropathy	
Grade 3 or 4 stomatitis	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:
Moderate (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. (3,4)

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.

DOXOrubicin

- ***Extravasation****: DOXOrubicin may cause pain and tissue necrosis if extravasated. (Refer to local extravasation guidelines).*
- ***Cardiac Toxicity:*** *DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction.*

DOCEtaxel

- **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 > 1.5x10^{9}cells/L.
- **Neutropenic Enterocolitis:** A number of cases of neutropenic enterocolitis have been reported in patients treated with DOCEtaxel in France. (5) 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.
- **Hepatic Dysfunction**: DOCEtaxel undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST) may lead to increased toxicity and usually requires a dose reduction

DRUG INTERACTIONS:

- Concurrent administration of calcium channel blockers with DOXOrubicin should be avoided as they may decrease the clearance of DOXOrubicin.
- 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:

DOXOrubicin - L01DB01
DOCEtaxel - L01CD02

REFERENCES:

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Version	Date	Amendment	Approved By
1	14/06/2017		Prof Maccon Keane
2	19/06/2019	Standardised Treatment table	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/

[ii] Cardiotoxicity is a risk associated with anthracycline therapy that may be manifested by early (acute) or late (delayed) effects.
Risk factors for developing anthracycline-induced cardiotoxicity include:
• high cumulative dose, previous therapy with other anthracyclines or anthracenediones
• prior or concomitant radiotherapy to the mediastinal/pericardial area
• pre-existing heart disease
• concomitant use of other potentially cardiotoxic drugs
In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors above and to the age of the patient