DOXOrubicin 50mg/m²/Docetaxel 75mg/m² (AT 50/75) Therapy
– 21 day cycle

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of Locally Advanced or Metastatic Breast Carcinoma</td>
<td>C50</td>
<td>00423a</td>
<td></td>
</tr>
</tbody>
</table>

If a reimbursement indicator (e.g. ODMS, CDS) is not defined, the drug and its detailed indication have not gone through the formal reimbursement process as legislated for in the Health (Pricing and Supply of Medical Goods) Act 2013.

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 patient's 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.

<table>
<thead>
<tr>
<th>Order of Admin</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>DOXOrubicin</td>
<td>50mg/m²</td>
<td>IV push</td>
<td>N/A</td>
<td>Repeat every 21 days</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>Docetaxel</td>
<td>75mg/m²</td>
<td>IV infusion</td>
<td>*250ml 0.9% sodium chloride or 5% glucose over 60min</td>
<td>Repeat every 21 days</td>
</tr>
</tbody>
</table>

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/m²
In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors outlined below 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

ELIGIBILITY:
- Indications as above
- ECOG 0-1
- Adequate haematological parameters (ANC > 1.5 x 10⁹/L, platelets > 100 x 10⁹/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 10⁹ cells/L
- Pregnancy or breast feeding
- Grade ≥ 2 peripheral neuropathy
NCCP Chemotherapy Regimen

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

TESTS:
Baseline tests:
- FBC, U&Es, LFTs
- ECG
- MUGA or ECHO (LVEF > 50% to administer doxorubicin) if > 65 years or clinically indicated.

Regular tests:
- FBC, U&Es, LFTs*
- 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

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5</td>
<td>and ≥ 100</td>
<td>100%</td>
</tr>
<tr>
<td>&lt;1.5</td>
<td>or &lt;100</td>
<td>Delay for 1 week</td>
</tr>
</tbody>
</table>

Renal and Hepatic Impairment:
Table 2: Dose modification in renal and hepatic impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOXOrubicin</td>
<td>No dose reduction required.</td>
<td>Serum Bilirubin</td>
</tr>
<tr>
<td></td>
<td>Clinical decision in severe impairment</td>
<td>(micromol/L)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20-51</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51-85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If AST 2-3 x normal give 75%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If AST &gt; 3 x ULN give 50%</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>No dose reduction required</td>
<td>See Table3 below</td>
</tr>
</tbody>
</table>

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens
Table 3: Dose modification of docetaxel in hepatic impairment.

<table>
<thead>
<tr>
<th>Alkaline Phosphatase</th>
<th>AST and/or ALT</th>
<th>Serum Bilirubin</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 2.5 ULN</td>
<td>and</td>
<td>&gt; 1.5 ULN</td>
<td>75 mg/m²</td>
</tr>
<tr>
<td>&gt; 6 ULN</td>
<td>and/or</td>
<td>&gt; 3.5 ULN (AST and ALT)</td>
<td>and</td>
</tr>
</tbody>
</table>

Management of adverse events:

Table 4: Dose modification schedule based on adverse events

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Recommended dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3 skin reaction</td>
<td>Decrease dose to 60mg/m²</td>
</tr>
<tr>
<td>Grade &gt;2 peripheral neuropathy</td>
<td>If the patient continues to experience these reactions at 60 mg/m², the treatment should be discontinued</td>
</tr>
<tr>
<td>Grade 3 or 4 stomatitis</td>
<td></td>
</tr>
</tbody>
</table>

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 (5,6)

OTHER SUPPORTIVE CARE: No specific recommendations

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 > 1.5x10⁹ cells/L.
- Neutropenic Enterocolitis: A number of cases of neutopenic 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:**
NCCP Chemotherapy Regimen

Tumour Group: Breast
NCCP Regimen Code: 00423

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.