DOCEtaxel Monotherapy 100mg/m² – 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>DOCEtaxel monotherapy is indicated for the treatment of patients with locally advanced or metastatic breast cancer.</td>
<td>C50</td>
<td>00202a</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.

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

<table>
<thead>
<tr>
<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>DOCEtaxel</td>
<td>100mg/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)

*75-185 mg dose use 250mL infusion bag. For doses > 185mg use 500mL infusion bag. Use non-PVC equipment

ELIGIBILITY:
- Indications as above
- ECOG 0-2

EXCLUSIONS:
- Hypersensitivity to DOCEtaxel or to any of the excipients
- Severe liver impairment
- Baseline neutrophil count < 1.5x10⁹ cells/L

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

TESTS:
Baseline tests:
- FBC, U&Es, LFTs

Regular tests:
- FBC, U&Es, LFTs*
- *See Adverse Effects/Regimen specific complications for guidelines regarding hepatic
DOSE MODIFICATIONS:
- Any dose modification should be discussed with a Consultant

Haematological:
Table 1: Dose modification of DOCEtaxel for haematological toxicity

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5</td>
<td>100mg/m²</td>
</tr>
<tr>
<td>0.5 to less than 1.5</td>
<td>Delay treatment until recovery</td>
</tr>
<tr>
<td>Febrile neutropenia or &lt;0.5 for more than 1 week</td>
<td>Reduce dose from 100 mg/m² to 75mg/m² and/or from 75 to 60 mg/m²</td>
</tr>
</tbody>
</table>

Renal and Hepatic Impairment:
No data available in patients with severely impaired renal function

Table 2. 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>Starting dose</td>
<td></td>
<td></td>
<td>100 mg/m²</td>
</tr>
<tr>
<td>&gt; 2.5 ULN</td>
<td>and &gt; 1.5 ULN</td>
<td>and &gt; ULN</td>
<td>75 mg/m²</td>
</tr>
<tr>
<td>&gt; 6 ULN</td>
<td>and or &gt; 3.5 ULN (AST and ALT)</td>
<td>and &gt; ULN</td>
<td>Stop treatment unless strictly indicated and should be discussed with a Consultant.</td>
</tr>
</tbody>
</table>

Management of adverse events:
Table 3: 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>Reduce dose from 100 mg/m² to 75 mg/m² and/or from 75 mg/m² to 60mg/m²</td>
</tr>
<tr>
<td>Grade &gt;2 peripheral neuropathy</td>
<td>Decrease dose to 60 mg/m²</td>
</tr>
<tr>
<td>Grade 3 or 4 stomatitis</td>
<td></td>
</tr>
</tbody>
</table>

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:
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.

- **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 10^9 cells/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:
NCCP Chemotherapy Regimen


<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10/02/2014</td>
<td></td>
<td>Dr Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>30/05/2015</td>
<td>Modification of premedication regimen</td>
<td>Dr Maccon Keane</td>
</tr>
<tr>
<td>3</td>
<td>23/05/2017</td>
<td>Updated with new NCCP regimen format</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>4</td>
<td>21/07/2017</td>
<td>Clarified use of G-CSF and updated re neutropenic enterocolitis</td>
<td>Prof Maccon Keane</td>
</tr>
</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1 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/profinfomedon/cdmp/

NCCP Regimen: DOCEtaxel
100mg/m² Monotherapy-21 day

Published: 10/02/2014
Review: 01/09/2019
Version number: 4

Tumour Group: Breast
NCCP Regimen Code: 00202
ISMO Contributor: Prof Maccon Keane

Page 4 of 4

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE’s terms of use available at http://www.hse.ie/eng/disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens