DOXOrubicin (60mg/m²) Therapy

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of unresectable or metastatic hepatocellular carcinoma not suitable for treatment with regional therapies</td>
<td>C22</td>
<td>00386a</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

*If the reimbursement status is not defined, 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 patient's individual clinical circumstances.

DOXOrubicin is administered once every 21 days for 3-6 cycles or until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

<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>DOXOrubicin*</td>
<td>60mg/m²</td>
<td>IV bolus</td>
<td>Slow bolus with 0.9% NaCl</td>
<td>Every 21 days for 3-6 cycles</td>
</tr>
</tbody>
</table>

*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.

ELIGIBILITY:
- Indications as above
- ECOG 0-3
- Adequate hepatic, renal, and bone marrow function

EXCLUSIONS:
- Hypersensitivity to DOXOrubicin or any of the excipients
- Pregnancy
- Lactation

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

TESTS:
Baseline tests:
- FBC, liver and renal profile
- Cardiac function using MUGA or ECHO (LVEF > 50% to administer doxorubicin) if >65 years or if clinically indicated (e.g. smoking history, hypertension).

Regular tests:
- FBC, liver and renal profile prior to each cycle
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 DOXOrubicin in haematological toxicity

<table>
<thead>
<tr>
<th>ANC (x10^3 /L)</th>
<th>Platelets (x10^3 /L)</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1 Or &lt;1</td>
<td>&gt;100 Or &lt;70</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delay</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
<th>Total Bilirubin (micromole/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dose modification required</td>
<td>Total Bilirubin (micromole/L)</td>
<td>Dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20-50</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>51-85</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;85</td>
<td>Omit</td>
<td></td>
</tr>
</tbody>
</table>

- If AST 2-3 x normal, give 75% dose.
- If AST >3x ULN, give 50% dose

SUPPORTIVE CARE:
EMETOGENIC POTENTIAL: Low-Moderate (Refer to local policy).

PREMEDICATIONS:
None usually required

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: Fever or other evidence of infection must be assessed promptly and treated appropriately.
- Cardiotoxicity: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction
- Extravasation: DOXOrubicin causes pain and tissue necrosis if extravasated (Refer to local policy).
NCCP Chemotherapy Regimen

DRUG INTERACTIONS:

- DOXOrubicin cardiotoxicity is enhanced by previous or concurrent use of other anthracyclines, or other potentially cardiotoxic drugs (e.g. 5-fluorouracil, cyclophosphamide or paclitaxel) or with products affecting cardiac function (e.g. calcium antagonists).
- Current drug interaction databases should be consulted for more information.

ATC CODE:
DOXOrubicin L01DB01

REFERENCES:

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20/12/2016</td>
<td></td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>26/11/2018</td>
<td>Updated to new NCCP template. Standardisation</td>
<td>Prof Maccon Keane</td>
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<tr>
<td></td>
<td></td>
<td>of dosing in hepatic impairment</td>
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</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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/proinfo/medonc/cdmp/

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

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 responsibility of the prescribing clinician. and is subject to HSE’s terms of use available at http://www.hse.ie/eng/Disclaimer

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