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 metastatic breast cancer in adult patients who have failed</td>
<td>C50</td>
<td>00230a</td>
<td>Hospital</td>
</tr>
<tr>
<td>first-line treatment for metastatic disease and for whom standard,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>anthracycline containing therapy is not indicated.</td>
<td></td>
<td></td>
<td></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.

Nab-PACLitaxel (Abraxane®) is administered once every 21 days until disease progression or unacceptable toxicity develops. Discontinue treatment if no response after 2 cycles.

Facilities to treat anaphylaxis MUST be present when Nab PACLitaxel (Abraxane®) is administered.

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug (Abraxane®)</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nab PACLitaxel</td>
<td>260mg/m²</td>
<td>IV infusion</td>
<td>over 30mins</td>
<td>Repeat every 21 days</td>
</tr>
</tbody>
</table>

The use of medical devices containing silicone oil as a lubricant (i.e. syringes and IV bags) to reconstitute and administer Abraxane® may result in the formation of proteinaceous strands.

Administer Abraxane® using an infusion set incorporating a 15 μm filter to avoid administration of these strands. Use of a 15 μm filter removes strands and does not change the physical or chemical properties of the reconstituted product. If strands are present and a filter is not available, the product must be discarded.

ELIGIBILITY:

- Indications as above
- ECOG status 0-2
- Life expectancy > 3 months

EXCLUSIONS:

- Hypersensitivity to PACLitaxel, albumin, or to any of the excipients
- Patients who have progressed on prior taxane therapy
- Breast Feeding
- Severe hepatic impairment
- Grade ≥ 2 sensory or motor neuropathy
PRESCRIPTIVE AUTHORITY:
The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:
Baseline tests:
- FBC, renal and liver profile
- Assessment of cardiac function, e.g. ECHO/MUGA scan if significant cardiac history or previous anthracycline therapy

Regular tests:
- FBC, renal and liver profile prior to each cycle
- Cardiac function if clinically indicated

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 modifications for neutropenia and/or thrombocytopenia

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose of Nab-PACLitaxel (Abraxane®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5</td>
<td>and ≥100</td>
<td>260mg/m²</td>
</tr>
<tr>
<td>1-1.49</td>
<td>and ≥ 100</td>
<td>220mg/m²</td>
</tr>
<tr>
<td>&lt;1 OR &lt;100</td>
<td></td>
<td>Delay until ANC ≥ 1.5 x10⁹/L and platelets ≥ 100 x10⁹/L, then consider giving 220mg/m²</td>
</tr>
</tbody>
</table>

Table 2: Dose modifications for febrile neutropenia

<table>
<thead>
<tr>
<th>Occurrence</th>
<th>Dose modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Occurrence</td>
<td>Delay until recovery (ANC ≥ 1.5 x10⁹/L and platelets ≥ 100 x10⁹/L), then dose reduce to 220mg/m²*</td>
</tr>
<tr>
<td>Second Occurrence</td>
<td>Delay until recovery (ANC ≥ 1.5 x10⁹/L and platelets ≥ 100 x10⁹/L), then dose reduce to 180mg/m²*</td>
</tr>
</tbody>
</table>

*Dose reductions should be maintained for subsequent cycles and not re-escalated.
Renal and Hepatic Impairment:

**Table 3: Dose modification of NabPACLitaxel and gemcitabine in renal and hepatic impairment**

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr Cl (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td>≥30 to &lt;90</td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Insufficient data available to make recommendation</td>
</tr>
<tr>
<td></td>
<td>&gt;5 x ULN or &gt;10 x ULN</td>
</tr>
</tbody>
</table>

**The reduced dose may be escalated to the dose for patients with normal hepatic function if the patient is tolerating the treatment for at least two cycles.**

Management of adverse events:

**Table 4: Dose Modifications for Adverse Events**

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Recommended dose modification</th>
</tr>
</thead>
</table>
| Grade ≥3 motor or sensory neuropathy  
  First occurrence | Hold treatment until resolved to grade 2 or less, then reduce dose to 220mg/m²*** |
| Second occurrence | Hold treatment until resolved to grade 2 or less, then reduce dose to 180mg/m²*** |
| Grade 4 motor or sensory neuropathy  
  First occurrence | Hold treatment until resolved to grade 2 or less, then reduce dose to 220mg/m²*** |
| Second occurrence | Discontinue OR Hold treatment until resolved to grade 2 or less, then reduce dose to 180mg/m²*** |

***Dose reductions should be maintained for subsequent cycles and not re-escalated.***

**SUPPORTIVE CARE:**

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

**PREMEDICATIONS:** None usually required.

**OTHER SUPPORTIVE CARE:**
Myalgias and arthralgias may occur with PACLitaxel. Analgesic cover should be considered.

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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](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](http://www.hse.ie/NCCPchemoregimens).
ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

Abraxane is an albumin-bound nanoparticle formulation of PACLitaxel, which may have substantially different pharmacological properties compared to other formulations of PACLitaxel. It should not be substituted for or with other PACLitaxel formulations.

- **Hypersensitivity**: Rare occurrences of severe hypersensitivity reactions have been reported. If a hypersensitivity reaction occurs, the medicinal product should be discontinued immediately, symptomatic treatment should be initiated, and the patient should not be rechallenged with PACLitaxel.

- **Extravasation**: PACLitaxel causes pain and tissue necrosis if extravasated. (Refer to local policy).

- **Neutropenia**: Bone marrow suppression (primarily neutropenia) occurs frequently with Abraxane®. Neutropenia is dose-dependent and a dose-limiting toxicity. Frequent monitoring of blood cell counts should be performed during Abraxane® therapy. Patients should not be retreated with subsequent cycles of Abraxane until neutrophils recover to >1.5 x 10^9/L and platelets recover to >100 x 10^9/L (see Table 1). **Peripheral neuropathy**: Sensory neuropathy occurs frequently with Nab PACLitaxel (Abraxane®), although development of severe symptoms is less common. If grade 3 sensory neuropathy develops, treatment should be withheld until resolution to grade 1 or 2 followed by a dose reduction for all subsequent courses of Abraxane (see Table 4).

- **Hepatic Dysfunction**: Because the toxicity of PACLitaxel can be increased with hepatic impairment, administration of Nab PACLitaxel (Abraxane®) in patients with hepatic impairment should be performed with caution. Nab PACLitaxel (Abraxane®) is not recommended in patients that have total bilirubin > 5 x ULN or AST > 10 x ULN.

- **Cardiotoxicity**: Rare reports of congestive heart failure and left ventricular dysfunction have been observed among individuals receiving Nab PACLitaxel (Abraxane®). Most of the individuals were previously exposed to cardiotoxic medicinal products such as anthracyclines, or had underlying cardiac history.

- **Pneumonitis**: Even though the incidence is low, patients should be closely monitored for signs and symptoms of pneumonitis. During the conduct of a trial in metastatic pancreatic cancer, a higher rate of pneumonitis events was observed in patients receiving Abraxane® in combination with gemcitabine.

DRUG INTERACTIONS:

- Risk of drug interactions causing increased concentrations of PACLitaxel with CYP3A inhibitors. Patients should also be counselled with regard to consumption of grapefruit juice.

- Risk of drug interactions causing decreased concentrations of PACLitaxel with CYP3A inducers.

- Current drug interaction databases should be consulted for more information.

ATC CODE:

PACLitaxel - L01CD01

REFERENCES:

2. BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using PACLitaxel-NAB (ABRAXANE) BRAVABR October 2016

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>05/04/2014</td>
<td></td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>29/04/2014</td>
<td>Updated advice on filters for administration</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>3</td>
<td>08/04/2016</td>
<td>Updated dose modifications in renal and hepatic impairment and for adverse reactions (Table 1) as per SmPC</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>4</td>
<td>18/04/2018</td>
<td>Updated with new NCCP regimen template, Updated hepatoxicity adverse events as per SmPC</td>
<td>Prof Maccon Keane</td>
</tr>
</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1ODMS – 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/

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