Nab-PACLitaxel (Abraxane®) Monotherapy– 21 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of metastatic breast cancer in adult patients who have failed first-line treatment for metastatic disease and for whom standard, anthracycline containing therapy is not indicated.	C50	00230a	Hospital

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.

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

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Nab PACLitaxel (Abraxane®)	260mg/m^2	IV infusion	over 30mins	Repeat every 21days

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.

ELIGIBILTY:

- 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

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose of Nab-PACLitaxel (Abraxane®)
≥ 1.5	and	≥100	260mg/m^2
1-1.49	and	≥ 100	220mg/m^2
<1	OR	< 100	Delay until ANC≥ 1.5 $x10^9$/L and platelets ≥ 100 $x10^9$/L, then consider giving 220mg/m^2

Table 2: Dose modifications for febrile neutropenia

First Occurrence	Delay until recovery (ANC≥ 1.5 $x10^9$/L and platelets ≥ 100 $x10^9$/L), then dose reduce to **220mg/m^{2*}**
Second Occurrence	Delay until recovery (ANC≥ 1.5 $x10^9$/L and platelets ≥ 100 $x10^9$/L), then dose reduce to **180mg/m^{2*}**

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

Renal and Hepatic Impairment:

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

Renal Impairment		Hepatic Impairment			
CrCl (ml/min)	**Dose**	**Bilirubin**		**AST**	**Dose**
≥30 to <90	No dose adjustment necessary	> 1 to ≤ 1.5 x ULN	and	≤ 10 x ULN	No dose adjustment required
<30	Insufficient data available to make recommendation	> 1.5 to ≤ 5 x ULN	and	≤ 10 x ULN	20% dose reduction**
		>5 x ULN	or	>10 x ULN	Insufficient data to permit dosage recommendations

**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

Adverse reactions	Recommended dose modification
Grade ≥3 motor or sensory neuropathy	
First occurrence	Hold treatment until resolved to grade 2 or less, then reduce dose to 220mg/m^2***
Second occurrence	Hold treatment until resolved to grade 2 or less, then reduce dose to 180mg/m^2***
Grade 4 motor or sensory neuropathy	
First occurrence	Hold treatment until resolved to grade 2 or less, then reduce dose to 220mg/m^2***
Second occurrence	Discontinue OR Hold treatment until resolved to grade 2 or less, then reduce dose to 180mg/m^2***

***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.

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:

1. Gradishar WJ et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. J Clin Oncol 2005;23(31):7794-803

2. BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer usingPACLitaxel-NAB (ABRAXANE®) BRAVABR October 2016
3. MHRA, Drug Safety Update, Abraxane (paclitaxel, formulated as albumin-bound nanoparticles): potential presence of strands in intravenous infusion bag—if visible, filtration advised. February 2014, Available at http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON377646
4. ABRAXANE Summary of Product Characteristics. Last updated: 09/03/2020. Accessed April2020. Available at https://www.ema.europa.eu/en/documents/product-information/abraxane-epar-product-information_en.pdf
5. NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting. V2 2019. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

Version	Date	Amendment	Approved By
1	05/04/2014		Prof Maccon Keane
2	29/04/2014	Updated advice on filters for administration	Prof Maccon Keane
3	08/04/2016	Updated dose modifications in renal and hepatic impairment and for adverse reactions (Table 1) as per SmPC	Prof Maccon Keane
4	18/04/2018	Updated with new NCCP regimen template, Updated hepatoxicity adverse events as per SmPC	Prof Maccon Keane
5	29/04/2020	Reviewed.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.