nab-PACLitaxel Weekly Monotherapy–28 day

Note: This regimen is intended for the treatment of patients with hypersensitivity to standard PACLitaxel formulation.

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE Reimbursement status*
Treatment of metastatic breast carcinoma (mBC) in patients who have either failed or are not candidates for standard, anthracycline-containing therapy[i]	C50	00736a	N/A

*This is for post 2012 indications only

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 is administered on days 1, 8 and 15 of a 28 day treatment cycle as an alternative to weekly PACLItaxel for patients who are unable to receive standard PACLitaxel formulation for the above indication. Treatment should continue until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1, 8, 15	nab-PACLitaxel	100mg/m^2	IV infusion	over 30 minutes	Repeat every 28 days
The use of medical devices containing silicone oil as a lubricant (i.e. syringes and IV bags) to reconstitute and administer nab-PACLitaxel may result in the formation of proteinaceous strands. Administer nab-PACLitaxel using an infusion set incorporating a 15µm filter to avoid administration of these strands. Use of a 15µm 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

EXCLUSIONS:

- Hypersensitivity to nab-PACLitaxel, albumin, or to any of the excipients
- Baseline neutrophil count < 1.5 x 10^9/L
- Breastfeeding
- 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, (ECHO/MUGA scan) where clinically indicated such as significant cardiac history or previous anthracycline therapy

Regular tests:

- FBC, renal and liver profile prior to each cycle
- Day 8: FBC
- 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: nab PACLitaxel dose reduction levels

Dose Level	nab-PACLitaxel Dose (mg/m^2)
Full Dose	100
1st Dose Level Reduction	80
2nd Dose Level Reduction	60

Table 2: Dose modifications for neutropenia and/or thrombocytopenia

ANC (x10^9/L)		Platelets (x10^9/L)	Dose of nab-PACLitaxel
≥ 1.0	and	≥ 75	Full dose
0.5-1.0	and	50 -75	Delay until recovery, and continue with full dose
< 0.5	OR	< 50	Delay until recovery, and reduce by one dose level
Febrile neutropenia or previous delay for myelosuppression			Delay until recovery, and reduce by one dose level

Renal and Hepatic Impairment:

Table 3: Dose modification of nab-PACLitaxel in renal and hepatic impairment

Renal Impairment		Hepatic Impairment
CrCl (mL/min)	**Dose**	Mild: no dose adjustment is needed
≥30	No dose adjustment is needed	Moderate and severe: approximately 80% of original dose
<30	No need for dose adjustment is expected	Bilirubin > 5 x ULN or AST > 10 x ULN: contraindicated
Haemodialysis	No need for dose adjustment is expected	
Dose modifications from Giraud et al 2023		

Management of adverse events:

Table 4: Dose modification of nab-PACLitaxel 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 by one dose level **
– Second occurrence	Hold treatment until resolved to grade 2 or less, then reduce dose by a further dose level **
Grade 4 motor or sensory neuropathy	
– First occurrence	Hold treatment until resolved to grade 2 or less, then reduce dose to by one dose level **
– Second occurrence	Discontinue OR Hold treatment until resolved to grade 2 or less, then reduce by a further dose level **

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

SUPPORTIVE CARE:

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

PRE-MEDICATIONS: 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.

nab-PAClitaxel 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 nab-PACLitaxel. Neutropenia is dose-dependent and a dose-limiting toxicity. Frequent monitoring of blood cell counts should be performed during nab-PACLitaxel therapy. Patients should not be retreated with subsequent cycles of until neutrophils recover to >1.5 x 10^9/L and platelets recover to >100 x 10^9/L.
- **Peripheral neuropathy:** Sensory neuropathy occurs frequently with nab-PACLitaxel, 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 nab-PACLitaxel (see Table 4).
- **Hepatic Dysfunction:** Because the toxicity of PACLitaxel can be increased with hepatic impairment, administration of nab-PACLitaxel in patients with hepatic impairment should be performed with caution. nab-PACLitaxel 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. 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 nab-PACLitaxel in combination with gemcitabine.

DRUG INTERACTIONS:

- Risk of drug interactions causing increased concentrations of PACLitaxel with CYP3A4 and CYP2C8 inhibitors. Patients should also be counselled with regard to consumption of grapefruit juice.
- Risk of drug interactions causing decreased concentrations of PACLitaxel with CYP3A4 and CYP2C8 inducers.
- Current drug interaction databases should be consulted for more information.

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Version	Date	Amendment	Approved By
1	26/08/2022		Prof. Maccon Keane
2	13/03/2024	Reviewed. Updated renal and hepatic dose recommendations in line with Giraud et al 2023.	Prof. Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This regimen is outside its licensed indication in Ireland. Patients should be informed of the unlicensed nature of this indication and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be aware of their responsibility in communicating any relevant information to the patient and also in ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.