Nab-Paclitaxel use in patients with Taxane Hypersensitivity

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Version	Date published	Amendment	Approved By
1	23/07/2025	Version 1	NCCP Medical Oncology Clinical Leads Group

Contents

Summary of the recommendation

Nab-paclitaxel is a reasonable alternative to taxanes in patients with taxane-induced hypersensitivity reactions (HSRs). Evidence suggest comparable efficacy between nab-paclitaxel and taxanes in cancer treatments for many indications. Nab-paclitaxel addresses patients' unmet needs by allowing treatment completion after HSRs in either adjuvant or advanced settings of cancer treatments.

Nab-paclitaxel can be prescribed for patients with Grade 2 or 3 moderate to severe HSRs, anaphylaxis or anaphylactoid reactions or significant contraindications to taxanes that are not manageable despite the use of premedications and increased infusion durations.

There are expected benefits through reduced resource utilisation and reduced patient treatment burden.

Nab-paclitaxel is not considered high cost SACT and therefore will be funded through local hospital budgets. In addition, as nab-paclitaxel is not considered high cost its use does not require approval from the HSE Senior Leadership Team as per the HSE Overview of Medicines Funding Governance Processes.

Background

Taxane agents are used in the treatment of many types of cancers, and include paclitaxel, docetaxel, nab-paclitaxel, and cabazitaxel [1].

Studies have shown rates of immediate HSRs of up to 50% with paclitaxel and docetaxel infusions, resulting in the routine use of antihistamine and steroid medications prior to infusion [2,3]. However despite premedication HSRs occur in approximately 10% of patients and are severe in 1% [2].

Alongside this, hypersensitivity reactions to taxanes typically involves desensitisation or slower drug infusions which prolongs treatment times increasing the strain on patients, nursing and pharmacy staff and day unit capacity.

Nab-paclitaxel, which is routinely given without premedications is associated with a lower incidence of hypersensitivity reactions than other taxanes, which is thought to be due to the fact that it is not formulated with Cremophor EL or polysorbate 80 [1,4-5].

Guidelines, case reports and small clinical trials have described substituting *nab*-paclitaxel for other taxanes for example in the treatment of gynaecologic cancers [4-5,12-13] and breast cancers, [6-7,13] and have shown that nab-paclitaxel is safe and well-tolerated as a substitute to other taxanes. In addition to safety and tolerability, one paper demonstrated improved clinical effectiveness when compared with paclitaxel in relation to time to treatment discontinuation and time to next treatment for patients with breast cancer [8].

Nab-paclitaxel represents an appealing alternative for patients who develop significant HSRs to traditional taxanes which cannot be managed despite premedication use.

The appropriate use of nab-paclitaxel has the potential to reduce resource utilisation and reduce patient burden on treatment. In addition, by switching to nab-paclitaxel for hypersensitivity reactions, it allows the continuation of taxane therapy in the adjuvant curative setting or in the advanced setting where treatment could prolong life.

Currently reimbursed and licensed indications for nab-paclitaxel:

This guideline recommendation is not intended to alter clinical practice or reimbursement for nab-paclitaxel indications which are already approved for reimbursement by the HSE through the Oncology Drugs Management System (ODMS)/hospital budgets. Nor is this guidance intended to alter clinical practice for nab-paclitaxel indications which are already licensed or will be licensed in the future.

To note, nab-paclitaxel substitution would not invalidate the reimbursement status of other high cost SACT that was being administered in combination with paclitaxel i.e. if a patient is being treated with Pembrolizumab, Paclitaxel and Carboplatin and it is deemed suitable to use nab-paclitaxel instead of paclitaxel then the pembrolizumab reimbursement status would not be invalidated in this instance.

Nab-paclitaxel treatment guideline and considerations:

The use of nab-paclitaxel may not be standard of care for some indications. While there may be clinical evidence, the responsibility for the clinical appropriateness of the decision to use nab-paclitaxel instead of paclitaxel remains with the treating clinician.

Nab-paclitaxel is comparable to paclitaxel in terms of clinical efficacy based on some of the available studies that showed non inferiority efficacy for nab-paclitaxel compared to paclitaxel.

Nab-paclitaxel can be prescribed for patients who have one of the following characteristics:

- After a second grade 2 or first grade 3 moderate to severe hypersensitivity reaction to taxanes (according to Common Terminology Criteria for Adverse Events (CTCAE) not manageable despite the use of premedications and prolonged infusion times,
- anaphylaxis or anaphylactoid reactions,
- patients with significant contraindications to taxanes or premedications (e.g., high dose steroids)

Nab-paclitaxel for use in the above circumstances will be funded through the hospitals drug budget; nab-paclitaxel is no longer considered high cost. Local processes for the use of unlicensed medicines should be followed.

Nab-paclitaxel would not be suitable in the following situations:

- Taxane resistant/refractory disease
- Disease progression on prior taxane therapy
- Severe hepatic dysfunction contraindicating nab-paclitaxel
- Patients with greater than or equal to grade 2 sensory or motor neuropathy
- Patients with any contraindications to nab-paclitaxel as outlined in the Summary of Product Characteristics.

Based on a number of Phase 3 randomized controlled studies comparing the use of nab-paclitaxel to paclitaxel, there is evidence to support that nab-paclitaxel is comparable to paclitaxel in the treatment of patients with various solid organ tumours (e.g., breast, lung, and gastroesophageal cancers) [9-11].

Consider the use of nab-paclitaxel for patients with contraindications to high dose steroids such as in patients with difficult to control diabetes or steroid induced neurocognitive changes. To note HSR's

are less common with docetaxel and patients who experience HSR's to docetaxel should be managed similarly to those with HSR's to paclitaxel.

The dosing conversion between paclitaxel and nab-paclitaxel should be left to the discretion of treating clinicians and pharmacy teams. Appendix 1 provides an overview of common dosing regimens used.

Nab-paclitaxel should be prescribed in accordance with the same standards as for other anti-cancer medicines. Clinicians prescribing nab-paclitaxel will be responsible for verifying the doses, providing the prescriptions and administering the medications, according to acceptable standards of care. Use of nab-paclitaxel for licensed and unlicensed indications is the responsibility of the treating clinician.

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Appendix 1 Dosing Guidance

General points to note:

- Patients receiving nab-paclitaxel due to taxane hypersensitivity should be managed according to the primary treatment regimen for their tumour type.
- **Premedication** not required: unlike paclitaxel, nabpaclitaxel does not contain Cremophor EL, which is often the cause of HSRs. This makes it suitable for patients with previous paclitaxel HSRs.
- **Neuropathy risk**: Nab-paclitaxel is associated with higher incidence of peripheral neuropathy than solvent based paclitaxel, especially at higher doses
- **Myelosuppression**: Neutropenia is a common adverse effect, particularly in combination regimens
- **Dose adjustments**: Consider renal and hepatic function when dosing. Nab-paclitaxel is metabolised hepatically.

Note: Dosing may vary by institution or patient specific factors. The below table reflects common regimens found in literature and guidelines. See local protocols and product labelling for full dosing information.

Table 1: Nab-Paclitaxel Dosing in Taxane-Hypersensitive Patients by Tumour Type

TUMOUR TYPE	COMMON DOSING REGIMENS	DOSING FREQUENCY	KEY DOSING CONSIDERATIONS	KEY REFERENCES
METASTATIC BREAST CANCER	260 mg/m² q3wk IV 100–125 mg/m² IV weekly (e.g., days 1, 8, 15 of q28 cycle)	Q3wk or weekly	Dose reductions may be needed for neuropathy or myelosuppression. Weekly dosing is often better tolerated than q3wk	Gradishar WJ et al., J Clin Oncol. 2005 Abraxane SmPC
EARLY BREAST CANCER	125mg/m^2 IV weekly x 12 weeks	Weekly	Monitor closely for cumulative toxicity; dose delays or reductions common with neuropathy	Untch M et al., Lancet Oncol. 2016 Swain SM et al., N Engl J Med. 2015
NSCLC	100mg/m2 IV on days 1, 8, 15 of a 21 day cycle 260mg/m^2 IV q3wk	Weekly or q3wk	Haematologic toxicity may require dose delays. Weekly dosing is generally better tolerated	Socinski MA et al., J Clin Oncol. 2012 Abraxane SmPC
PANCREATIC CANCER	125mg/m^2 IV days 1, 8, 15 of a 28 day cycle	Weekly for 3 weeks in a 28 days cycle	High incidence of neutropenia may necessitate dose modifications. Reduce or hold dose for significant toxicity	Von Hoff DD et al., N Engl J Med. 2013 Abraxane SmPC
PROSTATE CANCER	100-125mg/m^2 IV weekly	Weekly	Limited data; dose based on tolerance. Adjust for fatigue or haematologic adverse events.	Small EJ et al., J Clin Oncol. 2004 Case series and retrospective reviews
OVARIAN CANCER	100mg/m^2 IV weekly	Weekly	Monitor for hematologic toxicity and fatigue; dose adjustments based on tolerability and response	Sehouli J et al., Gynecol Oncol. 2011 Penson RT et al., J Clin Oncol. 2015
BLADDER CANCER	100-125mg/m^2 IV weekly	Weekly or q3wk	Adjust dose based on performance status and toxicity; limited data to guide guide standard reductions	Apolo AB et al., Cancer. 2009 McKiernan JM et al., J Urol. 2014
ADVANCED OVARIAN CANCER	260mg/m^2 IV q3wk	q3wk	May require dose reductions for hematologic toxicity	Limited data; institutional protocols (BC Cancer Protocol) and extrapolation from breast cancer regimens.

PRIMARY PERITONEAL CANCER	260mg/m^2 IV q3wk	q3wk	Monitor for hematologic toxicity	Derived from ovarian cancer trial data; institutional practice.
ENDOMETRIAL CANCER	260mg/m^2 IV q3wk	q3wk	Dose adjustments based on tolerance, limited trial data	Miller DS et al., Gynecol Oncol. 2012; institutional reports.
GASTRIC CANCER	260mg/m^2 IV q3wk 100mg/m^2 IV weekly	Q3wk or weekly	Monitor for neutropenia and GI toxicity	Sakata Y et al., Invest New Drugs. 2010; early-phase studies. Shitara et al., Lancet Gastroenterol Hepatol. 2017; phase 3 trial