Canada's Drug and
Health Technology Agency

CADTH Reimbursement Recommendation

Nab-Paclitaxel

Reimbursement request: For patients who developed hypersensitivity reactions to taxanes
Final recommendation: Reimburse with conditions

Summary of Recommendation

The Formulary Management Expert Committee (FMEC) concluded that nab-paclitaxel is a reasonable alternative to taxanes in patients with taxane-induced hypersensitivity reactions (HSRs). FMEC reviewed several phase III randomized clinical trials and noted at least comparable efficacy between nanoparticle albumin-bound (nab)-paclitaxel and taxanes in cancer treatments; however, these results were based on patients without prior HSRs.

FMEC considered that nab-paclitaxel addresses patients' unmet needs by allowing treatment completion after HSRs in either adjuvant or advanced cancer treatment settings.

The expected cost of nab-paclitaxel remains unknown as publicly available prices for this drug may not reflect current prices paid by public payers and the price for generic nab-paclitaxel is not presently available.

FMEC concluded that nab-paclitaxel should be reimbursed for patients with grade 2 or 3 moderate to severe HSRs, anaphylaxis or anaphylactoid reactions, or significant contraindications to taxanes that may not be manageable despite the use of premedications and increased infusion durations.

Therapeutic Landscape

What Are Hypersensitivity Reactions to Taxanes?

HSRs can occur in 10% to 15% of patients receiving taxane chemotherapies for the treatment of solid organ tumours such as breast cancer, non–small cell lung cancer, gastroesophageal cancer, and gynecological malignancies. The traditional taxanes — paclitaxel and docetaxel — contain diluents that improve solubility but can cause immediate HSRs in some patients. Nab-paclitaxel is a nanoparticle albumin-bound paclitaxel and does not contain the previously mentioned diluents. Hence, the risk of HSRs with nab-paclitaxel is lower than with paclitaxel or docetaxel.

Why Did We Conduct This Review?

Public drug programs requested a Non-Sponsored Reimbursement Review and Recommendation of nab-paclitaxel in patients with HSRs to taxanes given variability in reimbursement across jurisdictions. Although most patients develop HSRs to taxanes for the treatment of breast cancers or gynecological cancers, the publicly funded drug programs requested a tumour agnostic approach, so nab-paclitaxel can be used as a treatment alternative for any taxanes-related HSRs.

Person With Lived Experience

A person with lived experience presented her journey with hypersensitive reactions to taxanes during treatment for stage II breast cancer. Following initiation of docetaxel, she described her initial symptoms as having acidity in her stomach, feeling heat in her upper body, and lower back pain. She then provided a detailed account of the desensitization process, during which she experienced anaphylactic shock, hives, and swelling in her face. After changing to nab-paclitaxel, she noted an improvement in her recovery from infusions, highlighting less fatigue and reduced reactions. She encouraged the committee to consider the delays to treatment and added challenges that hypersensitivity reactions cause and that the treatment of these reactions further deteriorates a patient's well-being, making chemotherapy more challenging to undergo. The most important outcomes to her included longevity so she could care for her child and quality of life, underscoring the need for treatments that limit long-term side effects, pain, and cognitive issues.

Input From Community Partners

What Did We Hear From Patients?

HSRs to taxane chemotherapies significantly affect patients and their families. Patients reported a wide array of debilitating side effects from taxanes, including fatigue, infection risk, nerve damage, and emotional trauma and profound anxiety about subsequent treatments, leading to hospitalizations and affecting their work, family life, and overall quality of life. Patients who have faced severe immediate HSRs stressed the importance of having an alternative to traditional or standard of care taxanes that have similar benefits.

What Did We Hear From Clinicians?

Clinician groups noted that nab-paclitaxel represents an appealing alternative for patients who develop significant HSRs to traditional taxanes that cannot be managed despite premedication use. They noted that in some jurisdictions, the limited public reimbursement of nab-paclitaxel for some cancers leads to the exclusion of taxanes from the treatment regimen when patients develop HSRs to these drugs.

What Did We Hear From the Pharmaceutical Industry?

No input was provided from the pharmaceutical industry.

What Did We Hear From Public Drug Programs?

Public drug programs inquired about considerations for initiation and prescribing of therapy. Questions centred around dosing equivalency, contraindications, and resource use.

Refer to the Stakeholder Input section of the CADTH report.

Deliberation

With a unanimous vote, FMEC concluded that nab-paclitaxel is a reasonable alternative to taxanes in certain circumstances such as HSRs. There is an expected benefit on reduced resource use and reduced patient burden on treatment. However, the cost implications remain unknown.

FMEC deliberated on the following 6 domains as illustrated in the Deliberative Framework (Figure 1):

- Clinical value: whether the drug under review provides clinical value
- Unmet clinical need: whether there is an unmet clinical need that available treatment(s) is or are not currently addressing
- Comparable efficacy: whether the drug under review is at least comparable to other available treatment(s) for the condition
- Patient perspective: whether the drug under review addresses patients' specific unmet needs and values
- Health system and social considerations: whether there are health system or social considerations (e.g., administration, testing, equity, access, ethical) for the drug under review
- Economic implications: what are the economic implications of reimbursing the drug under review based on public list prices

Figure 1: Deliberative Framework

Decision Summary

Table 1: Why Did FMEC Make This Recommendation?

Domains	Reason
Patient perspective: whether the drug under review addresses patients' specific needs and values	• FMEC noted that patients are in favour of safely completing their intended treatments after experiencing an HSR to avoid missing or stopping treatment. Patients wish to minimize and avoid the long infusion times required for desensitization protocols.
Clinical value: whether the drug under review provides clinical value **Comparable efficacy**: whether the drug under review shows at least similar efficacy to other available treatments for the condition	• FMEC discussed that the presented evidence suggested that there is less risk for hypersensitivity reactions on nab-paclitaxel than on paclitaxel; however, these studies did not include patients with prior HSRs specifically and there is uncertainty in how the study results apply to this patient population. • The clinical experts reiterated that nab-paclitaxel is an albumin-bound form of paclitaxel that does not contain any diluent that is likely the cause of HSRs. Both paclitaxel and nab-paclitaxel contain the same drug and only their formulations and adverse event profiles are different. • FMEC recognized that nab-paclitaxel is comparable to paclitaxel in terms of clinical efficacy based on some of the available studies that showed noninferiority efficacy for nab-paclitaxel compared to paclitaxel. • HSRs are less common with docetaxel and limited data were presented on this drug. However, FMEC acknowledged that patients who experience HSRs to docetaxel should be treated similarly to those with HSRs to paclitaxel.
Unmet clinical need: whether there is an unmet clinical need that available treatment(s) is or are not currently addressing	• FMEC recognized that HSRs are common in patients treated with taxanes. Although most reactions are mild or moderate, managing hypersensitivity reactions remains a challenge for clinicians. • Without access to nab-paclitaxel, some patients are unable to continue taxane therapy either in the adjuvant setting when their treatment could be curative or in the advanced setting when their treatment could prolong life.
Health system and social considerations: whether there are health system or social considerations for the drug under review	• FMEC recognized that there are equity issues with current public reimbursement of nab-paclitaxel for patients who are unable to receive taxanes across jurisdictions. • The current management of hypersensitivity reactions to taxanes involves desensitization or slower drug infusions that prolong treatment times, which patients have highlighted they would like to minimize. • Desensitization protocols and slower drug infusions increase the strain on nursing and pharmacy resources.

Domains	Reason
Economic implications: what are the economic implications of reimbursing the drug under review based on public list price	• FMEC discussed the cost considerations associated with a reimbursement recommendation for nab-paclitaxel in patients with HSRs to taxanes. The committee noted that using publicly available pricing information, the combined drug acquisition and administration costs of treatment with nab-paclitaxel were similar to or less than the combined drug acquisition and administration costs of treatment with paclitaxel, but they were greater than the combined drug acquisition and administration costs of treatment with docetaxel. • The committee discussed that the publicly available price of paclitaxel may not represent the prices paid by public payers in Canada; as such, treatment costs associated with paclitaxel may be less than estimated, suggesting nab-paclitaxel may be associated with increased costs. • The committee also acknowledged the review report, which noted the availability of a generic nab-paclitaxel (for which no price was available at the time of the review), which should reduce the cost of nab-paclitaxel.

FMEC = Formulary Management Expert Committee; HSR = hypersensitivity reaction; nab = nanoparticle albumin-bound.

Full Recommendation

With a unanimous vote, FMEC recommends that nab-paclitaxel be reimbursed for patients who developed hypersensitivity reactions to taxanes if the conditions presented in Table 2 are met.

Table 2: Conditions, Reasons, and Guidance

Reimbursement condition	Reason	Implementation guidance
Initiation		
Nab-paclitaxel should be reimbursed for patients who have 1 of the following characteristics: • grade 2 or 3 moderate to severe hypersensitivity reactions that may not be manageable despite the use of premedications and infusion prolonging • anaphylaxis or anaphylactoid reactions • significant contraindications to taxanes or premedications (e.g., high-dose steroids).	Based on at least 6 phase III 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).	Please refer to the Severity Grading of Immediate Hypersensitivity Reactions table (Table 3 of the clinical report). Consider reimbursement of nab-paclitaxel for patients with contraindications to high-dose steroids such as those with difficult to control diabetes or steroid-induced neurocognitive changes. The dosing conversion between taxanes and nab-paclitaxel should be left to the discretion of treating clinicians and pharmacy teams.
Discontinuation		
Treatment and assessment should be continued per usual practice.	—	—
Prescribing		
Nab-paclitaxel like other oncology drugs, should be prescribed by a medical specialist with training in the diagnosis and management of cancer.	Patients with cancer are expected to be under the care of an experienced clinical team to address the complexity of treatment, maximize potential benefits, and mitigate adverse events.	—

nab = nanoparticle albumin-bound.

Feedback on Draft Recommendation

Canadian Breast Cancer Network, Ontario Health Breast Cancer Drug Advisory Committee, Ontario Health Gynecology Cancer Drug Advisory Committee, Ontario Health Lung Cancer Drug Advisory Committee, and the Provincial Advisory Group provided feedback on the draft recommendation and agreed with the committee's recommendation. Patient and clinician partners requested clarification on the reimbursement criteria for nab-paclitaxel and suggested citing the Ontario Health's Management of Cancer Medication Infusion-Related Reactions guidelines. Of note, this reference is already included in the clinical report.

FMEC Information

Members of the committee: Dr. Emily Reynen (Chair), Dr. Alun Edwards, Ms. Valerie McDonald, Dr. Jim Silvius, Dr. Marianne Taylor, Dr. Maureen Trudeau, Dr. Dominika Wranik, and 1 medical oncologist from Manitoba and 1 medical oncologist from Ontario. One expert committee member did not attend.

Meeting date: May 10, 2024

Conflicts of interest: None

Special thanks: CADTH extends our special thanks to the individual who presented directly to FMEC on behalf of people with lived experience, as well as the patient organizations that represented the community of those affected by hypersensitive reactions to taxanes, notably the Canadian Breast Cancer Network, which include JK Harris, Bukun Adegbembo, and Milena Crosato.

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