Canada's Drug and Health Technology Agency

DRAFT Reimbursement Recommendation

Nab-paclitaxel

Reimbursement request: In combination with gemcitabine, for previously treated advanced (locally advanced unresectable or metastatic) pancreatic cancer

Draft Recommendation: Do not reimburse

Summary of Recommendation

The Formulary Management Expert Committee (FMEC) recommends that nab-paclitaxel in combination with gemcitabine not be reimbursed, for previously treated advanced (locally advanced unresectable or metastatic) pancreatic cancer. FMEC acknowledged there remains an unmet need in advanced pancreatic cancer, and there is inequity in treatment access to this regimen across the country. Yet, there is substantial uncertainty in the evidence to suggest any clinical benefit and a high probability of additional harms.

FMEC reviewed two multicenter, single-arm, open-label, phase II studies, two retrospective studies and one systematic review. Overall, the phase II studies did not address whether nab-paclitaxel with gemcitabine improves progression-free survival or overall survival compared to gemcitabine monotherapy, and the evidence from the remaining studies had significant limitations. In addition, FMEC noted that the combination therapy may lead to more adverse events compared to gemcitabine monotherapy. Health-related quality of life was not evaluated in any of the included studies.

Therapeutic Landscape

What Is Advanced Pancreatic Cancer?

Pancreatic ductal cell adenocarcinoma (PDAC) is the 7th leading cause of cancer-related death worldwide. Diagnosis is commonly established when the disease is locally advanced or metastatic and is often unresectable, leading to poor prognosis. First line treatment options in the advanced setting include chemotherapy with FOLFIRINOX, nab-paclitaxel in combination with gemcitabine, or gemcitabine with capecitabine. Approximately 40-50% of patients with advanced pancreatic cancer progress to receive second- or subsequent-line therapies. Patients who received FOLFIRINOX in the first-line setting have limited options for second-line treatment.

Why Did We Conduct This Review?

Clinicians shared that advanced pancreatic cancer is associated with high mortality and patients have limited treatment options in the advanced setting. As several but not all jurisdictions already fund this drug regimen for the indication under review in Canada, publicly funded drug plans requested a reimbursement review and recommendation for nab-paclitaxel with gemcitabine given the emergence of new evidence for this dual therapy. Nab-paclitaxel is later in the drug development lifecycle making this treatment eligible for review at FMEC.

Person With Lived Experience

Two people with lived experience, a patient and his wife based out of Toronto, Ontario, spoke to the committee. The patient was diagnosed with metastatic pancreatic cancer in April 2022 and his treatments included accessing therapies like FOLFIRINOX, olaparib, and nab-paclitaxel with gemcitabine, alongside participating in clinical trials. Despite challenges such as delays in diagnosis and financial burdens in paying for treatment, they continue to remain hopeful, sharing his motto; 'no stone left unturned'. After an unsuccessful clinical trial, nab-paclitaxel with gemcitabine was reintroduced in March 2024 and they described the experience as having manageable side effects and effective disease control, supporting a good quality of life. The treatment's short administration time and tolerable side effects have been crucial, describing it as a lifeline and bridge to other treatments options. They emphasized the importance of treatment outcomes that enhance quality of life and provide time with loved ones. Lastly, they expanded on the difficultly in navigating financial obstacles and insurance coverage, underscoring the need for equitable access to effective therapies for patients across Canada.

Input from Community Partners

What Did We Hear From Patients?

One patient group, Pancreatic Cancer Canada, submitted input provided by one patient and one caregiver. They shared that untreated disease had a significant impact on quality of life especially in the investigative stages when patients experienced considerable pain. They highlighted the need for better access to second-line treatment options.

What Did We Hear From Clinicians?

Input was received from one clinician group, which highlighted the current lack of effective treatment options for patients with advanced pancreatic cancer following progression after first-line treatment.

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 treatment implementation, relevant comparators, as well as system and economic issues. Questions were asked regarding patient eligibility, comparability to other treatment options. Drug programs highlighted that relevant comparators might include gemcitabine monotherapy or gemcitabine-based combination therapy.

Refer to Stakeholder Input section of the report.

Deliberation

With a 6 to 0 vote, the Formulary Management Expert Committee (FMEC) concluded that the evidence of clinical benefit demonstrated with nab-paclitaxel in combination with gemcitabine in patients previously treated in the setting of advanced PDAC setting was uncertain and insufficient, while there was high likelihood of additional harms to patients.

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/are not currently addressing.
- Comparable Efficacy: whether the drug under review shows at least similar efficacy to other available treatment(s) for the condition.
- Patient Perspective: whether the drug under review addresses patients' specific unmet needs and values.
- Health System & Social Considerations: whether there are health system or social considerations (e.g., administration, testing, equity, access, ethical) for the drug under review.
- Economic Implications: economic implications of reimbursing the drug under review based on public list prices.

Figure 1: Deliberative Framework

Alt Text: The committee deliberated on 6 domains: clinical value, unmet clinical need, comparable efficacy, patient values, health system& social considerations, and economic implications.

Decision Summary

Table 1: Why Did FMEC Make This Recommendation?

Domains	Reason
Clinical Value: whether the drug under review provides clinical value.	• FMEC discussed that there is insufficient evidence regarding the clinical value and benefits of nab-paclitaxel with gemcitabine compared to single-agent gemcitabine based on the limitations of the available evidence. Limitations include a high risk of selection bias and confounders within the study designs. • Two phase II, single-arm trials, two retrospective cohort trials and one systematic review examined the use of nab-paclitaxel and gemcitabine in the second-line setting and formed the evidence base for the FMEC recommendation. • FMEC also questioned whether the results of the measured outcomes (e.g. overall survival and progression free survival) reflect meaningful benefits based on clinicians' or patients' values.
Comparable Efficacy: whether the drug under review shows at least similar efficacy to other available treatment(s) for the condition.	• FMEC noted that the comparative efficacy is uncertain, when comparing nab-paclitaxel with gemcitabine to gemcitabine monotherapy. The comparative evidence was based on retrospective cohort trials and systematic reviews with important limitations including a high risk of selection bias and confounders with the study designs.
Unmet Clinical Need: whether there is an unmet clinical need that available treatment(s) is/are not currently addressing.	• FMEC agreed that metastatic pancreatic cancer is a severe condition that is not addressed adequately by available treatments. There is a need for more and better therapies for this disease. • Prognosis is very poor despite single-agent gemcitabine being offered in most jurisdictions after first-line FOLFIRINOX in the advanced setting.
Patient Perspective: whether the drug under review addresses patients' specific unmet needs and values.	• FMEC discussed that given the lack of clinical benefits and increased toxicity, this treatment is unlikely to satisfy unmet patient needs.

Domains	Reason
	• FMEC considered input from the person with lived experience, which suggests a benefit of nab-paclitaxel with gemcitabine in their individual's circumstances; however, there is insufficient evidence to support the use of the combination treatment in the broader population. • One opposing opinion discussed by FMEC was that this combination offers patients an additional treatment option for a disease with limited options something that patients strongly value. However, it is unclear whether this treatment addresses the need for treatments that offer greater longevity.
Health System & Social Considerations: whether there are health system or social considerations for the drug under review.	• FMEC discussed that this domain is not entirely applicable to this review, although it was highlighted that there is additional chair time associated with nab-paclitaxel infusion in the combination therapy. • FMEC emphasized that there is currently inequity in publicly funded access for this regimen across Canada.
Economic Implications: what are the economic implications of reimbursing the drug under review based on public list price.	• FMEC did not discuss economic implications for this review. The decision to not recommend reimbursement was based on clinical considerations.

Full Recommendation

Unanimously, FMEC recommends that nab-paclitaxel in combination with gemcitabine not be reimbursed, for previously treated advanced (locally advanced unresectable or metastatic) pancreatic cancer.

Feedback on Draft Recommendation

<to be updated after the stakeholder feedback period.>

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 a medical oncologist from Alberta.

Meeting date: July 4, 2024

Conflicts of interest: None

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