CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

Nab-paclitaxel

Non-Sponsored

Indication: For patients who developed hypersensitivity reactions (HSRs) to taxanes.

Jan 29, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings.

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CADTH and do not necessarily represent or reflect the views of CADTH. No endorsement by CADTH is intended or should be inferred.

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Canadian Breast Cancer Network
Réseau canadien du cancer du sein

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[redacted]
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April 16, 2024

Formulary Drug Expert Committee
CO: Canadian Agency for Drugs and Technologies in Health
600-865 Carling Ave
Ottawa, ON K1S 5S8

Subject: (project number PX0348-000) – The Canadian Breast Cancer Network's input on the reimbursement of nab-paclitaxel for hypersensitive reactions to taxane chemotherapies.

Dear members of the Formulary Management Expert Committee:

The Canadian Breast Cancer Network (CBCN) is a national, patient-directed organization committed to promoting the best quality of care for all Canadians affected by breast cancer. In response to the open call for input on nab-paclitaxel for patients with hyper-sensitive reactions (HSRs) to taxane chemotherapies (project number PX0348-000), we are writing to share evidence, patient values, and patient experiences to inform this decision.

Taxane chemotherapies are a treatment pillar for a significant portion of people diagnosed with breast cancer (1), but a HSR prevalence of up to 40% (2, 3) means that many will not be able to tolerate the side effects of this crucial treatment. In contrast, nab-paclitaxel has a low prevalence of HSRs and remains clinically effective in treating breast cancer (4). This is significant because access to nab-paclitaxel for patients with HSRs means they can achieve their treatment goals of survival, reduced risk of recurrence, manageable side effects, good quality of life (QoL), minimal impact to family and loved ones, and minimal financial burden. Presented below is a summary of patient reported values and experiences with taxane side effects, including mild, moderate, and severe HSRs.

As outlined in the appendix, CBCN heard from patients about their experiences with both taxane chemotherapies and nab-paclitaxel. When taking taxane chemotherapies, patients experienced debilitating fatigue, increased risk of infection after surgery, long term nerve damage, suicidal ideation, intense stomach acid, and post-traumatic stress disorder. Also when taking taxane chemotherapies, patients experienced extreme blistering on feet which prevented walking, rashes, plus temporary and long-term numbness in fingers and toes. Finally, all of the respondents were hospitalized either at the time of experiencing HSRs, or for long term side effects of their treatment.

Patients discussed how it was the cumulative effects of both HSRs and side effects that made it necessary to switch medications or reduce taxane doses. One patient had a very severe reaction that would not have been acceptable regardless of other side effects, but the remaining two respondents emphasized the cumulative impacts. For example, all three spoke about not knowing what treatment was causing which side effect, because all the side effects and treatment came

together. The combined impact of side effect and HSRs led to them switching to nab-paclitaxel (2 patients) or reducing taxane dosage (1 patient). Patients were then able to continue their treatment because even though they had side effects, the HSRs weren't compounding to make their experience intolerable.

All interview respondents spoke about the impact treatment has had on their family or loved ones, work or productivity, and quality of life. Those with children were largely unable to participate in childcare duties during treatment. In terms of work or productivity, some left their responsibilities temporarily, while another still struggles with employment due to lasting anxiety and diminished cognitive function. One respondent's HSRs were so severe, her loved ones have lasting emotional trauma, and she relied on her husband as a caregiver during treatment.

All respondents experienced a diminished QoL during treatment, but experience with current QoL varied. Two respondents spoke about the tension post-treatment QoL presents because they are grateful for survival without recurrence but recognized their abilities have changed. One respondent viewed their current focus on breast cancer advocacy as a positive impact their cancer treatment has had on their current QoL. Yet, another stated that their current QoL was worse than before and shared that "…when we talk about quality of life, I have nothing to compare it to, because that person who was there before isn't there anymore."

Finally, one respondent who switched to nab-paclitaxel was initially told it was not being offered due to cost, rationale they viewed as unjust. Treatment with taxanes caused her rashes and blistering that were excruciatingly painful and acute, long-term mental anguish, suicidal ideation, and hospitalization. This respondent now raises awareness about her experiences in the hopes that others do not have to endure the same physical pain and emotional distress she did for what she views as financial reasons.

CBCN welcomes a recommendation that bolsters equitable access to nab-paclitaxel. Research, patient values, and patient experiences agree that doing so will help people living with breast cancer access chemotherapy treatments which do not cause avoidable HSRs. These findings are corroborated anecdotally in the patient testimony presented above.

On behalf of the Canadian Breast Cancer Network, thank you for considering our letter, and we look forward to a recommendation that incorporates the values and experiences of breast cancer patients.

Sincerely,

JK Harris,

Health Policy and Advocacy Lead
Responsable, Politiques de santé et défense des droits des patients
Canadian Breast Cancer Network/Réseau canadien du cancer du sein

Cathy Ammendolea,

Patient Advocate & Chair of the Board,
Défenseure des droits des patients et présidente du conseil d'administration
Canadian Breast Cancer Network/ Réseau canadien du cancer du sein

1. Gradishar, W.J. (2012). Taxanes for the Treatment of Metastatic Breast Cancer. *PubMed Central, 6: 159–171.* https://doi.org/10.4137%2FBCBCR.S8205
2. Health Canada. (2023). *Product monograph including patient mediaciton information docetaxel injection.* https://pdf.hres.ca/dpd_pm/00074216.PDF
3. Health Canada. (2013). *Product monograph paclitaxel for injection*. https://pdf.hres.ca/dpd_pm/00021796.PDF
4. Vishnu, P. & Roy, V. (2011). Safety and Efficacy of nab-Paclitaxel in the Treatment of Patients with Breast Cancer. *SageJournals.* https://doi.org/10.4137/BCBCR.S5857

Appendix
Patient input sources for CBCN's nab-paclitaxel submission to CADTH

Information for this submission was collected via:

Key informant interviews – A total of four people completed a phone interview; one interview was deemed out of scope and therefore excluded from this submission and the following demographic details. The three remaining interview participants all experienced HSRs to taxanes. Two were switched to nab-paclitaxel due to severe reactions, and one was able to remain on taxanes with dose adjustments and pre-treatments for HSRs. All three respondents had early-stage breast cancer, and were diagnosed within the last 5 years. One had a BRCA mutation. Their ages ranged from mid-30s to early 50s at the time of diagnosis.

Personal communications – On facebook, two people commented on their experiences with taxane side effects, but not HSRs. It's unclear if those who commented experienced HSRs. By email, one person shared their experience with taxane side effects, but did not experience HSRs.

Past CBCN submissions – Patient reported treatment goals were identified from past submissions that routinely include findings from our 2022 Triple Negative Breast Cancer Patient Survey, 2017 Metastatic Breast Cancer Patient Survey, and 2012 Metastatic Breast Cancer Patient and Caregiver Survey Report.

Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No. All research, interviews and outreach to patients was conducted independently by the Canadian Breast Cancer Network, as was the compilation of information and data for the writing of this submission.

   As a member of the Canadian Cancer Action Network, the Canadian Breast Cancer Network is committed to adhering to the Code of Conduct Governing Corporate Funding.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No. The Canadian Breast Cancer Network compiled and wrote this submission independently.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Gilead				X
Eli Lilly				X
Novartis				X
Roche				X
Pfizer				X
AstraZeneca				X
Janssen			X	
Merck				X

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: JK Harris
Position: Health Policy and Advocacy Lead
Patient Group: Canadian Breast Cancer Network (CBCN)
Date: April 16, 2024

CADTH

CADTH Reimbursement Review
Patient Input Template

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Nab-paclitaxal
Indication: Patients who developed hypersensitivity reactions (HSR's) to taxanes
Name of Patient Group: Rethink Breast Cancer
Author of Submission: Jenn Gordon

1. About Your Patient Group

Rethink Breast Cancer (Rethink) is a Canadian charity known for making positive change. Rethink educates, empowers and advocates for system changes to improve the experience and outcomes of those with breast cancer, focusing on historically underserved groups: people diagnosed at a younger age, those with metastatic breast cancer and people systemically marginalized due to race, income or other factors. We foster spaces to connect, listen, empower and rethink breast cancer, together. Rethink's strategic priorities and organizational direction are guided by the unique, unmet needs identified by breast cancer patients and their families.

Programs and Activities

- Rethink Breast Cancer builds community, bringing patients with various stages of breast cancer together through our private and public social spaces as well as in-person events
- Rethink runs patient retreats and facilitates peer-support
- Rethink creates and runs education forums and conferences
- Rethink creates support and education tools, resources and content
- Rethink funds and supports breast cancer research

You can find out more by visiting:

Rethink Breast Cancer Instagram
Rethink Breast Cancer Website

2. Information Gathering

For over 20 years, Rethink has been working closely with breast cancer patients in Canada. We learn from and listen to the community to understand their values, priorities and pain points to help drive change and system improvements. Each year, we learn from the patients we serve, survey and collaborate with. We learn from the 40 individuals that we work extremely closely with as key

patient advisors; the 100 patients that share their stories on our blog; the 500 patients that participate in our virtual support groups; the 2,000 members of our private peer-support network; the 40,000 people that have joined our Instagram community; and the 150,000 individuals reached each month through the reach of that channel. We listen, learn, engage and have conversations in all these spaces.

Rethink also benefits from regular knowledge exchange with our Scientific Advisory Committee, which includes some of the leading clinical scientists in Canada who treat breast cancer.

For this submission, we have drawn on our general observations and insights gathered through programming and meetings with breast cancer patients as described above. Rethink also conducted an in-depth virtual interview in January 2024 with a patient, **Ila**, who is living with metastatic triple negative breast cancer (mTNBC) and has experience with being treated with nab-paclitaxel as a result of having a hypersensitive reaction to a taxane.

3. Disease Experience

Most people in the Rethink community are diagnosed at a younger age. When young people get breast cancer it may be more aggressive, which can lead to tougher treatments. In addition, those diagnosed in their 20s, 30s and early 40s face age-specific issues such as fertility or family-planning challenges, diagnosis during pregnancy, childcare, impact on relationships, body image, dating and sexuality, feeling isolated from peers who don't have cancer, career hiatuses, and financial insecurity. The physical and emotional toll that a breast cancer diagnosis and treatment take on a young person's life is devastating and traumatic.

In Canada, 82% of female breast cancer patients are diagnosed at an early stage (stage I or II), with a 5-year net survival of 89%; however, fear of recurrence is a reality for our community and for good reason. Despite improvements made with early detection and treatment for early-stage breast cancer, there's approximately a 20-30% chance that early breast cancer will metastasize. Moreover, 5-10% of newly diagnosed breast cancers are metastatic. There is currently no cure for metastatic breast cancer and patients' goal with treatment is to live as well as they can for as long as they can.

Processing this reality of a breast cancer diagnosis is extremely difficulty and the emotional impacts on quality of life cannot be understated. The physical and psychosocial challenges of a breast cancer diagnosis negatively impact both the patients and their loved ones who are often their caregivers.

When asked about the importance of reducing the risk of recurrence, patients with early-stage breast cancer shared the following:

"I think when anyone gets a cancer diagnosis, you're always scared of the illness coming back. Especially when I have young kids that I want to be there for, and I have a lot of things I want to do myself. It's not only my kids, but also my life too. I want to be able to enjoy it. Because I feel that I'm

doing anything and everything that's available out there to have a lower chance of recurrence, it gives me peace of mind. It gives me less anxiety in my life."
***Negar** – diagnosed with early-stage breast cancer*

"I want to try anything to prevent recurrence, I want to add it to my exercise routine and healthy diet in my bag of tricks."
***Jessica** – diagnosed with early-stage breast cancer*

4. Experiences With Currently Available Treatments

Taxanes, including paclitaxel and docetaxel, are one of the most commonly used chemotherapy agents for the treatment of breast cancer. Even with the advancement of targeted therapies for the treatment of breast cancer, taxanes remain an important cornerstone for the treatment of both early stage and advanced or metastatic breast cancer. However, some patients can have hypersensitive reactions to taxanes that can cause serious consequences and prevent them from continuing treatment.

Hypersensitive reactions to taxanes include itchiness, chest pain, tightness in the throat, shortness of breath, racing heart, irregular heart-beat and flushing. **Ila,** the patient that Rethink spoke interviewed in January 2024, experienced several of these symptoms when she had a hypersensitive reaction to paclitaxel. **Ila,** was diagnosed with early stage triple negative breast cancer in September of 2020; when she recurred with metastatic triple negative breast cancer in April 2023 she knew how important chemotherapy would be for the treatment of this hard to treat sub-type of metastatic breast cancer. Here is how she describes her first treatment with paclitaxel:

"Almost immediately [after receiving paclitaxel] my heart was racing, I was nauseous, I was flush, I had a severe immediate reaction. It was traumatizing, which compounded the trauma I was already experiencing from being diagnosed with metastatic triple negative breast cancer"

She went on to explain that the nurses immediately responded by administering high doses of Benadryl to allow her to complete the treatment, but that the experience left her incredibly anxious going into the second treatment:

"At my second treatment I explained to the nursing staff that I was very anxious about whether or not I would have the same reaction again, which I immediately did upon having the paclitaxel administered. It was traumatizing because I didn't know if I was going to happen again, when it was going to happen, or how long I would have this reaction for."

Once again, the nurses administered high doses of Benadryl to allow **Ila** to continue her treatment but knowing that she was scheduled to return for another treatment continued to cause significant emotional and mental distress**.** This cycle continued for a third and fourth treatment, compounding the trauma that **Ila** experienced during each treatment and the anxiety leading up to it.

Ila met with her oncologist after her fourth treatment and shared the impact that the hypersensitivity was having on her overall physical, emotional and mental health. He informed her that he would be able to switch her treatment to nab-paclitaxel because she had met the criteria to switch.

5. Improved Outcomes

When it comes to breast cancer therapies, patients are looking for options that treat their disease and minimize the chances of recurrence, or in the case of metastatic breast cancer, manage their disease and to prolong their life while providing a good quality of life. Although they are not without toxicities, taxanes are an important part of achieving these important outcomes for patients, both in the early stage and metastatic setting; however, patients who experience hypersensitivity to taxanes may not be able to tolerate treatments long enough to receive these life-saving benefits.

Several patients explain what outcomes matter to them and how this translates into value in their lives:

"…those months could be the difference that lets me see my son start kindergarten; they could be the ones that give me time to get him off diapers before it all falls on dad; Or they could be the first time he says I Love You. While a few months are short on time they are bursting with possibility. Life happens in moments after all. Every scan matters."
***Jessica** – living with HR+ metastatic breast cancer*

There is now over a decade of evidence to support the use of nab-paclitaxel for breast cancer patients with hypersensitive responses to taxanes. Rethink's scientific advisory committee was unanimous in their support of providing access and reimbursement to nab-paclitaxel for this patient population.

6. Experience With Drug Under Review

We spoke with one patient, **Ila,** who had experienced hypersensitivity to paclitaxel and was prescribed nab-paclitaxel as a result.

"I did not have any of the hypersensitivities to nab-paclitaxel that I experienced with paclitaxel. While there are still significant side effects to this treatment, they have been manageable and tolerable compared with what I experienced when taking paclitaxel. In addition to the 4 treatments of paclitaxel that I received, I have been able to undergo fourteen treatments of nab-paclitaxel. Even with the side effects from the nab-paclitaxel, I have never been hospitalized, have been able to continue working and running my own business. It's been difficult, but feasible.

In my most recent scan, my oncologist informed me that all of the tumours had shrunk, two had completely disappeared, and there was no new growth, which was the absolute best possible news especially with a diagnosis of metastatic triple negative breast cancer. Eighteen treatments of

paclitaxel would have broken me; I would have never been able to have these results with my first line of therapy.

I understand that I have far fewer treatment options with metastatic triple negative breast cancer, so having something that works as a first line treatment is pretty spectacular"

When asked if she thinks this is an important treatment option for patients with hypersensitivity to taxanes, **Ila** responded with a "*full body yes. There is no way I could have continued with paclitaxel and had these results".* She was surprised to learn that this isn't already an accessible option for all patients in Canada who have experienced a hypersensitivity to taxanes.

7. Companion Diagnostic Test

None

8. Anything Else?

No

Appendix: Patient Group Conflict of Interest Declaration

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
None				

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Jenn Gordon
Position: Lead Strategic Operations and Engagement
Patient Group: Rethink Breast Cancer
Date: January 29, 2024

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PX0348
Generic Drug Name (Brand Name): nab-paclitaxel
Indication: For patients who developed hypersensitivity reactions (HSRs) to taxanes
Name of Clinician Group: Ontario Health Cancer Care Ontario Breast Cancer Drug Advisory Committee
Author of Submission: Dr, Andrea Eisen

1. About Your Clinician Group

OH-CCO's Cancer Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered by email.

3. Current Treatments and Treatment Goals

This is for breast cancer.

- Current standard is to administer premedication when paclitaxel is used.
- There is a specific protocol for HSR despite premedication (i.e., corticosteroids, antihistamines, H2 receptor antagonists, montelukast)
- If patients continue to have reactions despite this in the advanced disease setting, we use nab-paclitaxel. However, in early stage disease due to limited access to nab-paclitaxel, taxanes generally are dropped from the regimen. It is not the standard of practice to use docetaxel in the setting of a serious reaction to paclitaxel when optimal HSR prevention and treatment strategies have been used.
- In addition, docetaxel and paclitaxel are not interchangeable in terms of efficacy in the treatment of breast cancer.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.Patients with serious HSRs to paclitaxel despite optimal prevention and treatment strategies do not have access to taxanes in early stage disease, as nab-paclitaxel is not funded in this setting.

- Patients with serious HSRs to paclitaxel despite optimal prevention and treatment strategies do not have access to taxanes in early stage disease, as nab-paclitaxel is not funded in this setting.

- Paclitaxel is one of the most active drugs in the treatment of breast cancer.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?A switch to nab-paclitaxel would be indicated if the patient continued to experience HSR despite optimal prevention and treatment strategies.

- There is evidence now supporting the use of nab-paclitaxel as an upfront treatment in early stage breast cancer.[1,2]

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

- Any patient with any stage of breast cancer who has a serious HSR to paclitaxel despite optimal treatment and prevention strategies.
- About 1 to 3% of patients have a serious HSR to paclitaxel despite the use of premedication[3, 4]

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

- Nab-paclitaxel would be used in the setting of HSR to paclitaxel however we want to ensure that there is evidence that the drug is safe and effective in the setting.[1, 2]

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

- We are proposing a substitution of nab-paclitaxel for paclitaxel in patients who have severe HSRs to the latter. The same criteria for deciding on treatment discontinuation should be applied as for their original treatment. This will depend on the stage of disease and treatment intent.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

- Same setting as paclitaxel administration.
- Switching to nab-paclitaxel would result in less premedication and monitoring for HSRs.

6. Additional Information

References

[1] Gianni L, Mansutti M, Anton A, et al. Comparing neoadjuvant nab-paclitaxel vs paclitaxel both followed by anthracycline regimens in women with ERBB2/HER2-negative breast cancer – the Evaluating Treatment with Neoadjuvant Abraxane (ETNA) trial. JAMA Oncol 2018;4(3):302-308

[2] Untch M, Jackisch C, Schneeweiss A, et al. Nab-paclitaxel versus solvent-based paclitaxel in neoadjuvant chemotherapy for early breast cancer (GeparSepto-GBG 69): a randomised, phase 3 trial. Lancet Oncol 2016;17(3):345-356.

[3] Kwon JS, Elit L, Finn M, Hirte H, Mazurka J, Moens F, Trim K. A comparison of two prophylactic regimens for hypersensitivity reactions to paclitaxel. Gynecol Oncol. 2002 Mar;84(3):420-5. doi: 10.1006/gyno.2001.6546.

[4] Eisenhauer EA, ten Bokkel Huinink WW, Swenerton KD, Gianni L, Myles J, van der Burg ME, Kerr I, Vermorken JB, Buser K, Colombo N, et al. European-Canadian randomized trial of paclitaxel in relapsed ovarian cancer: high-dose versus low-dose and long versus short infusion. J Clin Oncol. 1994 Dec;12(12):2654-66. doi: 10.1200/JCO.1994.12.12.2654.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   OH-CCO provided a secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Andrea Eisen
Position: Lead, OH-CCO Breast Cancer Drug Advisory Committee
Date: 22-12-2023

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Haider Samawi
Position: Member, OH-CCO Breast Cancer Drug Advisory Committee
Date: 15-01-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PX0348
Generic Drug Name (Brand Name): nab-paclitaxel
Indication: For patients who developed hypersensitivity reactions (HSRs) to taxanes
Name of Clinician Group: Ontario Health (CCO) Gynecology Cancer Drug Advisory Committee
Author of Submission: Dr. Sarah Ferguson

1. About Your Clinician Group

OH-CCO's Cancer Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered by email.

3. Current Treatments and Treatment Goals

Current options for preventing hypersensitivity reactions includes premedicating with corticosteroids, diphenhydramine, and/or famotidine, and to administer a slower infusion of the taxane. For patients who react to paclitaxel, docetaxel can be used; however the risk of an HSR still remains.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

There are patients who cannot be given paclitaxel, and the number of patients in this setting is small. These include:

1. Patients who still experience an HSR even after premedication or a slower infusion rate
2. Patients who have a severe reaction that was life-threatening
3. Those who are intolerant to steroids i.e., if they have poorly controlled diabetes.

Although docetaxel has been used as a substitution in the event of a HSR from paclitaxel, patients may still experience a HSR with docetaxel.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Nab-paclitaxel would be considered an option if patients experience conditions listed in section 4.1.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

<Enter Response Here>

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

<Enter Response Here>

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

<Enter Response Here>

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

<Enter Response Here>

6. Additional Information

There is a single-institution retrospective analysis[1] which evaluated patients with stage IIIc to stage IV ovarian cancer treated with first line carboplatin/nab-paclitaxel (with or with bevacizumab) after experiencing a HSR with paclitaxel and/or docetaxel.

A retrospective chart review[2] was performed at an institution to evaluate the incidence of a HSR to nab-paclitaxel after a prior HSR to taxanes. There were no HSRs observed with the use of nab-paclitaxel.

1. Parisi A, Palluzzi E, et al. First-line carboplatin/nab-paclitaxel in advanced ovarian cancer patients, after hypersensitivity reaction to solvent-based taxanes: a single-institution experience. Clin Transl Oncol. 2020 Jan;22(1):158-162. doi: 10.1007/s12094-019-02122-x.
2. Maurer K, Michener C, Mahdi H, Rose PG. Universal tolerance of nab-paclitaxel for gynecologic malignancies in patients with prior taxane hypersensitivity reactions. J Gynecol Oncol. 2017 Jul;28(4):e38. doi: 10.3802/jgo.2017.28.e38.

7. Conflict of Interest Declarations

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1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   OH-CCO provided a secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Sarah Ferguson
Position: Member, Ontario Health (CCO) Gynecology Cancer Drug Advisory Committee
Date: 16-01-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Orit Freedman
Position: Member, Ontario Health (CCO) Gynecology Cancer Drug Advisory Committee
Date: 14-01-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Julie Ann Francis
Position: Member, Ontario Health (CCO) Gynecology Cancer Drug Advisory Committee
Date: 14-01-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Stephen Welch
Position: Member, Ontario Health (CCO) Gynecology Cancer Drug Advisory Committee
Date: 14-01-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

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CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PX0348
Generic Drug Name (Brand Name): nab-paclitaxel
Indication: For patients who developed hypersensitivity reactions (HSRs) to taxanes
Name of Clinician Group: Ontario Health (CCO) Lung Cancer Drug Advisory Committee
Author of Submission: Dr. Donna Maziak, Dr. Peter Ellis, Dr. Andrew Robinson, Dr. Mihaela Mates

1. About Your Clinician Group

OH-CCO's Cancer Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered by email.

3. Current Treatments and Treatment Goals

The difference in lung cancer versus other cancers (i.e., ovarian) are that there are other alternatives to be used for taxanes. For example, if a patient reacts to paclitaxel in neoadjuvant/adjuvant setting, can use cisplatin/gemcitabine or carboplatin/gemcitabine (with or without immunotherapy), or cisplatin/vinorelbine, etc. In the metastatic first line setting, prior approval is requested for cisplatin/gemcitabine/pembrolizumab or cisplatin/vinorelbine/pembrolizumab. In the concurrent setting, patients can receive carboplatin/etoposide, vinorelbine, vinblastine, and other options.

In the second line setting (post-platinum doublet with immunotherapy if appropriate), taxanes may be used as monotherapy. So, in rare instances of a hypersensitivity reaction, nab-paclitaxel would be a preferrable alternative.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

In lung cancer, current use of paclitaxel is as follows:

- weekly carboplatin and paclitaxel concurrent with radiation in stage III NSCLC
- carboplatin and paclitaxel plus nivolumab in neoadjuvant therapy - primarily in patients with squamous cancer
- carboplatin and paclitaxel plus pembrolizumab in stage IV squamous NSCLC

Infusion reactions occur in 10-15% of patients receiving paclitaxel. The majority of these are mild to moderate and can be managed with premedication or treatment of infusion reactions. Severe reactions precluding the repeat dosing with paclitaxel are not common - probably 1 or 2%. While there are alternatives with gemcitabine, some physicians have concerns about gemcitabine and immunotherapy because it causes more lymphopenia. Having an alternative of similar efficacy but without the risk of infusion reactions should be available.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

This would have limited use in lung cancer. The use of nab-paclitaxel would be directed towards patients with a grade 3/4 reaction, or recurrent infusion reactions despite appropriate premedication.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

<Enter Response Here>

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Standard measures such as ORR, PFS / disease progression, improvement in symptoms would be used to determine benefit.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Treatment would be discontinued for disease progression, intolerable side effects or patient choice.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Patients would be under the care of an oncologist experienced in prescribing systemic therapy i.e., medical oncologist, hematologist, or gynecologic oncologist.

6. Additional Information

The trial by Socinski et al[1] compared every 3 week high dose ("American dosing") paclitaxel 200mg/m2 with 100mg/m2 weekly dose of nab-paclitaxel. Nab-paclitaxel was better tolerated.

[1] Socinski MA, Bondarenko I, Karaseva NA, Makhson AM, Vynnychenko I, Okamoto I, Hon JK, Hirsh V, Bhar P, Zhang H, Iglesias JL, Renschler MF. Weekly nab-paclitaxel in combination with carboplatin versus solvent-based paclitaxel plus carboplatin as first-line therapy in patients with advanced non-small-cell lung cancer: final results of a phase III trial. J Clin Oncol. 2012 Jun 10;30(17):2055-62. doi: 10.1200/JCO.2011.39.5848.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   OH-CCO provided a secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Donna Maziak
Position: Lead, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 08-12-2023

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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Add company name				
Add company name				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Andrew Robinson
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 04-12-2023

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS	X			
Add company name				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Peter Ellis
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 05-12-2023

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS	X			
Add company name				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Mihaela Mates
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 08-12-2023

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS	X			
Add company name				

* Place an X in the appropriate dollar range cells for each company.