Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

pembrolizumab (Keytruda)

(Merck Canada Inc.)

Indication: Treatment of adult patients with resectable locally advanced head and neck squamous cell carcinoma (HNSCC) as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without platinum-containing chemotherapy and then as monotherapy.

March 31, 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC 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. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Pembrolizumab

Indication: Treatment of adult patients with resectable locally advanced head and neck squamous cell carcinoma (HNSCC) as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without platinum-containing chemotherapy and then as monotherapy.

Name of Patient Group: Canadian Cancer Survivor Network (CCSN), Life-Saving Therapies Network (LSTN)

Author of Submission: Lindsay Timm for CCSN and Anris Kica for LSTN

1. About Your Patient Group

The Canadian Cancer Survivor Network (CCSN) is a national network of patients, families, survivors, friends, community partners, funders, and sponsors who have come together to take action to promote the very best standard of care, whether it be early diagnosis, timely treatment and follow-up care, support for cancer patients, or issues related to survivorship or quality of end-of-life care. https://survivornet.ca/

The Life-Saving Therapies Network is a patient-led network of clinicians, scientists, health economists, legal experts and patient organizations. Our aim is to expand access to life-saving therapies for patients with lethal disorders in a timely and efficient manner. We strive for regulatory, reimbursement and clinical reforms that ensure patients with lethal disorders get faster access to novel innovative therapies.

2. Information Gathering

Together, with the Life Saving Therapies Network, the two groups disseminated a survey to their networks to obtain responses. The Life Saving Therapies Network created the survey using SurveyMonkey and shared the link with CCSN to share in their newsletter, on their social media, and with their partner organizations. The survey was conducted from February 24, 2025 to March 17, 2025. All respondents to the survey are from Canada. From looking at the demographic data, it was identified that there was one (1) patient in active treatment, two (2) caregivers to someone with head and neck cancer, and five (5) head and neck cancer survivors. Three (3) of the respondents to the survey have received treatment with pembrolizumab in the past and one (1) of the respondents is currently receiving treatment with pembrolizumab. The Life-Saving Therapies Network also conducted interviews with head and neck cancer survivors that had previously been treated with pembrolizumab.

3. Disease Experience

The respondents to the survey were asked to rate on a five-point scale, zero being no impact and five being severe impact, how head and neck cancer has impacted their ability to conduct daily activities. There were five areas of their lives that we asked them to rate: working, socializing with family and friends, performing household chores, participating in hobbies or leisurely activities, and exercising. The top three that were most affected were participating in hobbies or leisurely activities with a weighted average of 3.25/5, exercising with a weighted average of 3.13/5, and working with a weighted average of 3.00/5.

The following are comments from the respondents on how head and neck cancer has affected their daily life:

“Almost 2 years cancer free. My partner was diagnosed with laryngeal cancer, and it was not easy caring for him. I don't believe we had it as bad as some other patients out there, but we were very fortunate to have a strong support system around us. I tell everyone I meet to get and HPV vax. It makes a difference according to the onco doc.”

“Hearing the words 'you are positive for cancer' is one of the most devastating experiences I've ever had. It is like being hit with a sledgehammer in the gut. I am overwhelmed with anxiety and uncertainty about what's to come. The pain and discomfort can be unbearable at times. Radiation therapy was brutal. It feels like my whole life has been turned upside down. I try to remain hopeful for the future but it's difficult not to worry about it spreading. I have difficulty sleeping.”

“It has had a huge impact. My ability to communicate at work and at home was impacted. I had and still struggle with trouble swallowing. After surgery, I struggled with self-esteem. I knew people were looking at my neck. It's one of the first things people would notice.”

“I am a caregiver, so it has affected me indirectly. It has been very difficult to navigate the clinical trial environment with my husband. The treatments with Cisplatin took a severe toll on us. It was very painful for my husband to eat or drink and difficult for our family to adjust our habits like dining out at restaurants and attending social events.”

“It has limited the ability to live a normal life. Pain and discomfort were a normal thing. It definitely hit my confidence in social or work situations. Talking, eating, laughing etc. became a challenge.”

“Radiation reduced thyroid function, produced hearing loss, made me sensitive to spicy foods and reduced my salivary function. Surgery was disfiguring and affected speech.”

“I’m back to normal now.”

“My speech is impaired. I have difficulty swallowing. I experience chemo brain. I do not produce saliva. I have stiffness in neck and shoulder area.”

From the discussion with head and neck cancer survivors that had been treated with pembrolizumab we learned that there are challenges in accessing immunotherapies.

A survivor told us that: “One of the main barriers that needs to be overcome is the inclusion of immunotherapies, including pembro but not only pembro, to the standard of care.”

Before being treated with immunotherapies, patients often go through other lines of treatment (e.g. surgery, radiation) which in their estimation are more physically and psychologically demanding than immunotherapy such as pembrolizumab.

4. Experiences With Currently Available Treatments

As you can tell from the comments above, there is a lot left to be desired from the currently available treatments. As you read from one respondent, they felt that the radiation treatment was brutal. Another respondent said that the treatment with Cisplatin took a severe toll on their loved one. A common theme amongst the responses is the hit that the patients take to their self-esteem after surgery whether it leaves them visually disfigured or creates an impairment for them to overcome, like a speech impediment.

5. Improved Outcomes

The head and neck cancer field is an ever changing one but there has been little innovation when it comes to treatment. As of 2023, treatment protocols for oral cavity, pharyngeal, and laryngeal cancers and for nasopharyngeal cancers include: 1. generalized first-line therapy based on stage, 2. chemoradiation therapy and induction chemotherapy for locally advanced disease, 3. First-, second-, and third-line chemotherapy for metastatic or recurrent disease (Stevenson, 2023). With the addition of treatments like pembrolizumab respondents rated on a scale from 0-100 how they would rate their quality of life while being treated with pembrolizumab and the average was rated at 68/100. This leads us to believe that their experience with the addition of pembrolizumab benefits the patient’s quality of life over the standard of care.

6. Experience With Drug Under Review

The following are comments made by the respondents who have received or are receiving pembrolizumab and their experiences with the treatment:

“We were very fortunate to have a medical team that took the time to walk us through our options. We spent a lot of time discussing PD1 inhibitors. Keytruda was floated as an option and my partner was able to live a relatively normal life while going through treatment. Some things were more difficult, and I would say I had more worries and questions than he did during treatment. I had never cared for someone with head and neck cancer, so it was a learning experience, but my partner has been cancer free for almost 2 years now and we are very fortunate for that.”

“Keytruda is definitely less intense of a treatment than radiation. I have a sore neck and back but haven't had any of the side effects I had with radiation.”

“Less harsh than chemo.”

“Overall satisfied. Some skin rashes from the treatments but I was given cream for it.”

The respondents were asked to rate on a scale of 0 no side effect to 5 severe/intolerable side effects, if they experienced any of the common side effects of pembrolizumab. The categories that they were asked to rate were confusion, sleepiness, memory problems, mood or behaviour change, balance problems, stiff neck, tingling or numbness in arms and legs, vision problems or eye pain, and muscle weakness, pain or cramps. The most severe symptoms experienced were muscle weakness, pain, or cramps weighted as a 2.00/5, stiff neck weighted as a 1.60/5, and tingling or numbness in arms and legs weighted as a 0.80/5. Even though these were on average the most experienced side effects, as you can see their effect on the patient was not so severe that they could not function.

The following are comments from the respondents as to whether they believe the benefits of the treatment with pembrolizumab outweigh the side effects:

“Yes, they do. We are grateful for the wonderful healthcare staff that told my partner about Keytruda.”

“I have only had one round of Keytruda, so I don't know if the good outweighs the bad. So far so good. Time will tell. It is not as severe of a treatment as others I have received.”

“Again, I haven't received it, but I know someone who has. They seemed to be in good spirits during their ordeal. I asked my care team about it, and they said I wasn't a candidate to receive Keytruda.”

“Definitely. Far better than chemotherapy.”

“Yes, I do.”

7. Companion Diagnostic Test

N/A

8. Anything Else?

CCSN is aware of the limitations of this submission given the small number of respondents to the survey. Even with a small number of responses, it is shown that there have been benefits to the respondents with the experience with pembrolizumab. With the addition of pembrolizumab to the treatment options it gives head and neck patients hope and reassurance that they have options where they may not have had any before. This is especially true for patients whose cancer may become metastatic or recurrent disease. For this indication, it may provide the

patient with the opportunity to shrink the tumour as much as possible to limit the invasiveness of the surgery or reduce the duration of the radiotherapy needed, therefore limiting discomfort and disfigurement.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, 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

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
Merck 2023 (CCSN)				X

Merck 2024 (CCSN)			X	
Merck 2024 (LSTN)			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: Lindsay Timm
Position: Community Engagement Manager
Patient Group: Canadian Cancer Survivor Network
Date: **March 31, 2025**

Name: Anris Kica
Position: Co-CEO
Patient Group: Life-Saving Therapies Network
Date: **March 31, 2025**

References

Stevenson, M. M. (2024, October 29). Head and neck cancer treatment protocols. Treatment Protocols. https://emedicine.medscape.com/article/2006216-overview?form=fpf

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0410-000
Generic Drug Name (Brand Name): pembrolizumab (Keytruda)
Indication: Treatment of adult patients with resectable locally advanced head and neck squamous cell carcinoma (HNSCC) as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without platinum-containing chemotherapy and then as monotherapy.
Name of Clinician Group: OH (CCO) Head and Neck Cancer Drug Advisory Committee ("OH (CCO) HN DAC")
Author of Submission: Dr. Michael Odell and members of the OH (CCO) HN DAC

1. About Your Clinician Group

OH(CCO)'s 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 collected via emails.

3. Current Treatments and Treatment Goals

Resectable locally advanced head and neck squamous cell carcinomas (HNSCC) are generally comprised of the following anatomic sub-sites: larynx, oral cavity, and hypopharynx. The treatment paradigm is generally upfront surgery followed by adjuvant radiation (60-66Gy in 30-33 fractions) and risk adapted addition of concurrent cisplatin chemotherapy (either weekly 40mg/m2 or high dose 3-weekly 100mg/m2 cisplatin) for those patients with a positive surgical margin and/or extranodal extension. The Keynote 689 study also included locally advanced oropharyngeal SCC but, in Canada in general, these patients undergo definitive chemoradiation rather than surgery followed by adjuvant therapy. This has been the standard of care for about 2 decades.

Unfortunately, approximately 50-60% will have a recurrence, and only a minority (~10-20%) can be salvaged with either further surgery or radiotherapy. Furthermore, patients without recurrence are at risk of long term sequelae that impact quality of life from extensive surgery, radiation and cisplatin toxicities.

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.

Unfortunately, approximately 50-60% will have a recurrence, and only a minority (~10-20%) can be salvaged with either further surgery or radiotherapy. Furthermore, patients without recurrence are at risk of long term sequelae that impact quality of life from extensive surgery, radiation and cisplatin toxicities. Therefore, there is a need to improve both oncologic outcomes (relapse free survival, overall survival) and to prevent some of the toxicities related to treatment.

5. Place in Therapy

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

In a press release in October 2024, the keynote 689 study was reported to have met the primary end-point of improving event-free survival, and secondary end-point of major pathologic response, with a trend towards improvement in overall survival to be evaluated at the next interim analysis. It has also been accepted for priority review by the FDA.

Pembrolizumab is current used alone or in combination with chemotherapy in the relapsed/metastatic setting and has substantially improved outcomes in that population. Unfortunately, there have also been failed trials of PD-(L)1 inhibitors in earlier stages of HNSCC (Keynote-412 and Javellin 100), where PD-(L)1 agents were evaluated in patients receiving radical chemoradiation (no surgery). Therefore, news that keynote 689 is positive is welcome, but the data has not yet been presented for a wholesome opinion on its place in the treatment landscape.

Assuming the topline data is indeed encouraging, important questions will be whether patient selection on biomarkers status (CPS PD-L1) is required, risks of primary progressive disease or toxicities that may hinder surgery, whether responses to neo-adjuvant pembrolizumab may actually convert patients from high to low risk (and therefore potentially spare the need for adjuvant cisplatin). Answers to these questions will help determine the breadth of impact on this patient population.

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?

It is difficult to comment on this without having seen the data, but important questions will be whether CPS PD-L1 testing will be required to select patients, risks of primary progressive disease or toxicities that may hinder surgery. The trial enrolled patients that were deemed resectable upfront- how this gets rolled out in the real world is an open question. Finally, the trial enrolled cisplatin eligible patients, but whether the data can be extrapolated to upfront non-cisplatin eligible patients is unclear though there isn't a clear biological reason why it wouldn't.

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?

Neo-adjuvant systemic treatment of LAHNSCC is not generally SOC in Canada, but a clinical assessment (ideally with the treating surgeon) prior to each cycle and surgery would be key, in addition to re-staging cross-sectional imaging (CT and/or MRI) prior to planned surgery.

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

Disease progression and toxicities from pembrolizumab.

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]?

Treatment of LAHNSCC is generally done at regionalized cancer programs involving multi-disciplinary teams (surgical, medical and radiation oncology), and the neo-adjuvant and concurrent pembrolizumab doses should probably be monitored in multi-disciplinary clinics to mitigate risks of primary progressive disease (depends on the data). However, the adjuvant component of pembrolizumab (post adjuvant radiation +/- chemotherapy) will add significant new volume, and the impact on resources needs to be considered.

6. Additional Information

NA

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) PDRP provided 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. Michael Odell
Position: Lead, OH (CCO) HN DAC
Date: 28-03-2025

☒ **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. Martin Smoragiewicz
Position: Member, OH (CCO) HN DAC
Date: 05-03-2025

☒ 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**
Merck	X			
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. Eric Winquist
Position: Member, OH (CCO) HN DAC
Date: 25-03-2025

☒ 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

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Merck	X			
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: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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

Company	Check appropriate dollar range*			
	$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 5

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	$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.