CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

nirmatrelvir/ritonavir (Paxlovid)

(Pfizer Canada ULC)

Indication: For the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death

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February 2, 2024

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0808-000-000
Brand name (generic)	Paxlovid (Nirmatrelvir/Ritonavir)
Indication(s)	Mild to moderate COVID-19, treatment
Organization	Asthma Canada
Contact information[a]	Name: Jeffrey Beach

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Asthma Canada disagrees with the draft recommendation and wishes to express our concerns regarding the reimbursement conditions, particularly from the perspective of Canadians living with asthma and other respiratory health conditions. We implore CADTH to extend the reimbursement criteria recommendations to include those living with asthma and other chronic lung health conditions and cardiopulmonary diseases, due to their risk of progression to a severe form of the disease, and risk of hospitalization or death.

Asthma Canada is the only national, patient driven charitable organization solely devoted to enhancing the quality of life for people living with asthma and respiratory allergies. For 50 years, Asthma Canada has proudly served as the national voice for Canadians living with asthma. We empower patients with evidence-based information, education programs and support asthma research in Canada. We advocate for equitable access to the treatment options and healthcare programs that people with asthma need to manage their disease, and for environmental issues that affect air quality.

Asthma is the one of the most common, chronic lung disease which restricts airflow into the lungs, making it difficult for over 4 million Canadians to breathe. It is a leading contributor to workplace absenteeism, hospitalizations, and emergency department visits (more than 82,000 in 2021 alone). The cost of asthma to the Canadian economy is expected to climb to $4.2 billion by 2030.

People with asthma and other chronic lung health conditions are at risk of developing more severe disease or outcomes from COVID-19 and adults with severe asthma are at increased risk of COVID-19 hospitalization. Asthma is also associated with several comorbidities that further put individuals at risk of more severe outcomes, hospitalization, or death.

Severe asthma affects as many as 230,000-465,000 Canadians and is associated with frequent exacerbations, poor symptom control and significant morbidity from the disease itself, as well as the high dose inhaled, and systemic steroids used to treat it. Severe asthma represents a significant burden to the patient, as symptoms frequently interfere with day-to-day living, sleeping, and physical activity. In addition, patients experience frightening and unpredictable exacerbations/attacks. Severe asthma is responsible for approximately 50% of all direct asthma related costs.

The current and future implications of COVID-19 on the health of Canadians living with asthma are unknown. We are grateful that many Canadians have been immunized and continue to follow recommendations for COVID-19 and other respiratory viral disease vaccinations. However, recent COVID-19 outbreaks in long-term care facilities and other institutions provide warning that COVID-19 continues to pose serious health risks to the most vulnerable among us.

The draft CADTH recommendations on reimbursement conditions for Paxlovid would further contribute to the health inequities and poorer health outcomes that many face in our country. Asthma Canada's own research and that of other researchers have found that those who are economically disadvantaged, those living in urban communities and indigenous communities have higher rates of asthma than others, and often do not have equitable access to healthcare resources and coverage for medications they need to control their disease.

On behalf of Canadians living with asthma, we ask that these serious concerns be taken into consideration, and that CADTH revise its reimbursement conditions for Paxlovid to be in line with those issued by INESSS for more equitable and appropriate access.

Given the fact that more than 4 million Canadians live with asthma, and that approximately 5-10% of those have severe asthma that is extremely difficult to manage and treat effectively, access to medication like Paxlovid can be the difference between a positive health outcome following mild-to-moderate COVID-19 and potentially severe complications, including not being able to function or even breathe.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐

N/A Asthma Canada did not previously provide stakeholder input to CADTH for this review.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

The current and future implications of COVID-19 on the health of Canadians living with asthma are unknown. We are grateful that many Canadians have been immunized and continue to follow recommendations for COVID-19 and other respiratory viral disease vaccinations. However, recent COVID-19 outbreaks in long-term care facilities and other institutions provide warning that COVID-19 continues to pose serious health risks to the most vulnerable among us.

The draft CADTH recommendations on reimbursement conditions for Paxlovid would further contribute to the health inequities and poorer health outcomes that many face in our country. Asthma Canada's own research and that of other researchers have found that those who are economically disadvantaged, those living in urban communities and indigenous communities have higher rates of asthma than others, and often do not have equitable access to healthcare resources and coverage for medications they need to control their disease.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☒

It is not clear that the recommendations take into account that people with asthma and other chronic lung health conditions are at risk of developing more severe disease or outcomes from COVID-19 and adults with severe asthma are at increased risk of COVID-19 hospitalization. Asthma is also associated with several comorbidities that further put individuals at risk of more severe outcomes, hospitalization, or death.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- 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 feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Jeffrey Beach*
Position	*President & CEO*
Date	*18/02/2024*
☒	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.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☒
Pfizer – met with Pfizer medical representatives to discuss information and studies related to Paxlovid and individuals with asthma and lung health conditions.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☒
	Yes	☐

D. New or Updated Conflict of Interest Declaration

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**
AstraZeneca	☐	☐	☐	☒
GSK	☐	☐	☐	☒
Sanofi	☐	☐	☐	☒
Pfizer	☐	☐	☒	☐
Novartis	☐	☒	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0808-000
Brand name (generic)	nirmatrelvir/ritonavir
Indication(s)	Mild-to-moderate COVID-19, treatment
Organization	Canadian Breast Cancer Network
Contact information[a]	Name: JK Harris

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

CBCN thanks CADTH for the opportunity to comment on the draft recommendation for nirmatrelvir/ritonavir. We respectfully disagree with the committee recommendations concerning the following points:

- People receiving cancer treatment are an indicated population to receive funding for Paxlovid, however the equitability of this access remains unclear.
- Which populations benefit most from treatment needs further examination but is presumed to includes people receiving cancer treatment due to immune suppressed state.
- Implementation and prescribing guidelines are available through CADTH, but remains at the discretion of each jurisdiction leading to equity concerns.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

If not, what aspects are missing from the draft recommendation?

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

CBCN would note that the concerns expressed about inequitable access due to varied prescribing criteria nationally remains unaddressed. We appreciate that CADTH recommendations must not be mandates, and that prescribing processes (i.e. centralized vs decentralized) are a jurisdictional prerogative, however CADTH is able to offer advise on how this can be done equitably but has not done so in this recommendation.

	Yes	☒

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

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A. Patient Group Information	
Name	*JK Harris*
Position	*Health Policy and Advocacy Lead*
Date	*January 29, 2024*
☒	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.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

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

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0808-000-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Paxlovid (nirmatrelvir/ritonavir)
Indication(s)	Mild-to-moderate COVID-19, treatment
Organization	Gastrointestinal Society
Contact information[a]	Jaymee Maaghop

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

COVID-19 still exists and continues to affect the health of individuals across the country, with many resulting in hospitalizations and/or deaths. Thank you for recognizing the need for effective treatments among people living with acute or chronic diseases and disorders who are at increased risk for severe COVID-19. This is especially important since Paxlovid™ is the first and only oral therapy available in Canada to treat COVID-19.

Due to varying definitions on eligibility requirements, specifically risk factors for severe disease and hospitalization, healthcare providers across the country need clarity and evidence-based guidance for Paxlovid™. We appreciate that CADTH provided a comprehensive definition on the severely or moderately immunosuppressed individuals eligible for treatment and we hope that this provides clarity for public drug plans and healthcare providers across Canada.

We also welcome CADTH's call for investments in rapid antigen test kits and recognition that testing strategies must be "timely, accessible, and equitable" (page 5). Hospitals continue to be overwhelmed and understaffed, and there is wide variation in the availability of rapid test kits across Canada, even within urban centres.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

The draft recommendation lacked highlighting that there are very few medications available to treat COVID-19. It stated that the first line treatment is "supportive care" but they did not define what this consists of. They noted Veklury® (remdesivir) as second-line treatment but it is not as accessible since it is administered by intravenous infusion, requiring immunocompromised patients to go in-person, and it is also given to patients who are already hospitalized. By comparison, Paxlovid™ is an oral medication so patients can stay at home and prevent transmission of the virus.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

In Table 2 (page 10), CADTH recommends that Paxlovid™ should not be prescribed for patients travelling out of the country and it issued this without any explanation. Further areas that need clarification are listed under the following question.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

CADTH did not provide guidance on how jurisdictions can ensure that patients have timely access to therapy, which is crucial for Paxlovid™ since it has a limited treatment window of five days within symptom onset. The recommendation also lacked emphasis on the importance of public drug plans addressing this critical issue. To prevent additional barriers to an already confusing treatment pathway for COVID-19 therapies, CADTH must work with Health Canada and public drug plans in achieving consistency with the eligibility criteria and definitions for severely and moderately immune suppressed individuals.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

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A. Patient Group Information	
Name	*Jaymee Maaghop*
Position	*Health Policy & Outreach Manager*
Date	*29-01-2024*
☒	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.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0808-000-000
Brand name (generic)	Paxlovid - nirmatrelvir/ritonavir
Indication(s)	Mild-to-moderate COVID-19, treatment
Organization	Save Your Skin Foundation: **List of supporters:** 1. The Colorectal Cancer Resource & Action Network (CCRAN) 2. The Leukemia & Lymphoma Society of Canada 3. Kidney Cancer Canada 4. Lung Cancer Canada 5. Canadian Cancer Survivor Network 6. Cancertainty 7. Canadian Skin Patient Alliance (CSPA) 8. Canadian Psoriasis Network
Contact information[a]	Name: Kathleen Barnard

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

-This review gives limited access to patients. It is recognized that the landscape of Covid-19 has changed, however, it would be ill-advised to leave the health of vulnerable populations to herd immunity when vaccination and infection does not guarantee protection against another Covid-19 infection. Some individuals in the vulnerable populations were unable to receive the vaccine in the first place and are in need of a treatment like Paxlovid - nirmatrelvir/ritonavir to prevent serious infection or hospitalization. They must rely on reactive treatment versus proactive treatment should they contract the virus.

It is recognized that there are many medications that conflict with Paxlovid - nirmatrelvir/ritonavir. This should not be a reason to exclude an entire segment of the population, like the elderly, based on the assumption that they would be prescribed too many medications that could put them at risk for drug interactions. We find this to be very paternalistic. The information provided by the manufacturer is detailed and provides thorough guidance on the drug interactions, and the severity, that paired with a knowledgeable pharmacist, there should be no reason why any person should not have the option to

discuss having Paxlovid - nirmatrelvir/ritonavir as a treatment option. Given the variety of medications that interact with Paxlovid - nirmatrelvir/ritonavir it also does not seem like a fair assessment that only the elderly would have medications that would interact when many of the medications listed could be taken by anyone at any age. Therefore, the point that elderly individuals are the only ones at a higher risk for drug interactions does not seem like a fair assessment.

As stated in the recommendation, there should be work done by the jurisdictions to establish infrastructure for testing and prescribing. With many of the at home tests expiring in 2024, and many of the testing centers having closed, it is becoming increasingly more difficult to obtain a test in the five-day time frame to prove a positive result to obtain Paxlovid - nirmatrelvir/ritonavir should you be eligible. There should also be discussions around making the eligibility criteria for Paxlovid - nirmatrelvir/ritonavir more uniform across the jurisdictions so that access is more equitable across the country.

Overall, it is our view that the conditions that were made in the recommendation make it even more difficult for a decision to be made between a medical professional and patient whether Paxlovid - nirmatrelvir/ritonavir should be a treatment used should someone meet the eligibility criteria to acquire a prescription. Paxlovid - nirmatrelvir/ritonavir was brought in to help the at-risk populations and these recommendations picks and chooses which segments to support.

-The conditions included in Table 1 are quite restrictive and are not in line with the current eligibility criteria provided under the emergency use authorization, the reimbursement recommendation provided by INESSS, nor the manufacturer's indication. Indeed, INESSS has issued a funding recommendation that is far more inclusive when compared to CADTH and this threatens our equitably-minded, morally and ethically-based universal health care system that we have in place in Canada. The recommendations need to be consistently aligned to ensure equity and distributive justice across Canada.

Cancer patients and survivors have made it abundantly clear they want the opportunity to avail themselves of this life-saving medication regardless of their treatment status. Cancer patients and survivors are frequent users of the healthcare system, and thus, at increased risk of contracting nosocomial COVID-19 infections, through exposure to diagnostic imaging, visits to the emergency department, or blood draws as part of a surveillance plan, for example. Cancer survivors, particularly those over the age of 60, have often endured several months of toxic and invasive therapies, which include chemotherapeutics, radiotherapies, and surgical procedures, and may no longer feel their bodies are capable of persevering through potentially deadly COVID-19 infections.

Further, while CCRAN supports CADTH's utilization of real-world evidence, the referenced Dormuth et al study was conducted between February 1, 2022, and February 3, 2023 when the Omicron variant, associated with less severe disease, was the primary circulating variant in Canada. Currently in Canada (as of January 2024), subvariant B.A.2.86 [Health Canada] represents the most dominant lineage, for which no data is available. Dormuth et al cautioned that their results may not be applicable to other variants. Given the tumultuous nature of the ongoing pandemic, ever-evolving variants of concern, and the significant strain on the current healthcare system, taking a more judicious approach to avoiding unnecessary hospitalization or death from COVID-19 is most certainly warranted to ensure our Canadian patient populations are protected.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?
Partially

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☒

If not, please provide details regarding the information that requires clarification.

Most of the details are clearly stated. However, it is not clear why the "***older age***" demographic in the recommendation, which has been identified as a relevant risk factor for progressing to severe disease, is not included in the reimbursement criteria listed in Table 1. What is further ill-defined is why "***older age***" is being considered as > 80 years old, particularly in the context of "the changing nature of the pandemic, and the viral evolution" when Schwartz et al noted the most significant benefit in those 70 and older and the EPIC-HR RCT demonstrated benefit at **a median age of 45**, despite including only unvaccinated individuals. In the absence of strong, high-level evidence, it is unclear why the Dormuth et al observational study, with the most restrictive criteria, was utilized.

The provided patient perspective is undeniable: patients with co-morbidities, such as cancer, want and deserve access to this potentially life-saving therapeutic, regardless of their current treatment regimen status. Patient groups shared that patients feel that "because of their condition, they [are] at higher risk for worst outcomes from COVID-19 than the general population, and that COVID-19 complications also posed a risk of worsening their baseline condition."

Patients with co-morbidities spend a disproportionate amount of time in the hospital, and congruently, utilize a disproportionate amount of increasingly scarce healthcare resources. The therapeutic under review can potentially help these patients to avoid a hospital admission or emergency department visit due to COVID-19 infection and/or complications, yet the reimbursement criteria is not inclusive of all individuals in this disadvantaged group. It is not clear why this input was not taken into account when determining the eligibility for reimbursement.

Additionally, any Canadian diagnosed with moderate to severe COVID-19 disease should be permitted to access Paxlovid to ensure best outcomes and reduce the burden on the healthcare system. We strongly urge this expert review committee to revisit the funding recommendation criteria by expanding and including patient populations.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

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- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name: Save Your Skin Foundation*
Position	*Please state currently held position: President*
Date	*Please add the date form was completed (DD-MM-YYYY)01/02/2024*
☐	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.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☒
If yes, please detail the help and who provided it. Above listed PAG's		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

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**
Pfizer	☐	☐	☒	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0808-000-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Nirmatrelvir-Ritonavir (Paxlovid)
Indication(s)	for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death
Organization	Sickle Cell Awareness Group of Ontario
Contact information[a]	Name: Lanre Tunji-Ajayi, M.S.M

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale. Though the study by Dormuth et al., which compared to patients who did not receive nirmatrelvir-ritonavir, treatment with nirmatrelvir-ritonavir was associated with statistically significant relative reductions in prevention of death or admission to hospital in the severely immunocompromised patients (risk difference [RD], −2.5%, 95% CI, −4.8% to −0.2%) and the moderately immunocompromised patients (RD, −1.7%; 95% CI, −2.9% to −0.5%); it was alarming that immune-compromised diseases are not included in the CADTH recommendations. People with sickle cell disease have compromised immune system and are highly susceptible to infections We are of the opinion that immune compromised patients should be included in the recommendations.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒
If not, what aspects are missing from the draft recommendation? Though individuals with sickle cell disease would benefit from this drug, this group of patients was not included. The recommendations focused on moderate or severe primary immunodeficiency and this is not complete in our opinion.		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
	Yes	☒

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	No	☐
If not, please provide details regarding the information that requires clarification.		

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A. Patient Group Information	
Name	*Please state full name Lanre Tunji-Ajayi, M.S.M*
Position	*Please state currently held position President/CEO*
Date	*Please add the date form was completed (30-01-2024)*
☒	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.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

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Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Pfizer Canada	☐	☒	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0808-000-00
Brand name (generic)	Nirmatrelvir/Ritonavir
Indication(s)	COVID
Organization	Nova Scotia Emerging and Re-emerging Infections Therapeutics And Prophylactics Recommendations Group
Contact information[a]	Name: [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Thank you to the CADTH Canadian Drug Expert Committee for the thoughtful and thorough review of data on the use of nirmatrelvir/ritonavir for prevention of hospitalization and death in at risk individuals.

We would like to contribute some information and data from the Nova Scotia context that may be useful for consideration in the final recommendations. We include an individual patient care lens and a system viability lens given the current Canadian health system climate.
There are two domains in which more nuanced usage recommendations may be helpful:

1. The safety of nirmatrelvir/ritonavir in the context of older and frail individuals
2. Uncertainty as to whether nirmatrelvir/ritonavir treatment in older COVID positive individuals who are **not** immunocompromised reduces hospitalization or death

The Nova Scotia nirmatrelvir/ritonavir prescribing and COVID care context
Nirmatrelvir/ritonavir has been prescribed only by designated physician and pharmacist prescribers to high risk individuals 12 years of age and older with non-severe COVID who meet the following criteria:

- Symptom onset within 5 days AND
- Positive SARS-CoV-2 PCR test or rapid antigen test AND
- Not sufficiently vaccinated as defined in the NS referral criteria AND
- ≥ 1 high risk factor for progression as defined in the NS referral criteria

Over 100,000 people have been virtually assessed, and 6,578 nirmatrelvir/ritonavir treatment courses have been prescribed. Those in inpatient and long term care (LTC) settings were also evaluated and prescribed nirmatrelvir/ritonavir when criteria were met. As such, there is a reasonably large documented cohort experience.

Section A: Nova Scotia safety, outcome, and prescription data in older and frail individuals
In our data, 1,549 people greater than 65 years old with a risk factor for progression and under vaccinated were prescribed nirmatrelvir/ritonavir. **As a surrogate of frailty, 211 long term care (LTC) residents prescribed nirmatrelvir/ritonavir were assessed.** Discontinuation of nirmatrelvir/ritonavir and adverse events were the same or lower than those not in LTC. LTC residents had a significantly lower occurrence of side effects secondary to nirmatrelvir/ritonavir treatment (11.7% vs. 52.8%, $p<0.001$) and were significantly less likely to discontinue treatment due to side effects (6.7% vs. 35.5%, $p=0.022$) than those not in LTC. More LTC residents completed greater than 90% of the nirmatrelvir/ritonavir treatment course than those not in LTC (92.5% vs. 86.4%, $p=0.015$).

Of those 65 years of age and older who received nirmatrelvir/ritonavir, LTC residents vs those not in LTC were no more or less likely to be hospitalized after starting nirmatrelvir/ritonavir treatment (4.0% vs. 6.3%, p=0.196) and there was no significant difference in requiring ICU care (0.0% vs. 4.7%, p=1.000). There was no significant difference in all-cause death at 30 days post nirmatrelvir/ritonavir treatment in LTC residents vs those not in LTC (3.2% vs. 2.1%, p=0.342).
Therefore, based on the experiences in Nova Scotia, it is possible to safely prescribe nirmatrelvir/ritonavir in elderly and frail people, and it is well tolerated in a designated prescriber model. Outcomes in elderly nirmatrelvir/ritonavir treated non-LTC individuals are similar to those for elderly LTC residents.

Outcome data was assessed in 301 immunocompromised people greater than 65 years old and 1,174 non-immunocompromised people greater than 65 years old that met nirmatrelvir/ritonavir prescribing criteria. Of those greater than 65 years old, there was no significant difference in immunocompromised people and non-immunocompromised people after starting nirmatrelvir/ritonavir in hospitalization (6.3% vs. 6.1%, p=0.9196), ICU care (3.2% vs. 5.0%, p=0.748), or all cause death (2.6% vs. 2.4%, p=0.813).

And therefore, if one were to consider treating immunocompromised people, it may be reasonable until further data are available to consider treating other higher risk older people as well.

Section B: Biologic / immunologic plausibility for why older frail under vaccinated individuals may maintain higher risk for progressive infection
It is well recognized that the immunologic correlate of preventing severe disease is a robust T cell response[1,2,3] . Data from Dr. Barrett's lab (pers communication) demonstrate lower functional T cells responses to SARS-CoV-2 in older LTC adults, which is exacerbated in frail individuals, suggesting a biologic predisposition to more severe disease. Older adults also elicit lower T cell immunity to COVID vaccination[4]. Age-related decline in T cell immunity poses increased risk of severe COVID disease, higher risk of hospitalization, intensive care, and death due to COVID-19.

Canadian health care climate consideration: The Canadian health care system in emergency departments and acute care settings is in crisis and that is likely to continue into the foreseeable future until care of the older person/long term care, human resource and other factors have long term fixes. The primary goal at this point is to maintain health and prevent visits to the emergency departments and need for hospitalization.

Rationale for our suggestions: There is considerable uncertainty as to whether nirmatrelvir/ritonavir prevents hospitalization or death in people greater than 65 years old without immunocompromise with other significant health issues, especially in those under vaccinated or greater than 6 months from last vaccination. There are, however, pieces of real world data from our province (section A), as well as immunologic plausibility data (section B), that suggest at least some of these people may benefit from treatment. Data suggest that treatment of frail and older people (section A) can be safely done with robust prescribing safety protocols especially now that drug-drug interactions are far better described after 2 years of real world experience.

Suggestion for panel consideration:
1.It would be helpful to articulate that safe treatment of older frail individuals may be possible with proper oversight and pharmacist involvement.
2. It would also be helpful to highlight treatment benefit for comorbid and/or under vaccinated older individuals is unclear but until that is clarified, these individuals remain at high risk of poor outcomes, and treatment consideration in a stressed system may be reasonable until further data become available.

References:

[1]E. John Wherry, Dan H. Barouch, T cell immunity to COVID-19 vaccines. Science 377,821-822(2022).DOI:10.1126/science.add2897

[2]Rydyznski Moderbacher C, et al. Antigen-Specific Adaptive Immunity to SARS-CoV-2 in Acute COVID-19 and Associations with Age and Disease Severity. Cell 183, 996–1012 e1019 (2020)

[3]Moss, P. The T cell immune response against SARS-CoV-2. Nat Immunol 23, 186–193 (2022). https://doi.org/10.1038/s41590-021-01122-w

[4]Jo, N., Hidaka, Y., Kikuchi, O. *et al.* Impaired CD4⁺ T cell response in older adults is associated with reduced immunogenicity and reactogenicity of mRNA COVID-19 vaccination. *Nat Aging* **3**, 82–92 (2023). https://doi.org/10.1038/s43587-022-00343-4

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐
If not, what aspects are missing from the draft recommendation? N/A, this is the first time providing feedback on the recommendation.		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A, we are not providing feedback on that component.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A, we are not providing feedback on that component.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification. N/A, we are not providing feedback on that component.		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- 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 feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please 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 declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Tasha Ramsey*
Position	*Co-chair, Nova Scotia Emerging and Re-emerging Infections Therapeutics And Prophylactics Recommendations Group*
Date	*February 14, 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.

Conflict of Interest Declaration				
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**
***None* (no** companies or organizations have provided with financial payment)	☒	☒	☒	☒

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0808
Name of the drug and Indication(s)	Nirmatrelvir-Ritonavir (Paxlovid) for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification. Clarification is required to explain the rationale for excluding patients with advanced age as a sole risk factor from the recommended reimbursement population, particularly given the following excerpt from the Clinical Evidence section below: "In two studies with subgroup analyses according to age group, there was a greater magnitude of effect with nirmatrelvir-ritonavir treatment versus no treatment in patients at least 70 years of age, compared with patients who were less than 70 years. The overall incidence of hospitalization was also greater in both treatment and control groups in patients with older age."

b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification. Guidance is required regarding definitions for the following terms used in the reimbursement conditions: “severe primary immunodeficiencies” and “moderate primary immunodeficiencies”.
c) Implementation guidance
Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.