CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

upadacitinib (Rinvoq AD)

(Abbvie Corporation)

Indication: Atopic dermatitis

March 31, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0685-000
Brand name (generic)	Upadacitinib (Rinvoq)
Indication(s)	Atopic dermatitis
Organization	Dermatologist and allergist group managing atopic dermatitis (Formerly the Atlantic Specialist group managing atopic dermatitis - expanded to include experts from other regions in Canada)
Contact information[a]	Name: Dr. Irina Turchin; [redacted]

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

The Dermatologist and allergist group managing atopic dermatitis (AD) disagrees with the following recommendations presented in Table 1:

"Patients must have had an adequate trial or be ineligible for each of the following therapies: phototherapy (where available), methotrexate, and cyclosporine" (Initiation Reimbursement Condition, page 4). This criterion imposes several critical barriers to the safe and effective treatment of moderate-to-severe AD and is not aligned with published data nor clinical expertise:

- There is no evidence to suggest that failure of prior treatment with methotrexate and cyclosporine is a useful prerequisite in selecting patients who are likely to respond to upadacitinib as prior treatment with these agents was not required for inclusion in upadacitinib's clinical trial program.[1-4] Furthermore, data in support of these agents in AD treatment are sparse, inconsistent, and historic.
- Given the safety concerns associated with both methotrexate and cyclosporine,[5-6] imposing at least 24 weeks of treatment with these agents on patients with moderate-to-severe AD places them at considerable risk of medical complications, infectious complications in those already vulnerable to skin infection, and in particular for adolescent patients and patients of childbearing potential.
    - Similarly, the draft recommendations give limited guidance related to ineligibility for systemic therapies. **Methotrexate and/or cyclosporine treatments should be immediately discontinued upon the emergence of adverse events, and medical contraindications to these agents should be exempted from upadacitinib initiation criteria.**
- Multiple trials of systemic agents will be cost-prohibitive for many moderate-to-severe AD patients and would unnecessarily limit their access to upadacitinib.
    - **We recommend that corticosteroids (i.e. prednisone IM Kenalog) be added as a systemic option prior to initiation of upadacitinib** as these treatments are more accessible to patients and are commonly prescribed for moderate-to-severe AD, including in combination with other systemic treatments.
    - Furthermore, **patients should be required to have an adequate trial to only one of the systemic agents prior to initiating upadacitinib, rather than multiple trials with multiple agents**. This is reflected using "methotrexate, and/or cyclosporine", which is present elsewhere in the description of this reimbursement condition.
- Additionally, the expert who was consulted by CADTH stated that AD-treaters would be likely to choose methotrexate and cyclosporine ahead of upadacitinib (page 8); this statement does not reflect our clinical experience and should not be used to craft reimbursement recommendations.

Current use of methotrexate and cyclosporine for the treatment of moderate-to-severe AD is a result of the forced treatment ladder, and access to safer, more effective treatments such as upadacitinib would circumvent these options in clinical practice.

"Adequate control and refractory disease are optimally defined using similar criteria to those used in the upadacitinib trials, such as achieving an EASI-75" (Initiation Implementation Guidance, page 4), and "The physician must provide the EASI score and Physician Global Assessment score at the time of initial request for reimbursement" (Initiation Reimbursement Condition, page 4). The consideration of disease severity at special sites (i.e. face, hands, and feet) is currently missing from these recommendations, and the decision to implement EASI-75 may preclude clinically meaningful improvements associated with lower EASI scores.

- Because the minimally clinically important difference of the EASI score is unknown, smaller EASI score differences may have been clinically meaningful in clinical trials. A nonarbitrary EASI improvement cut-off has yet to be clearly defined for AD.
- **Atopic dermatitis present at special sites may have significant negative impact on the functioning and quality of life of moderate-to-severe AD patients and DLQI (≥10), patient-reported pruritus NRS, and PGA scores (moderate or severe) at special site should be considered in the assessment of disease severity for initiation and renewal of upadacitinib.**

"For renewal after initial authorization, the physician must provide proof of beneficial clinical effect…defined as a 75% or greater improvement in the EASI score (EASI-75)…" (Renewal Reimbursement Condition, pages 4-5) and "For subsequent renewal, the physician must provide proof of maintenance of EASI-75 response…" (Renewal Reimbursement Condition, page 5). These conditions lack consideration for patient-reported outcomes and other clinically meaningful results of AD treatment, and do not consider the involvement of special sites (i.e. face, hands, and feet).

- **Conditions for upadacitinib renewal should be revised to include EASI-75 or EASI-50 along with improvement of other patient-reported outcome parameters including 5-point improvement in DLQI and 4-point improvement in pruritus NRS.**
- **Additionally, the above criteria, when assessed at special sites (face, hands, and/or feet), should be sufficient for renewal of upadacitinib.**

"The patient must be under the care of a dermatologist" (Prescribing Reimbursement Condition, page 5). This condition does not reflect the reality of AD care in Canada and would result in unnecessary delays in access to upadacitinib along with excessive use of health care resources.

- **Allergists, clinical immunologists, and pediatricians knowledgeable in the management of moderate-to-severe AD should be included in the list of prescribing specialists for upadacitinib.**

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 following important aspects of the Atlantic Specialist group managing atopic dermatitis's input appear to have been excluded from the draft recommendations:

- **The importance of patient-reported, and quality of life outcomes in determining disease severity and clinically meaningful treatment response.**
  - Patient-reported itch reduction (4-point reduction on the NRS, or a total NRS score of less than 3), and improved quality of life (DLQI ≥10) are important indicators of treatment success, as indicated in our response to question 6.9 on the Clinical Input Template.

- **The high risk of side effects and low efficacy associated with off-label systemic treatments (methotrexate and cyclosporin).**
    - These treatments carry significant safety concerns, especially in the long-term, and have limited efficacy and low durability of response, especially when compared to novel medications like upadacitinib which target AD's underlying pathogenesis, as described in our response to question 3.1 of the Clinical Input Template.

- **The lack of evidence for the efficacy and feasibility of phototherapy as an initiation criterion for upadacitinib.**
    - Phototherapy is associated with poor accessibility, long wait times, low efficacy, and exposure to UV radiation, and should be removed from the forced treatment ladder, as indicated in our response to question 5.1 on the Clinical Input Template.
    - We acknowledge that we disagree with the clinical expert consulted by CADTH on this topic.

- **The range of specialists who frequently treat moderate-to-severe AD and who would be qualified to initiate upadacitinib treatment.**
    - Our clinical group includes allergists/clinical immunologists who frequently treat moderate-to-severe AD in patients with common comorbidities such as asthma, allergic rhinitis/nasal polyps, and anaphylactic food allergies. These specialists were included as critical to an ideal care pathway for AD in our response to question 6.13 of the Clinical Input Template.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒
Apart from the duration of initial authorization (page 4), clinical evidence is missing from the provided rationale behind the initiation and renewal conditions (pages 4-5). Please provide additional explanation, especially as it relates to upadacitinib's clinical trial data, for the reasoning behind the recommendations.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
The definition of an "adequate trial" of systemic therapies (page 11) requires clarification and further exploration. Specifically, there is no indication of how to handle treatment interruptions or adverse events, and it is not clear why 12 weeks was determined as the minimum trial duration for cyclosporine. Clinical experience suggests that responders to cyclosporine will experience symptom improvement in 4-6 weeks and maintaining patients on ineffective therapy for more than twice that duration serves no clinical benefit. Moreover, cyclosporine is a short-term therapy for acute flares and is not appropriate for medium-to long-term management due to its impact on blood pressure and renal function. Additional evidence is required to support the requirement of immunomodulator trials prior to initiating upadacitinib.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
In the first initiation reimbursement condition, the phrase "methotrexate, and cyclosporine" appears to contradict the phrase "methotrexate, and/or cyclosporine" and the third point under "Implementation Guidance" which states that 2 out of 4 systemic immunomodulators be trialed prior to initiating upadacitinib. This criterion should be clarified, and we suggest that failure of a single systemic agent be sufficient for upadacitinib initiation (see above response to question 1). The rationale behind matching upadacitinib's initiation and renewal reimbursement criteria to those of dupilumab appear to be the result of a single expert's opinion and are not sufficiently explained. Although both are indicated for the treatment of AD, their distinct formulations, efficacy/safety profiles, and disease-modifying mechanisms of action [4,7] necessitate separate consideration.		

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

References:

1. Evaluation of upadacitinib in adolescent and adult patients with moderate to severe atopic dermatitis (eczema) (Measure Up 1). ClinicalTrials.gov identifier: NCT03569293. Updated February 3, 2022. Accessed March 25, 2022. https://clinicaltrials.gov/ct2/show/NCT03569293

2. A study to evaluate upadacitinib in adolescent and adult subjects with moderate to severe atopic dermatitis (Measure Up 2). ClinicalTrials.gov identifier: NCT03607422. Updated September 5, 2021. Accessed March 25, 2022. https://clinicaltrials.gov/ct2/show/NCT03607422

3. A study to evaluate upadacitinib in combination with topical corticosteroids in adolescent and adult participants with moderate to severe atopic dermatitis (AD Up). ClinicalTrials.gov identifier: NCT03568318. Updated September 2, 2021. Accessed March 25, 2022. https://clinicaltrials.gov/ct2/show/NCT03568318

4. A study to compare safety and efficacy of upadacitinib to dupilumab in adult participants with moderate to severe atopic dermatitis (Heads Up). Updated February 2, 2022. Accessed March 25, 2022. https://clinicaltrials.gov/ct2/show/NCT03738397

5. van der Schaft J, Politiek K, van den Reek JMPA, et al. Drug survival for ciclosporin A in a long-term daily practice cohort of adult patients with atopic dermatitis. *Br J Dermatol*. 2015;172(6):1621-1627. doi:10.1111/bjd.13730

6. Politiek K, van der Schaft J, Coenraads PJ, de Bruin-Weller MS, Schuttelaar ML. Drug survival for methotrexate in a daily practice cohort of adult patients with severe atopic dermatitis. *Br J Dermatol.* 2016;174(1):201-203. doi:10.1111/bjd.13961

7. AbbVie. RINVOQ™ (upadacitinib) Achieved Superiority Versus DUPIXENT® (dupilumab) For Primary and All Ranked Secondary Endpoints in Phase 3b Head-to-Head Study in Adults with Atopic Dermatitis. Accessed: March 25, 2022. Available at: https://news.abbvie.com/news/press-releases/rinvoq-upadacitinib-achieved-superiority-versus-dupixent-dupilumab-for-primary-and-all-ranked-secondary-endpoints-in-phase-3b-head-to-head-study-in-adults-with-atopic-dermatitis.htm)

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: • Dr. Wayne Gulliver • Dr. Ian Landells • Dr. Kamal Ohson • Dr. Catherine Rodriguez • Dr. Irina Turchin		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Dr. Kirk Barber	
Name	*Kirk Barber, MD*
Position	*Clinical Professor, Department of Medicine (Dermatology) and Department of Community Health Sciences, University of Calgary, Calgary, Alberta*
Date	*17- 03- 2022*
☒	**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**
AbbVie Canada	☐	☐	☐	☒
Galderma	☐	☐	☐	☒
Sanofi / Regeneron	☐	☐	☐	☒

New or Updated Declaration for Dr. Marc Bourcier	
Name	*Marc Bourcier, MD*
Position	*Dermatologist*
Date	*30/03/2022*
☒	**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**
AbbVie	☐	☐	☐	☒
Amgen	☐	☐	☒	☐
Bausch Health	☐	☒	☐	☐
BMS	☒			
GSK		☒		
Janssen			☒	
Paladin	☒			
Eli Lilly		☒		
Novartis	☒			
Pfizer	☒			
RBC	☒			
Sanofi			☒	
Sandoz			☒	
Sun Pharma		☒		

New or Updated Declaration for Dr. Sameh Hanna	
Name	*Sameh Hanna, MD*

Position	*Clinical Lead Dermatologist, Dermatology on Bloor*
Date	*30-03-2022*
X	**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

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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**
AbbVie Canada	☐	☒	☐	☐

New or Updated Declaration for Dr. Vipul Jain

Name	*Vipul Jain, MD*
Position	*Allergy & Clinical Immunology*
Date	*30-03-2022*
☒	**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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Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
AbbVie	☒	☐	☐	☐
Medexus	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐

New or Updated Declaration for Dr. Gina Lacuesta

Name	*Gina Lacuesta, MD*
Position	*Assistant Professor, Faculty of Medicine, Dalhousie University, Consultant Physician in Allergy and Clinical Immunology Nova Scotia Health Authority*
Date	*21-03-2022*
☒	**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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Company	Check Appropriate Dollar Range

	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie – advisory board, sponsorship for Supplement co-authorship	☐	☒	☐	☐
Pfizer – advisory board	☒	☐	☐	☐
Sanofi – advisory board, speaker	☐	☒	☐	☐

New or Updated Declaration for Dr. Martin Leblanc	
Name	*Martin Leblanc, MD*
Position	*Dermatologist*
Date	*30-03-2022*
☒	**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

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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
Abbvie	☒	☐	☐	☐
Genzyme	☒	☐	☐	☐
Janssen	☒	☐	☐	☐
Leo Pharma	☒	☐	☐	☐
Novartis	☒	☐	☐	☐

New or Updated Declaration for Dr. Jason Lee	
Name	*Jason K Lee, MD*
Position	*MD, FRCPC, FAAAAI, FACAAI*
Date	*30-03-2022*
☒	**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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	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie	☐	☒	☐	☐
Pfizer	☒	☐	☐	☐
Leo Pharma	☒	☐	☐	☐

New or Updated Declaration for Dr. Hermenio Lima	
Name	*Jose Hermenio Cavalcante Lima Filho, MD*
Position	*LEADER Research Director and Associate Clinical Professor divisions of Clinical Immunology, Allergy and Dermatology McMaster University.*
Date	*29-03-2022*
☒	**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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AbbVie	☐	☒	☐	☐
Sanofi Genzyme	☐	☒	☐	☐

New or Updated Declaration for Dr. Charles Lynde	
Name	*Charles Lynde, MD*
Position	*Dermatologist & Principal Investigator*
Date	*31-03-2022*
☒	**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

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	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
AbbVie	☐	☐	☒	☐
Amgen	☐	☒	☐	☐
Basuch Health	☐	☒	☐	☐
Dermavant	☐	☒	☐	☐
Eli Lilly	☐	☒	☐	☐
Janssen	☐	☒	☐	☐
LEO Pharma	☐	☒	☐	☐
Novartis	☐	☒	☐	☐
Pfizer	☐	☐	☒	☐
Sandoz	☐	☒	☐	☐

New or Updated Declaration for Dr. Kim Papp	
Name	*Kim Papp, MD*
Position	*Founder and President of Probity Medical Research Inc. Waterloo, Ontario*
Date	*28-03-2022*
☒	**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

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	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie	☒	☐	☐	☐
Acelyrin	☒	☐	☐	☐
Akros	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Anacor	☒	☐	☐	☐
Aralez Pharmaceuticals	☒	☐	☐	☐
Arcutis	☒	☐	☐	☐
Avillion	☒	☐	☐	☐
Bausch Health/Valeant	☒	☐	☐	☐
Boehringer Ingelheim	☒	☐	☐	☐
Bristol-Myers Squibb	☒	☐	☐	☐
Can-Fite Biopharma	☒	☐	☐	☐
Celgene	☒	☐	☐	☐
Celltrion	☒	☐	☐	☐
Coherus	☒	☐	☐	☐
Dermavant	☒	☐	☐	☐
Dermiria	☒	☐	☐	☐
Dice Pharmaceuticals	☒	☐	☐	☐
Dow Pharma	☒	☐	☐	☐
Eli Lily	☒	☐	☐	☐
Evelo	☒	☐	☐	☐
Forbion	☒	☐	☐	☐
Galderma	☒	☐	☐	☐
Gilead	☒	☐	☐	☐
GSK	☒	☐	☐	☐

Incyte	☒	☐	☐	☐
Janssen	☒	☐	☐	☐
Kyowa Hakko Kirin	☒	☐	☐	☐
Leo	☒	☐	☐	☐
Meiji Seika Pharma	☒	☐	☐	☐
Merck (MSD)	☒	☐	☐	☐
Mitsubishi Pharma	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐
Regeneron	☒	☐	☐	☐
Reistone	☒	☐	☐	☐
Roche	☒	☐	☐	☐
Sanofi-Aventis/Genzyme	☒	☐	☐	☐
Sandoz	☒	☐	☐	☐
Sun Pharma	☒	☐	☐	☐
Takeda	☒	☐	☐	☐
UCB	☒	☐	☐	☐
vTv Therapeutics	☒	☐	☐	☐
Xencor	☒	☐	☐	☐

New or Updated Declaration for Dr. Sanjay Siddha	
Name	*Sanjay Siddha, MD*
Position	*Dermatologist*
Date	*30-03-2022*
☒	**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

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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**
None to declare	☐	☐	☐	☐

New or Updated Declaration for Dr. Timothy Vander Leek	
Name	*Timothy Vander Leek, MD*
Position	*President, Canadian Society of Allergy and Clinical Immunology*

Date	*28-03-2022*
☒	**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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Miravo Healthcare	☐	☒	☐	☐
Bausch Health	☒	☐	☐	☐
Pfizer Canada	☒	☐	☐	☐

New or Updated Declaration for Dr. Wade Watson

Name	*Wade Watson, MD*
Position	*President, Atlantic Society of Allergy and Clinical immunology*
Date	*28-03-2022*
☒	**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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None to declare	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0685-000
Brand name (generic)	Rinvoq (upadacitinib)
Indication(s)	atopic dermatitis
Organization	Fraser Health Dermatology Group
Contact information[a]	Name: Dr. Gurbir Dhadwal

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

- We disagree with Table 1. Initiation 1 – Patients must have had an adequate trial or be ineligible for each of the following therapies: phototherapy (Where available), methotrexate, and cyclosporine.
- In the same table under implementation guidance 2. It is noted that the clinical expert noted that a trial of two of the four immunomodulators (methotrexate, cyclosporine, mycophenolate mofetil, and azathioprine) should be considered before initiating upadacitinib. This implies any two of the noted immunomodulators rather than specifically methotrexate and cyclosporine
- On page 8 – input from clinical expert consulted by CADTH, "the clinical expert believed that many practitioners would still consider a trial of methotrexate and cyclosporine before initiating treatment with Upadacitinib"
- The clinician input from The Atlantic Specialist Group contradicts the clinical expert as they felt that the place for upadactinib would be after lifestyle measures and topical steroids. We would tend to agree with the Atlantic specialist group that upadacitinib could be used post topical steroids, and we would disagree with the clinical expert that many physicians would consider a trial of methotrexate AND cyclosporine before treating with upadacitinib; unless they were compelled by reimbursement criteria. Cyclosporine has a significant side effect profile including malignancy and renal impairment, and it often leads to polypharmacy to manage the hypertension and hyperlipidemia it causes.
- In summary we disagree with the recommendation to have had adequate trials or be ineligible for both methotrexate and cyclosporine. We agree with the Atlantic Specialist group that many physicians would consider upadactinib after topical therapy. Further if we were to recommend a trial of another systemic before upadactinib it would be methotrexate alone.

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	☐

No applicable

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

- It is not clear why the recommendation specifically recommends both methotrexate AND cyclosporine as neither the input from the clinical expert nor the clinician input appeared to recommend this		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
- We have the same comments regarding implementation issues regarding the rational for requirement for specifically both methotrexate and cyclosporine		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
- Once again we have the same comments regarding reimbursement conditions regarding the rational for the requirement for specifically both methotrexate and cyclosporine		

[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		
2. 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.		
3. 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		
4. 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	*Gurbir Dhadwal*
Position	*Community Dermatology*
Date	*30-03-2022*
☒	**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**
Abbvie	☐	☐	☒	☐
Sanofi	☐	☐	☒	☐
Leo	☐	☒	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Se Mang Wong*
Position	*Community Dermatologist*
Date	*30-03-2022*
☒	**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**
Abbvie	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Aaron Wong*
Position	*Community Dermatologist*
Date	*30-03-2022*
☒	**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**
Abbvie	☐	☒	☐	☐
Sanofi	☐	☒	☐	☐

New or Updated Declaration for Clinician 4

Name	*Gordon Jung*
Position	*Community dermatologist*
Date	*30-03-2022*
☒	**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**
Abbvie	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Michael Samycia*
Position	*Community Dermatologist*
Date	*30-03-2022*
☒	**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**
Abbvie	☐	☒	☐	☐
Sanofi	☐	☒	☐	☐

New or Updated Declaration for Clinician 1	
Name	*Chih-ho Hong*
Position	*Please state currently held position*
Date	*30-03-2022*
☒	**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.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0685-000
Brand name (generic)	Rinvoq (upadacitinib)
Indication(s)	Atopic dermatitis
Organization	Canadian Skin Patient Alliance & Eczéma Québec
Contact information[a]	Rachael Manion, Canadian Skin Patient Alliance Charlie Bouchard, Director, Eczéma Québec

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

The Canadian Skin Patient Alliance and Eczéma Québec appreciate the rigorous approach of the committee to this recommendation. However, we have concerns regarding certain of the eligibility criteria.

We feel there is a high burden placed on patients by requiring them to fail cyclosporine and methotrexate (in addition to phototherapy where it is available) before they are eligible to access reimbursement for Rinvoq (upadacitinib). Cyclosporine can cause kidney damage and methotrexate can damage the liver. Methotrexate is contraindicated in pregnancy and breastfeeding. We urge the Canadian Drug Expert Committee (CDEC) to reconsider requiring patients – especially young patients and women of childbearing age – to take and fail on these therapies before having access to Rinvoq (upadacitinib).

Currently, many atopic dermatitis patients are treated with older therapies that are like a hammer for their system. The hope for patients is that tailored treatments for the underserved atopic dermatitis community that focus on the underlying disease mechanisms would replace immunosuppressants that were not initially developed to treat skin conditions such as atopic dermatitis.

Some atopic dermatitis patients experience these lesions on "special sites" like their hands and face. Having atopic dermatitis on these sites on the body is particularly debilitating, difficult to treat, and has significant impacts on patients' mental health. It is not uncommon for skin patients with lesions on special sites to have access to innovative therapies without the months-long (or even years-long) trial and error process. For example, people living with psoriasis in their genital area can access biologics without failing on multiple other therapies. Drawing on the experience of the psoriasis community, we urge CDEC to include exceptions for special sites in its recommended reimbursement criteria – specifically, the face and hands.

We urge CDEC to not restrict the prescribing criteria to dermatologists. Some patients are managed by other specialists such as allergists or pediatricians. It is not uncommon for young people with atopic dermatitis to be under the care of a pediatrician, not a dermatologist. While there are pediatricians in Canada who focus on dermatology, they would not technically meet the prescribing criteria outlined in the draft recommendation. This is a disservice to young patients. There is currently no pediatric dermatology specialization recognized by the Royal College of Physicians and Surgeons in Canada.

Further, Canada has some of the poorest access to dermatologists when compared with 7 other comparable countries: there are only 1.7 dermatologists per 100,000 people in Canada. (Global Patient Initiative to Improve Eczema Care, Access Measure 1: Access to Dermatologists, https://www.improveeczemacare.com/dashboard)

To help improve access to dermatology care, an increasing number of primary care physicians with an interest in dermatology are expanding care to patients. Excluding them from accessing this treatment for their patients with moderate to severe atopic dermatitis can exacerbate the barriers to care for this community.

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	☒

Because of the heterogenous nature of atopic dermatitis, many people only have mild symptoms, and some outgrow this disease as they age. *This is not the case for everyone. We are concerned that this is inadvertently creating an assumption that atopic dermatitis is not as serious as it is in fact for people who live with it.* We want to ensure that CDEC members understand that moderate to severe atopic dermatitis can have a major impact on Health-Related Quality of Life (HRQoL) and is frequently associated with comorbid anxiety and depression. Many patients with uncontrolled disease will experience close to no remission in a year. Imagine living with uncontrolled itch (imagine mosquito bites) 24 hours a day, 7 days a week, for a whole year with no reprieve.

The stakeholder input that was included in the draft recommendation does not include any of the testimonials that people shared with us – and that we included in our submission. As patient advocates, we go out of our way to present the stories that patients share with us as directly as possible. We did not see those stories that people shared with us reflected in the high-level, numbers-focused summary. It is hard to tell whether CDEC members were told those stories and we must assume they weren't. Did they hear the words of the young woman who felt her raw skin rip every time she removed her bra? Did they understand the agony from people who haven't been able to sleep properly for many years and who told us they felt like the constant itch they felt might only end when they died?

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.		
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

- 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	*Rachael Manion*
Position	*Executive Director*
Date	*30-03-2022*
☒	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. CSPA and Eczéma Québec collaborated to prepare this feedback on the draft recommendation.		
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. CSPA and Eczéma Québec collaborated to prepare this feedback on the draft recommendation. CSPA met with the manufacturer, AbbVie Canada, to share CSPA's thoughts on the draft recommendation but the manufacturer had no opportunity to draft, review or input into this feedback.		

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	☐	☐	☐	☐

A. Patient Group Information	
Name	*Charlie Bouchard*
Position	*Director, Eczéma Québec*
Date	*30-03-2022*
☐	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		
4. 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.

CSPA and Eczéma Québec collaborated to prepare this feedback on the draft recommendation.

5. 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.

CSPA and Eczéma Québec collaborated to prepare this feedback on the draft recommendation. CSPA met with the manufacturer, AbbVie Canada, to share CSPA's thoughts on the draft recommendation but the manufacturer had no opportunity to draft, review or input into this feedback.

C. Previously Disclosed Conflict of Interest		
2. 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

6. 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

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
Brand name (generic)	Rinvoq (Upadacitinib)
Indication(s)	Upadacitinib (Rinvoq) for the treatment of adults and adolescents 12 years and older with moderate to severe atopic dermatitis (AD) who are candidates for systemic therapy.
Organization	Eczema Society of Canada
Contact information	Amanda Cresswell-Melville, Executive Director

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.

The Eczema Society of Canada (ESC) is pleased to see the positive recommendation for upadacitinib and pleased that CADTH recognizes the needs of patients with atopic dermatitis (AD). AD is a complex disease, and it is common for patients living with uncontrolled moderate to severe atopic dermatitis to have complex treatment needs, with a need for effective treatments, as well as a need for equitable access to approved treatments. Equitable access also includes criteria that is fair, safe, reasonable, and appropriate.

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?

ESC thanks CADTH for their careful consideration and review of patient and clinician input during the review process. Safe and effective medications are essential to help patients manage their conditions. For patients living with uncontrolled moderate to severe AD, the itch, pain, and discomfort associated with the condition can have a profoundly negative impact on quality of life. New treatment options like upadacitinib, which patients reported brought rapid improvement of both itch and skin symptoms, bring hope and promise for better treatment outcomes.

"Upadacitinib was extremely helpful in managing my AD. When I think back to where I started, I don't know where I would be if I hadn't tried it."

"Before our involvement in the clinical trial for upadacitinib, there were no good solutions for [my child]. The lack of options impacted their mental health as well as their physical health, and it is a side of eczema that people don't realize, understand, acknowledge, or treat."

[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	Amanda Cresswell-Melville
Position	Executive Director, Eczema Society of Canada
Date	March 24th, 2022
☒	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**
Same as initial submission; no new or updated information since initial submission.	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0685
Brand name (generic)	RINVOQ (upadacitinib)
Indication(s)	For the treatment of adults and adolescents 12 years of age and older with refractory moderate to severe atopic dermatitis who are not adequately controlled with a systemic treatment (e.g., steroid or biologic) or when use of those therapies is inadvisable.
Organization	AbbVie Corporation (Sponsor)
Contact information[a]	[redacted]

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

Overall, AbbVie Corporation (the Sponsor) agrees with the recommendation. There are however certain aspects of the reimbursement conditions that in our opinion limit the eligibility of moderate-to-severe AD patients to RINVOQ:

- [Page 4 – Initiation condition] **Use of both methotrexate (MTX) and cyclosporin (CyA)** as systemic treatments that must be tried before initiating therapy with RINVOQ. This limits flexibility to prescribers in selecting appropriate step therapy as other systemic agents may be used and may be preferred to MTX and CyA, based on patient presentation. As outlined on p. 35 of the clinical review report, a group of experts indicated that "upadacitinib would be used after initial treatments for AD, such as lifestyle measures and topical steroids and after the patient has been diagnosed with moderate to severe AD. In their opinion, upadacitinib would replace systemic therapies that are currently used off-label to treat moderate to severe AD, as well as phototherapy."
- Furthermore, the NEORAL (cyclosporine) product monograph warns that "NEORAL® should only be prescribed (…) by physicians experienced with its use. It also warns that "Psoriasis patients previously treated with PUVA and to a lesser extent, methotrexate, (…) are at an increased risk of developing skin malignancies when taking cyclosporine". Therefore, the sequential use of both MTX and CyA could put patient at risk for serious adverse events and several dermatologists, with little experience with CyA, may decide to keep patients sub-optimally treated with topical corticosteroids and/or oral prednisone if they believe the risk-benefit of using CyA is inacceptable.
    - AbbVie suggests amending the recommendation to: "Patients must have had an adequate trial or be ineligible for each of the following therapies: phototherapy (where available) and at least one oral systemic (including oral corticosteroids). Patients who have had an adequate trial of phototherapy and/or an oral systemic must have documented refractory disease or intolerance".
- [Page 4 – Initiation condition] The recommendation does not distinguish between **adults and adolescents**. Use of immunomodulator agents in adolescents may be contra-indicated. For instance, the NEORAL product monograph indicates that: "NEORAL® is not recommended in children of non-transplant indications other than nephrotic syndrome". In the APO-METHOTREXATE product monograph, a similar caution is provided: "Safety and effectiveness in pediatric patients have not been established, other than in cancer

chemotherapy. Therefore, APO-METHOTREXATE should not be used as a DMARD in pediatric patients".
    - Given the documented risk of MTX and CyA in the pediatric population, AbbVie suggests amending the recommendation to limit the use of immunomodulator agents to adults. In adolescents, the recommendation could be: "Patients must have had an adequate trial or be ineligible for one systemic agent (including oral corticosteroids)".
- [Page 5 – Prescribing] The recommendation limits RINVOQ eligibility to patients under the care of a dermatologist. AbbVie agrees that health care providers with experience with the management of moderate-to-severe atopic dermatitis are better suited in selecting the appropriate treatment option. Specialists, other than dermatologists, are experienced in treating AD. These include allergists, immunologists, and pediatricians. Limiting to dermatologists the treatment of moderate-to-severe AD would results in delayed care and inappropriate use of health care resources as other specialists would be required to refer their patients to a dermatologist before they can be eligible to RINVOQ.
    - Abbvie suggests amending the recommendation to: "The patient must be under the care of a specialist or a pediatrician with experience in the management of moderate to severe atopic dermatitis".

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	☐

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.

- [Page 4 – Initiation condition] The definition of an adequate trial for methotrexate and cyclosporine, particularly the duration of this trial, provide little flexibility to the health care provider in selecting the appropriate treatment sequence in patients showing no response to the systemic therapy shortly after treatment initiation. This would unnecessarily delay the achievement of proper treatment outcomes and leave patients suffering unnecessarily.
    - Abbvie suggests amending the recommendation to:
    - "
      6. For methotrexate: in atopic dermatitis an adequate trial of methotrexate would be 10 to 20 mg per week for 12 weeks unless no improvement is observed within the first 4 weeks.
      7. For cyclosporine: in atopic dermatitis an adequate trial of cyclosporine would be 2.5 to 5 mg/kg/day for 12 weeks unless no improvement is observed within the first 4 weeks.
      "

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