CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

upadacitinib (Rinvoq)

(AbbVie Corporation)

Indication: ankylosing spondylitis

April 27, 2023

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0759-000
Brand name (generic)	Rinvoq (upadacitinib)
Indication(s)	For the treatment of adults with active ankylosing spondylitis who have had an inadequate response to a biologic DMARD or when use of those therapies is inadvisable.
Organization	
Contact information[a]	Name: Dr. Sherry Rohekar, rheumatologist

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

I disagree with the following statement in the committee's recommendations:

"If treatment with an TNF or IL-17i does not result in adequate efficacy within 3 months or if their use is not advisable, a JAK inhibitor should be an option."

In fact, the above statement directly contradicts sentence immediately preceding it, which states:

"Clinical expert believes the clinician should be allowed to decide when a JAK might be most appropriate."

Support for upadacitanib's clinical efficacy in axSpA may be found in the SELECT AXIS-1 and SELECT AXIS-2 trials (van der Heijde D. *et al*., 2022), double-blind, placebo-controlled trials of upadacitanib 15 mg od vs. placebo in patients with radiograpic axSpA who were biologic-naive and biologic inadequate responders, respectively.

As I am making an argument that upadacitanib should be used in patients with radiographic axSpA who are biologic naïve, I will focus on data from SELECT AXIS-1.

In SELECT AXIS-1 (bDMARD naive), significantly more patients treated with upadacitinib met ASAS40, ASDAS, and MRI spine endpoints than those treated with placebo. 52% of upadacitanib treated patients acheived an ASAS40 response by week 14 vs. 26%% of placebo, with a rapid differentiation between groups by week 2, and maintained through 2 years. Sustained efficacy was also shown for other clinically relevant composite endpoints (ASDAS LDA, ASAS PR, ASDAS ID) (van der Heijde D. *et al*., 2022). Back pain and physical function were also improved in the upadacitinib group, as was pain (van der Heijde D. *et al*., 2022, McInnes IB *et. al,* 2022).

Support that upadacitanib treats the underlying disease process may be found in evidence that it prevents progression of inflammatory radiographic spinal changes in axSpA. Radiographic changes are completely objective and do not rely on patient report. In SELECT AXIS-1 (van der Heijde D. *et al*., 2022), biologic disease modifying anti-rheumatic drug (bDMARD) naïve patients with axSpA were treated with upadacitinib 15 mg daily for 104 weeks (with a 14-week placebo-control arm that was later switched to active treatment). In this study, MRI spine and SI joint scores decreased from baseline to week 14 and 104 in the upadacitinib groups, as did modified Stoke Ankylosing Spondylitis

Spine Scores (mSASSS). As such, a strong argument may be made that upadacitinib addresses the underlying disease process in axSpA rather than merely providing symptomatic treatment.		
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	☒
Consideration should also be given to the unique nature of upadacitinib in that it has an oral route of administration, rather other advanced therapeutics for radiographic axSpA that are given as injections or intravenous infusions. Many patients with axSpA are young and are busy at school, work, or travel. The once-daily oral administration of upadacitinib would be ideal for this patient population.		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒
The draft recommendations contradict themselves by stating that “the clinician should be allowed to decide when a JAK might be most appropriate”, but then restricting the use of upadacitinib to second line, after the failure of TNFi or IL-17i. It is unclear why the clinician’s clinical judgement as to when JAKi should be used in an individual patient cannot be relied upon.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
More detail is required as to why upadacitinib is placed as second-line therapy after TNFi and IL-17i.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

[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 clincian 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	*Sherry Rohekar*
Position	*Associate Professor, Western University*
Date	*22-04-2023*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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	☐	☒	☐	☐
BioJAMP	☐	☐	☐	☐
Celltrion	☒	☐	☐	☐
Eli-Lilly	☐	☐	☒	☐
Fresenius Kabi	☐	☒	☐	☐
Janssen	☐	☒	☐	☐
Merck	☐	☒	☐	☐
Novartis	☐	☐	☒	☐
Organon	☒	☐	☐	☐
Roche	☐	☒	☐	☐
Sandoz	☐	☒	☐	☐
UCB	☐	☐	☒	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*

Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 4

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 5

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0759 Rinvoq AS
Brand name (generic)	Rinvoq
Indication(s)	Ankylosing Spondylitis
Organization	
Contact information[a]	Name: Dr. Robert Inman

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.		

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	☒

Dear Panel:

I would add a strong endorsement and a word of encouragement for approval of upadacitinib for the treatment of ankylosing spondylitis.

There is currently an unmet need for treatment of AS in general, with current biologics (TNFi and IL-17i) achieving sustained low disease activity in small percentage of patients. The studies with upadacitinib for patients with prior biologic inadequate response found an excellent response rate regardless if whether the prior biologic was a TNFi or an IL-17i, or if >2 biologics had been tried.

In addition the efficacy of upadacitinib in inflammatory bowel disease is a very supportive piece of evidence since 12% of AS patients have IBD, and up to 60% of AS patients have subclinical bowel inflammation. Having an option which effectively treats both gut and joint inflammation is compelling.

In addition the young patient population (younger say than RA) generally find an oral option far more acceptable than an injection, which is required for the TNFi and IL-17i agents.

The excellent efficacy (with ASAS 40 responses equal to or greater than TNFi or IL-17i) and excellent safety profile (particularly in this younger population) make upadacitinib an extremely valuable addition to the treatment options in AS.

Best regards,

R Inman, MD

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

Appendix 1. Conflict of Interest Declarations for Patient Groups

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A. Patient Group Information	
Name	*Please state full name* ***Robert D Inman***
Position	*Please state currently held position* ***Professor, University of Toronto***
Date	*Please add the date form was completed (DD-MM-YYYY)* ***09-05-2023***
☒	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**
Abbvie	☐	☒	☐	☐
Novartis	☐	☒	☐	☐
Janssen	☐	☒	☐	☐

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  - 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	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0759
Name of the drug and Indication(s)	Upadacitinib (Rinvoq) for ankylosing spondylitis
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.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
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.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0759-000
Brand name (generic)	Upadacitinib (Rinvoq)
Indication(s)	Ankylosing spondylitis
Organization	Arthritis Society Canada, Canadian Arthritis Patient Alliance, Canadian Spondylitis Association, CreakyJoints Canada
Contact information[a]	Margretha Gonsalvez

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.)

We are pleased with the recommendation to reimburse upadacitinib (Rinvoq) for people with ankylosing spondylitis (AS). People with AS have limited treatment options and some will benefit tremendously from the committee's recommendation. However, the limited scope of the recommendation may present access issues for those who respond well to Rinvoq. We also believe that Rinvoq should be considered as a first-line treatment option. We think it is important to take into consideration patient values and preferences - some patients may prefer oral medications over injectables (subcutaneous treatment). Taking patient preference into account may also help with adherence to treatment. Moreover, treatment for conditions such as AS is not sequential, and studies have shown that failure first/step therapy approaches can be harmful to patients and can greatly worsen health outcomes. See here for an example from the United States.

We ask that information be added about simplifying medication renewals in order to reduce the impact on people with AS who are often over-burdened with managing their health and health care.

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?)

We appreciate that CADTH and CDEC have recognized the heterogeneity of the disease and the need for multiple treatment options given that treatment responses can vary significantly among patients. Going forward, we recommend that patient organizations and people with AS be actively engaged with CADTH in developing and implementing real-world evidence in support of ongoing reviews of upadacitinib (Rinvoq) and other AS medications and treatments.

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.

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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*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	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	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0759
Brand name (generic)	Rinvoq (upadacitinib)
Indication(s)	For the treatment of adults with active ankylosing spondylitis who have had an inadequate response to a biologic DMARD or when use of those therapies is inadvisable. Upadacitinib may be used as monotherapy or in combination with nonsteroidal anti-inflammatory drugs (NSAIDs).
Organization	AbbVie Corporation
Contact information[a]	[redacted]

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

AbbVie agrees with the recommendation to reimburse RINVOQ (upadacitinib) for the treatment of adults with active ankylosing spondylitis (AS) who have had an inadequate response to a biologic DMARD or when use of those therapies is inadvisable.

However, AbbVie noted inconsistencies in the definition of inadvisable throughout the recommendation. In the Table 1, the reimbursement condition (initiation and renewal) *[CADTH draft recommendation p. 4 Table 1 "… are intolerant, or who have contraindications to other bDMARDs."]* and the implementation guidance (renewal) *[p. 4 Table 1 "Upadacitinib should not be considered a first-line treatment option."]* are misaligned with the stakeholder feedback, the CADTH Clinical expert recommendation, the CADTH Clinical expert response to the drug program questions and the approved Health Canada indication.

Stakeholder feedback mentions the need for oral options in rural settings.

The Canadian Rheumatology Association clinical input mentions that *"Since upadacitinib is an orally administered advanced therapeutic, it would be a reasonable treatment option for any of our axSpA patients.* ***It will be particularly useful for our large rural and remote population, who have difficulty coming to an infusion center or getting deliveries of injectable biologic medications from specialty pharmacies. Oral administration is also great for those who travel frequently and do not want to carry ice packs and the other paraphernalia needed with injectable biologics****. Many patients also have phobias of needles, even in an auto-injector format, so oral administration is very helpful for this population". [Clinical Review Report Appendix 6 Question 5.5 p.164].* The Canadian Rheumatology Association clinical input mentions the need for upadacitinib in patients in patients living in rural and remote areas, the CDEC reimbursement conditions as well as the implementation guidance does not consider upadacitinib use in this patient population.

CADTH clinical expert recommended patient preference should be considered.

Additionally, the clinical expert consulted by CADTH mentions *"The drug under review would provide further options to treat patients either due to contraindications to TNF/IL-17 inhibitors, previous failures to these drugs,* ***convenience to patients giving them an oral option,*** *and efficacy in patients with both IBD and axSpA." [Clinical Review Report p.28 paragraph 4]. Patients who also have active IBD,* ***prefer an oral option****, or have failed/have a contraindication to a TNF/IL-17 inhibitor may also benefit. [Clinical Review Report p.28 paragraph 5].* Patient convenience is currently not considered with the current reimbursement recommendation.

Inconsistency between the reimbursement conditions and the response to questions from Drug Programs provided from the CADTH clinical expert.

Finally, the drug program asked CADTH "is it possible to define for which patients bDMARDs are inadvisable?" [*CADTH draft recommendation p. 10 Table 2] the response was the following:*
"CDEC heard from the clinical expert that patients must be comfortable with therapy and that the absolute serious infection risk is quite small with bDMARDs; however, a patient must be comfortable with that risk.
Circumstances where one agent would be preferrable might include:

- *Pregnancy/lactation: TNFi*
- *Active malignancy: IL-17i*
- *Active IBD: TNFi or JAKi*
- *Previous CVD: TNFi or IL-17i*
- *CHF: IL-17i*
- *Severe psoriasis: IL-17i*
- *Paradoxical psoriasis: IL-17i or JAKi*
- *Recurrent/severe uveitis: TNFi*
- ***Preference for oral option: JAKi***
- *Personal/family history of multiple sclerosis: IL-17i and possibly JAKi"*

Once more, JAKi were recommended if a patient prefers oral therapies.

We recommend that the committee consider stakeholder feedback, the CADTH Clinical expert recommendation, and the CADTH Clinical expert response to the drug program questions, and therefore allow the use of upadacitinib in patients where a bDMARD is inadvisable (e.g., rural setting, patient preference, oral option).

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	☐
Please see response to Question #1		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
As mentioned in our response to Question 1, on page 4 table 1 CDEC recommended "*Upadacitinib should not be considered a first-line treatment option." However, if a bDMARD is inadvisable Upadacitinib can be considered as a first-line treatment option.*		
	Yes	☒

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

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