CADTH

CADTH REIMBURSEMENT REVIEW

# Stakeholder Feedback on Draft Recommendation

**upadacitinib (Rinvoq)**

(AbbVie Corporation)

**Indication:** For the treatment of adult patients with moderately to severely active Crohn's disease who have demonstrated prior treatment failure, i.e., an inadequate response to, loss of response to, or intolerance to at least one of conventional and/or biologic therapy.

**November 30, 2023**

CADTH

# CADTH Reimbursement Review
# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | SR0775-000 |
| Brand name (generic) | RINVOQ (upadacitinib) |
| Indication(s) | Crohn's disease |
| Organization | The Canadian IBD Specialist Group |
| Contact information[a] | Name: Dr. Mark MacMillan |

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

The Canadian Inflammatory Bowel Disease (IBD) Specialist Group acknowledges the positive recommendation provided by the Canadian Agency for Drugs and Technologies in Health (CADTH) for the reimbursement of upadacitinib for the treatment of adults with moderately to severely active Crohn's disease (CD). Below are our recommendations and feedback:

Table 1, Reimbursement Condition 1 (page 4):

- We believe that the reimbursement condition does not consider the opinion of the clinical expert on 5-ASA therapy. "In particular, the current requirements for prior drug failures in prescribing advanced therapies includes 5-aminosalicylates (5-ASA), which is considered by the clinical expert to be out-of-date due to its known lack of efficacy in this population." (Input from the clinical expert consulted by CADTH, last paragraph page 9).
- We recommend removing "who have an inadequate response, a loss of response or intolerance to conventional or biologic therapies" from the reimbursement condition 1 based on our clinical experience, the opinion of the clinical expert, and the needs of our patients with CD.

Table 1, Reimbursement Condition 2 (page 4):

- The recommendation acknowledges the existence of data supporting the extended induction of upadacitinib in patients who do not achieve clinical response in the first 12-weeks of treatment. However, the Canadian Drug Expert Committee (CDEC) concludes that the evidence is insufficient without further explanation (Discussion points, 3rd bullet page 5). We suggest that extended induction be allowed as it would be the best approach in clinical practice.
- We recommend that the reimbursement condition 2 state: "The patient must have achieved clinical response within 24 weeks after 12 weeks of induction therapy" allowing for patients to continue treatment for an additional 12 weeks at 30 mg if clinical response is not achieved by the end of the induction period.

Background (page 6):

- We believe that emphasis should be placed on highlighting the distinctiveness of upadacitinib compared to biologic therapies. It is the first oral therapeutic for the treatment of CD which obviates the need for an infusion network. In addition, there is no immunogenicity with upadacitinib, which sets it apart from advanced biologic treatments.

Input from the Clinical Expert Consulted by CADTH (page 8):

- "The expert described that combinations would typically include a low-risk, safe agent such as an anti-integrin with other more systemically active agents" - We recommend replacing "safe agent" by "an agent with a more favourable safety profile".
- "Although there are no clear "stages" of CD, objective measures such as endoscopic activity and the requirement or dependence on corticosteroids are important while are not reliable and less predictive of disease course- The Montreal classification classifies disease behaviour as B1: inflammatory, B2: stricturing, B3: penetrating. These are associated with the progression to adverse outcomes (e.g., disease flare, hospitalisation, surgery). We recommend removing "Although there are no clear "stages" of CD".

Table 2 (page 11):

- "Combinations would typically include a low-risk, safe agent such as an anti-integrin with other more systemically active agents" - We recommend replacing "a low risk, safe agent" with "a low-risk agent with a more favourable safety profile."

Clinical Evidence, paragraph 1 (page 12)

- "Irritable Bowel Disease Questionnaire [IBDQ]"- should be "Inflammatory Bowel Disease Questionnaire [IBDQ]".

| **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 recommendation demonstrates that the committee has considered the stakeholder input that was provided to CADTH by the Canadian IBD Specialist Group. | | |

| **Clarity of the draft recommendation** | | |
|---|---|---|
| **3. Are the reasons for the recommendation clearly stated?** | Yes | ☒ |
| | No | ☐ |
| The reasons for the recommendation are clearly stated throughout. | | |
| **4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?** | Yes | ☒ |
| | No | ☐ |
| The implementation issues are clearly articulated and adequately addressed in the recommendation. | | |
| **5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?** | Yes | ☒ |
| | No | ☐ |
| The reimbursement conditions are clearly stated and the rational for the conditions are provided in this recommendation. | | |

[a] CADTH may contact th s person f comments requ re c ar f cat on.

## Appendix 2. Conflict of Interest Declarations for Clinician Groups

| A. Assistance with Providing the Feedback | | |
|---|---|---|
| **1. Did you receive help from outside your clinician group to complete this submission?** | No | ☐ |
| | Yes | ☒ |
| Kataka Medical Communication helped us fill out the feedback form | | |
| **2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?** | No | ☒ |
| | Yes | ☐ |

| 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. Mark MacMillan
- Dr. Charles N. Bernstein
- Dr. Mark Borgaonkar
- Dr. Brian Bressler
- Dr. John Igoe
- Dr. Peter L Lakatos
- Dr. Christopher Ma
- Dr. Jeffrey McCurdy
- Dr. Neeraj Narula
- Dr. Remo Panaccione
- Dr. A. Hillary Steinhart
- Dr. Michael Stewart

### C. New or Updated Conflict of Interest Declarations

| New or Updated Declaration for Clinician 1 | |
|---|---|
| **Name** | *Vipul Jairath* |
| **Position** | *Professor of Medicine* |
| **Date** | *29-11-2023* |
| ☒ | **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* | ☐ | ☐ | ☒ | ☐ |
| *Alimentiv Inc* | ☐ | ☐ | ☐ | ☒ |
| *Altrubio* | ☐ | ☒ | ☐ | ☐ |
| *Amgen* | ☒ | ☐ | ☐ | ☐ |

| | | | | |
|---|---|---|---|---|
| *Arena* | ☒ | ☐ | ☐ | ☐ |
| *Asieris* | ☒ | ☐ | ☐ | ☐ |
| *Astra Zeneca* | ☐ | ☐ | ☒ | ☐ |
| *BMS* | ☐ | ☐ | ☒ | ☐ |
| *Celltrion* | ☒ | ☐ | ☐ | ☐ |
| *Eli Lilly* | ☒ | ☐ | ☒ | ☐ |
| *Endpoint Health* | ☐ | ☒ | ☐ | ☐ |
| *Enthera* | ☒ | ☐ | ☐ | ☐ |
| *Fresenius Kabi* | ☒ | ☐ | ☐ | ☐ |
| *Galapagos* | ☐ | ☒ | ☐ | ☐ |
| *GSK* | ☒ | ☐ | ☐ | ☐ |
| *Genentech* | ☒ | ☐ | ☐ | ☐ |
| *Gilead* | ☐ | ☒ | ☐ | ☐ |
| *Janssen* | ☐ | ☐ | ☒ | ☐ |
| *MRM Health* | ☒ | ☐ | ☐ | ☐ |
| *Mylan* | ☒ | ☐ | ☐ | ☐ |
| *Pandion* | ☒ | ☐ | ☐ | ☐ |
| *Pendopharm* | ☐ | ☒ | ☐ | ☐ |
| *Pfizer* | ☐ | ☐ | ☒ | ☐ |
| *Protagonist Therapeutics* | ☒ | ☐ | ☐ | ☐ |
| *Prometheus Biosciences* | ☐ | ☒ | ☐ | ☐ |
| *Reistone Biopharma* | ☐ | ☒ | ☐ | ☐ |
| *Roche* | ☐ | ☒ | ☐ | ☐ |
| *Roivant* | ☐ | ☒ | ☐ | ☐ |
| *Sandoz* | ☒ | ☐ | ☐ | ☐ |
| *Sorriso* | ☒ | ☐ | ☐ | ☐ |
| *Takeda* | ☐ | ☐ | ☒ | ☐ |
| *Teva* | ☒ | ☐ | ☐ | ☐ |
| *Ventyx Biosciences* | ☐ | ☒ | ☐ | ☐ |
| *Vividion* | ☒ | ☐ | ☐ | ☐ |

| New or Updated Declaration for Clinician 2 | |
|---|---|
| **Name** | *Yvette Leung* |
| **Position** | *Gastroenterologist Staff, St Paul's Hospital* |
| **Date** | *29-11-2023* |
| ☒ | **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* | ☐ | ☐ | ☒ | ☐ |
| *Celltrion* | ☒ | ☐ | ☐ | ☐ |
| *Eli Lilly* | ☐ | ☐ | ☒ | ☐ |
| *Janssen* | ☐ | ☐ | ☒ | ☐ |
| *Pfizer* | ☐ | ☐ | ☒ | ☐ |
| *Sandoz* | ☒ | ☐ | ☐ | ☐ |
| *Takeda* | ☐ | ☐ | ☒ | ☐ |

| New or Updated Declaration for Clinician 3 | |
|---|---|
| **Name** | *John Marshall* |
| **Position** | *Professor of Medicine* |
| **Date** | *27-11-2023* |
| ☒ | **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* | ☐ | ☒ | ☐ | ☐ |
| *Bausch Health* | ☐ | ☒ | ☐ | ☐ |
| *Bristol Myers Squibb* | ☐ | ☐ | ☒ | ☐ |
| *Celltrion* | ☐ | ☒ | ☐ | ☐ |
| *Ferring* | ☐ | ☒ | ☐ | ☐ |
| *Fresenius Kabi* | ☒ | ☐ | ☐ | ☐ |

| | | | | |
|---|---|---|---|---|
| *Janssen* | ☐ | ☐ | ☒ | ☐ |
| *Lilly* | ☐ | ☐ | ☒ | ☐ |
| *Organon* | ☐ | ☒ | ☐ | ☐ |
| *Pfizer* | ☐ | ☐ | ☒ | ☐ |
| *Pharmascience* | ☒ | ☐ | ☐ | ☐ |
| *Roche* | ☒ | ☐ | ☐ | ☐ |
| *Sandoz* | ☐ | ☒ | ☐ | ☐ |
| *Takeda* | ☐ | ☐ | ☒ | ☐ |
| *Viatris* | ☒ | ☐ | ☐ | ☐ |

| **New or Updated Declaration for Clinician 4** | |
|---|---|
| **Name** | *Cynthia Seow* |
| **Position** | *Professor, Division of Gastroenterology and Hepatology, Department of Medicine, University of Calgary, Alberta, Canada* |
| **Date** | *27-11-2023* |
| ☒ | **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** |
| *Janssen* | ☐ | ☒ | ☐ | ☐ |
| *AbbVie* | ☐ | ☒ | ☐ | ☐ |
| *Takeda* | ☐ | ☒ | ☐ | ☐ |
| *Pfizer* | ☐ | ☒ | ☐ | ☐ |
| *Fresenius Kabi* | ☒ | ☐ | ☐ | ☐ |
| *Bristol Myers Squibb* | ☒ | ☐ | ☐ | ☐ |
| *Pharmascience* | ☒ | ☐ | ☐ | ☐ |

| **New or Updated Declaration for Clinician 5** | |
|---|---|
| **Name** | *Dr. Chadwick Williams* |
| **Position** | *Assistant Professor of Medicine, Dalhousie University* |
| **Date** | *29-11-2023* |
| ☒ | **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* | ☐ | ☐ | ☒ | ☐ |
| *Janssen* | ☐ | ☐ | ☒ | ☐ |
| *Pfizer* | ☐ | ☐ | ☒ | ☐ |
| *Eli Lilly* | ☐ | ☐ | ☒ | ☐ |
| *Takeda* | ☐ | ☐ | ☒ | ☐ |

# CADTH Reimbursement Review

# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | SR0775 |
| Name of the drug and Indication(s) | Upadacitinib (Rinvoq)<br>For the treatment of adult patients with moderately to severely active Crohn's disease who have demonstrated prior treatment failure, i.e., an inadequate response to, loss of response to, or intolerance to at least one of conventional and/or biologic therapy. |
| Organization Providing Feedback | FWG |

| **1. Recommendation revisions**<br>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 | ☐ |
| | **No requested revisions** | X☐ |

| **2. Change in recommendation category or conditions**<br>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**<br>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.<br>2. |
| **2. Please specify other implementation questions or issues that should be addressed by CADTH** |
| 1.<br>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

# CADTH Reimbursement Review
# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | SR0775-000-000 |
| Brand name (generic) | Rinvoq (upadacitinib) |
| Indication(s) | Crohn's disease |
| Organization | Crohn's and Colitis Canada |
| Contact information[a] | Name:Patrick Tohill |

| 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.

Reimbursement condition #1 should be further clarified by adding the words "one or more" before the phrase "conventional or biologic therapies". Without this clarification, some provinces may understand condition #1 as meaning that patients are required to "have had an inadequate response, a loss of response, or intolerance to" *all* conventional therapies.

In our stakeholder input submission, we sought to make clear that most Crohn's and colitis patients would like to avoid steroid use if possible. In the unmet needs survey we cited, "at least 7 in 10 respondents scored 7 and above for fewer medications and 9 in 10 for minimizing chronic steroid use (on a sliding scale of 0 (not important at all) to 10 (extremely important), with an additional option of "I don't know")."

As detailed in our submission, one of the three patients we interviewed who had used the study drug had been prescribed "unsustainable" levels of corticosteroids in a failed effort to control symptoms of Crohn's disease (CD). His experience, sadly, is not unique. We hear this story time and time again. In addition to the frequently debilitating symptoms of CD, patients like the one whose story we related in our submission, must also contend with adverse effects from corticosteroid usage.

Further, as noted by the GI Society in the recommendation report: "First line treatments include 5-ASA and corticosteroids to reduce inflammation in moderate to severe cases of CD. When one medication fails, patients must try another to keep a normal routine. According to the patient input, these treatments are inconvenient therapies that make it difficult for patients to keep a normal routine."

In other words, upadacitinib ideally would be available as a first line treatment option, consistent with the principle that physicians be able to prescribe the right medication for the right patient at the right time. The clinical expert cited in the recommendation report seemingly agrees, for he notes that "the first-prescribed therapy has the best chance for improvement and healing due to the aforementioned pattern of lower likelihood of robust response with subsequent advanced therapies. Selecting the most optimal therapy from the start is a challenge and is based on disease phenotype, disease severity, and the risks and expected onset of action of each available therapy; for instance, particularly severe disease would warrant the selection of a therapy with rapid onset, high efficacy, and steroid-sparing effects (e.g., anti-TNFs or anti IL 23 and 12/23)."

This is made even clearer a few paragraphs later: “The clinical expert indicated that upadacitinib would be used as a first agent for patients receiving advanced therapies for CD, and that there is no mechanistic, efficacy, or sequencing-based argument to require the failure of other advanced agents before initiation of upadacitinib”. Indeed, all stakeholders attested to upadacitinib’s effectiveness in treating the symptoms of CD. As noted in the recommendation report, all three patients we interviewed for our submission as well as those interviewed by the GI Society “had experience with Upadacitinib and reported near-immediate improvements in their health, alleviation of the disease symptoms, and symptoms of their CD with no side-effects or few mild side-effects such as weight gain.” Of the three patients we interviewed, two had no prior experience with conventional or biologic therapy.

The recommendation also acknowledges, but in our opinion downplays upadacitinib’s value as the first oral therapy available to treat CD: ” Patients noted the convenience of pill-based administration and no need to refrigerate the medication nor to attend a clinic for infusions.” In our patient input submission the first of the three patients we interviewed cited upadacitinib’s contribution to her “work life balance” as a result of not having “to schedule your life around IV infusions” as well as other benefits such as not being exposed to nosocomial infections in a clinic or hospital setting. Our second interviewee cited the benefits of not having to take a day off work for infusions, not having to arrange for a ride home, etc. The third spoke to the benefit of not having to refrigerate the medication for travel and visiting family.

The Canadian IBD Specialist Group, in their submission, also speak to upadacitinib’s value as an oral medication, pointing out “that upadacitinib has a new mechanism of action, and it is the first oral therapy for CD that has ever been evaluated to meet the treatment goals.”

Additionally, we would also like to note that the recommendation report is using old estimates for the number of Canadians living with Crohn’s disease. On page 6, in the section headed “Background” the report states that “The predicted prevalence of CD in 2018 was 368 per 100,000 population, which translates to approximately 135,000 people in Canada living with CD.” These numbers are taken from our report *2018 Impact of Inflammatory Bowel Disease in Canada* and as such are out-of-date. Today, in 2023, per our report *2023 Impact of Inflammatory Bowel Disease in Canada* the prevalence rate is estimated at 410 per 100,000 for Crohn’s disease. The current incidence rate for Crohn’s disease is 12.2 per 100,000 for Crohn’s disease.

**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?

While the recommendation report fairly summarized our input on disease experience, as stated above, our input on patient experiences with and concerns around systemic steroid use appear to have been for the most part overlooked as was feedback from others such as the GI Society, the clinician group and the clinical expert that speak to upadacitinib as a first line treatment option. We also feel that while the report acknowledges the convenience of the study drug’s oral route of administration, noted by patients and stakeholders alike, that the value of this attribute is scarcely given the attention it merits.

| 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.<br><br>Declined to answer this question. | | |
| **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.<br><br>Declined to answer this question. | | |

[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** | *Patrick Tohill* |
| **Position** | *Director, Advocacy and Government Affairs* |
| **Date** | *21-11-2023* |
| ☒ | 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.<br><br>Initial analysis of data in the unmet needs survey cited in our feedback submission was conducted by Leger. | | |

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

**D. New or Updated Conflict of Interest Declaration**

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

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

CADTH

# CADTH Reimbursement Review
# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | SR0775-000-000 |
| Brand name (generic) | Rinvoq® (upadacitinib) |
| Indication(s) | Crohn's disease |
| Organization | Gastrointestinal Society |
| Contact information[a] | Gail Attara |

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

We are grateful that the recommendation provides flexibilities for patients and physicians given the realities of our strained healthcare system. We agree with the recommendations allowing physicians experienced in the diagnosis and management of Crohn's disease to prescribe upadacitinib. It also did not require endoscopy within 12 weeks of treatment initiation and left the determination of clinical response up to the treating physician.

As we've mentioned in past submissions and feedback to new treatments for inflammatory bowel disease (primarily Crohn's disease and ulcerative colitis), patients with moderate to severe disease should not have to trial conventional therapies that are only effective for a short term (i.e., immunosuppressants, corticosteroids, 5-ASAs) before they can access advanced treatments such as biologics and JAK inhibitors. Trialing these therapies can take a toll on patients and the clinical expert highlighted that the "current requirements for prior drug failures in prescribing advanced therapies… [is] out-of-date due to its known lack of efficacy in this population." As the clinical expert mentioned, and what we have heard from communities as well, is that this results in short prescriptions of 5-ASAs to meet the requirements, which can contribute to avoidable healthcare spending.

We know that some provinces have made progress toward this approach, and we appreciate that the CADTH recommendations have left determination of eligibility up to the public drug plans. However, we encourage CADTH to take on leadership as well by also conducting a review on the emerging trends and technologies in Crohn's disease, similar to the horizon scan for ulcerative colitis that CADTH released in April 2023.[1]

Thank you for helping individuals living with Crohn's disease have access to new and advanced treatment options, such as Rinvoq®!

| 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 recommendation did not capture the significance of upadacitinib as the first oral, advanced therapy for Crohn's disease. It also did not reflect patients' preferences for a medicine that suited their needs and lifestyle. For patients, an oral medication is not just about "convenience." Having the option to take an oral drug instead of one administered by infusion or subcutaneous injection can have beneficial effects to their life, including self-perception, employment, and time.

The patients we interviewed firmly expressed their preference for a medication that was easy to administer. One was adamant in not trying corticosteroids, due to side effects and lack of efficacy in

long-term use as a stand-alone therapy, and biologics due to the burdens of going in for infusions, especially during the COVID-19 pandemic. Patients also emphasized the financial impacts of lost wages if they had to go in for infusions. They already need to take time off every year for colonoscopies. One patient had just started their career and had their first child, so losing wages from taking time off was not a feasible option.

Regarding self-perception, one patient said (and as mentioned in our submission), "Oral medication makes travelling easy. I don't have to schedule my life around I.V. infusions. It's very discreet. Nobody has to know you're taking it." Clearly, there is still stigma surrounding Crohn's disease.

Oral medicines can also lead to healthcare resource savings since it does not require patients to go in for infusions or require training and assistance for administering subcutaneous injections. We hope that CADTH considers these cost-savings when conducting a cost-effectiveness review with comparators.

| 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 | ☐ |
| **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 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** | *Gail Attara* |
| **Position** | *President and Chief Executive Officer* |
| **Date** | *29/11/2023* |
| ☒ | 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** |
| *Add company name* | ☐ | ☐ | ☐ | ☐ |
| *Add company name* | ☐ | ☐ | ☐ | ☐ |
| *Add or remove rows as required* | ☐ | ☐ | ☐ | ☐ |

[1] Canadian Agency for Drugs and Technologies in Health. An Overview of Emerging Trends and Technologies in Ulcerative Colitis. 2023. Available at: https://www.cadth.ca/overview-emerging-trends-and-technologies-ulcerative-colitis.

CADTH

# CADTH Reimbursement Review
# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | SR0775 |
| Brand name (generic) | RINVOQ (upadacitinib) |
| Indication(s) | For the treatment of adult patients with moderately to severely active Crohn's disease (CD) who have demonstrated prior treatment failure, i.e., an inadequate response to, loss of response to, or intolerance to at least one of conventional and/or biologic therapy. |
| 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 adult patients with moderately to severely active Crohn's disease (CD) who have demonstrated prior treatment failure, i.e., an inadequate response to, loss of response to, or intolerance to at least one of conventional, and/or biologic therapy.

| 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 | ☒ |

While AbbVie agrees with the recommendation to reimburse RINVOQ (upadacitinib) for CD, we would ask the CDEC to kindly consider the following proposed changes:

**1. There remains a considerable probability that upadacitinib may be more efficacious than other comparative treatments.**
On page 5 of the draft recommendation, under Discussion Points, it is stated that "CDEC was unable to determine the relative efficacy and safety of upadacitinib compared to biologic therapies in the Canadian setting."

AbbVie respectfully disagrees with CADTH's assertion regarding the assumption of no meaningful difference demonstrated in efficacy or safety outcomes between upadacitinib and other advanced therapies as well as the statements around substantial imprecision, unresolved heterogeneity etc. Indeed, while there is uncertainty due to the lack of direct evidence and the sparse network, we note that all NMAs inherently contain a degree of uncertainty. However, it is important to consider the whole body of evidence available. AbbVie maintains that it is more appropriate to acknowledge the potential improved efficacy of upadacitinib vs. available therapies, rather than stating that conclusions about its comparative efficacy cannot be established. The submitted ITC demonstrated that upadacitinib is an effective therapy with instances of improved efficacy vs. appropriate comparative therapies across key endpoints relevant to the expressed unmet needs of patients and clinicians. Furthermore, the safety profile of upadacitinib, placebo, and other advanced treatments appears generally consistent.

AbbVie is requesting that the following statement be included to reflect upadacitinib's potentially improved efficacy vs. other advanced CD therapies and requests that CADTH acknowledge the stringent endoscopic outcome data for upadacitinib in the context of this limitation for comparators:

"*CDEC was unable to determine the relative efficacy and safety of upadacitinib compared to biologic therapies in the Canadian setting with certainty. While the submitted indirect treatment comparison did face limitations, there is some evidence of probable benefit of upadacitinib vs. appropriate comparator therapies across key endpoints relevant to the expressed unmet needs of patients and clinicians.*"

**2. The value of upadacitinib to the Canadian healthcare system extends beyond delivering high rates of clinical remission and endoscopic improvements alone. Upadacitinib may aid in the resolution of EIMs, support reduced steroid use and offers these benefits as a novel MoA (JAKi) for CD patients and the first oral advanced therapy for moderate-to-severe Crohn's disease.**
AbbVie would like to further highlight benefits of upadacitinib which may have been overlooked. Upadacitinib is the first oral advanced therapy for moderate-to-severe Crohn's disease and provides a new mechanism of action (MoA), as a selective and reversible Janus kinase (JAK) inhibitor. To date, CD patients only have access to anti-TNF, anti-integrin, and IL-12/23 therapies, and with the highly refractory nature of the disease, additional mechanisms of action and routes of administration are needed. Additionally, an oral treatment option may also be of value to Canadians with more limited access to infusion resources or to help reduce the strain on the healthcare system associated with infusion procedures.

Patients with CD also face challenges with corticosteroid use, typically implemented to combat flares associated with suboptimal treatment response to existing therapies. We are hopeful that upadacitinib may be able to aid in the reduced reliance upon corticosteroids for CD patients given the robust steroid-free efficacy demonstrated with upadacitinib, where steroid-free remission was seen as early as induction.

Many patients with IBD suffer from extraintestinal manifestations (EIMs) of disease as well. Up to 40% of patients with IBD will experience EIMs and up to 20% of patients suffer with musculoskeletal EIMs included IBD-related arthritis, peripheral arthritis, axial arthritis, and enthesitis.[1] Upadacitinib is the only IBD treatment indicated for the broad treatment of a number of these rheumatologic conditions, potentially offering significant value to patients suffering with CD and musculoskeletal involvement.

Lastly, AbbVie would like to highlight that the upadacitinib clinical trials incorporated some of the most recently recommended treatment goals, as outlined in the STRIDE-II guidelines, such as the long-term goal of mucosal healing. Importantly, these trials are some of the first to evaluate disease activity by endoscopic measurement in all patients, to prospectively evaluate patient-reported outcomes, and to incorporate both symptomatic clinical remission and endoscopic response as co-primary outcomes in all three phase 3 trials.

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

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

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

References:


1. Rogler, Gerhard et al. "Extraintestinal manifestations of inflammatory bowel disease: Current concepts, treatment, and implications for disease management." Gastroenterology, 161(4), 1118–1132. https://doi.org/10.1053/j.gastro.2021.07.042