

CADTH COMMON DRUG REVIEW

# Patient Input

**Upadacitinib (TBC)**

(AbbVie)

Indication: Arthritis, Rheumatoid

CADTH received patient input from:

**Arthritis Consumer Experts**

**Canadian Arthritis Patient Alliance (CAPA) & The Arthritis Society**

July 22, 2019

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**C/O:** Canadian Agency for Drugs and Technologies in Health (CADTH)

**Re:** Patient Input for upadacitinib for rheumatoid arthritis

**Date of submission:** July 22, 2019

**Section 1 — General Information**

**Name of the drug:** upadacitinib

**Indication of interest:** rheumatoid arthritis

**Name of patient group:** Arthritis Consumer Experts

**Name of the primary contact for this submission:**

[REDACTED]  
[REDACTED]  
[REDACTED]

**Name of author (if different):**

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**Patient group's contact information:**

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**Permission is granted to post this submission:** Yes

**Section 1 – About your Patient Group**

Canada's largest, longest running national arthritis patient organization headquartered in Vancouver, BC, Arthritis Consumer Experts (ACE) provides free, science-based information and education programs in both official languages to people with arthritis. ACE serves people living with all forms of arthritis by helping them take control of their disease and improve their quality of life through education and (em)powerment. Founded and led by people with arthritis, ACE also advocates on arthritis health policy issues, through ACE's

JointHealth™ family of programs and the Arthritis Broadcast Network, directly to consumers/patients, media and government. ACE operates as a non-profit in a fully transparent manner and is guided by a strict set of guiding principles, set out by an advisory board comprised of leading scientists, medical professionals and informed arthritis consumers. Ultimately, we are guided by the needs of our members, who are people living with arthritis, and their caregivers.

Link to website: [www.jointhehealth.org](http://www.jointhehealth.org)

## **Section 2 – Information Gathering**

The information was gathered in Canada on the ACE Survey Monkey platform from June to July 2019, without assistance or funding from an outside source. Input was compiled and made grammatically correct by [REDACTED] full time employees of ACE.

## **Section 3 — Disease Experience**

### **3.1 How does the disease impact the patients' day-to-day life and quality of life?**

Rheumatoid arthritis (RA) has a significant effect on the lives of people living with it and they constantly consider the state of their disease and decide what they can, or more likely, cannot, cope with or achieve, how they can go about their daily lives, and how much help they may need along the way.

- **Patient A:** Living with RA for approximately 30 years. RA limits many activities due to pain and stiffness. They also live with fibromyalgia, myasthenia gravis, and asthma.
- **Patient B:** Living with RA for 24 years. "It is a daily challenge to accept limitations affecting the use of my hands and knees." They also get pain in their other joints. Their quality of life has been improved with treatment and medications.
- **Patient C:** Living with RA for 11 years and is no longer able to work and receives CPP disability. Her husband is retired so he is able to do the shopping, cleaning, and laundry, which she is unable to do. She is in constant pain and always feels "miserable". A lot of time is spent travelling between doctors and health-related appointments. She also has fibromyalgia, myasthenia gravis, and asthma.
- **Patient D:** A caregiver to someone living with RA for 32 years. The person they care for gets inflamed joints and pain and have difficulty walking.
- **Patient E:** Living with RA since 1980. "Severely limits me in day to day life and reduces my quality of life. I need to constantly take meds throughout the day. I work in a low-level professional job, earning less money than I could if I didn't have a chronic illness, because I can't put in the hours. I have had countless hand surgeries making me less dexterous on the keyboard for office work." Any medication that controls inflammation, chronic pain, and stiffness will be helpful. Also lives with rheumatoid arthritis pulmonary fibrosis, chronic neutropenia, drug-induced high blood pressure, and dry eyes.

- **Patient F:** Living with RA for 18 years. “Limited movement, joint pain, muscle weakness, chronic fatigue, depression, limited social life due to inability to complete normal tasks, and require assistance.”

### 3.2 How does the disease impact the caregivers’ day-to-day life and quality of life?

Caregivers of people living with rheumatoid arthritis have indicated that time management is very important to them. When patients are in pain, caregivers have to help with house chores and many other aspects of life at home.

- **Patient A:** Their caregivers feel depressed at times.
- **Patient B:** This patient did not provide an answer to this section.
- **Patient C:** “It’s very hard for caregivers and it is such an unpredictable disease. Sometimes you feel good, sometimes you feel awful, but the caregiver has no way of knowing as RA is a silent disease. The impact of having to take multiple treatments significantly impacts our lives as there are a lot of appointments to organize and attend.”
- **Patient D:** No particular challenges.
- **Patient E:** “Dealing with the mental outlook of the patient with arthritis. Caregivers are often not educated on what they can do to help the patient and often suggest “old wives’ tales” cures. There is challenge in providing mental and physical support for the patient.”
- **Patient F** did not indicate any challenges exist for their caregivers.

### 3.3 Are there any aspects of the illness that are more important to control than others?

- **Patient A:** “Movement.”
- **Patient B:** “Painful joints” are more important to control. An adverse effect they can tolerate is fatigue.
- **Patient C:** “Pain!!! And the systemic effects it has on my body.”
- **Patient D:** “Inflamed joints, pain.”
- **Patient E:** “Inflammation, chronic pain, and stiffness.”
- **Patient F:** “Immune system response to turn off RA.”

## Section 4 – Experiences with Currently Available Treatments

**How well are patients managing their disease/condition with currently available treatments?**

- **Patient A:** Takes Humira injections. They are afraid of needles and have to get a nurse to do the Humira injections in the back of their arms. The medication is relatively good at controlling their symptoms and they do not experience any side effects from it. They admit that treatments are costly. Besides medication therapy, they also participate in aqua therapy.

- **Patient B:** Taking Humira and methotrexate and find the treatments helpful in controlling the symptoms of RA. They feel fatigue from their medication treatments. They expect new medication to help alleviate the discomfort in affected joints.
- **Patient C:** “I have to take multiple medications, inject myself weekly, and receive a 4 weekly infusion. A lot of my time is spent going to many doctors and health related appointments.” She is on a biologic, DMARDs, anti-inflammatory, opioids, and steroids. Currently, she is on her 4<sup>th</sup> biologic and finds it is losing efficacy. The injections cause bruising on her hand and “it is very uncomfortable at the clinic.” She adds: “The medication is very expensive, and the drug company limits how much annual co-payment they give me.”
- **Patient D:** Taking Simponi and the medication is effective in controlling her RA. In regards to new medication, they said: “My concerns are US reports of clots. I would be unwilling to switch from Simponi as I have had no clots and it has not been suggested I might get them. I would be unwilling to have the risk of clots as my family has heart attacks and strokes.”
- **Patient E:** Currently taking Rituxan infusions, Celebrex and prednisone and so far, the medications are effective in controlling her RA. She finds it difficult to tolerate the adverse effects of prednisone: “For example, moon face, thin skin, thinning of the bones, and water retention.” Current therapies are costly.
- **Patient F:** Currently taking upadacitinib. Please refer to Section 6 of this input for further information.

In general, the thousands of RA patients that ACE has interacted with over the past 19 years, have told us that having medication options is important to them, like it is for patients with cancer, HIV and other serious chronic diseases and illnesses. As stated in every patient input we have submitted on our members’ and the public’s behalf, patient input respondents consider the “best treatment” is one that causes the fewest adverse effects and puts patients into remission.

### **Section 5 – Improved Outcomes**

- **Patient A:** “For me, an unmet need is home care assistance.”
- **Patient B:** Has no unmet needs.
- **Patient C:** Stresses the need for medications that control pain.
- **Patient D:** Emphasizes that some patients are less controlled.
- **Patient E:** Experiences hardships in receiving current treatment but “I tolerate them because I know that if I don’t, I will be in extreme pain and my arthritis will come back with a vengeance.” Current unmet needs: “More occupational therapy counselling, counselling for coping with having a chronic illness, quicker access to see specialists for surgeries.”
- **Patient F:** The following are unmet needs: Affordable medications; lack of precision in the prescribing of treatments; poor/inadequate insurance.

### **Section 6 – Experience with Drug Under Review**

One of the patients interviewed has experience with taking upadacitinib for rheumatoid arthritis:

- **Patient F** is currently on upadacitinib, which they get via participation in a clinical trial. The medication is effective in treating their RA and is easier to use. They do not get adverse effects from the medication but do have to travel to and from appointments and do extensive tests. Also, the appointments are very long. Expects the medication to give people their “life back, to have freedom to care for themselves and their families, to work, to socialize.” They would also like to achieve remission. Upadacitinib “manages all of my symptoms by limiting inflammation, no pain, no morning stiffness, more energy, better mood, want to complete tasks and do more, able to work.”

Patients who have not tried upadacitinib also provided feedback for this section:

- **Patient A:** The medication should be “easy to get and take – perhaps something taken monthly.” Would like the “ability to do things without having to think twice regarding pain, effort, and energy, and have better health and no depression.”
- **Patient B:** Expects to achieve an improvement in their quality of life, to be independent, and gain relief from discomfort in their affected joints.
- **Patient C:** Expects to be in less pain and inflammation and the “downstream” damage those things do to the body.
- **Patient D:** “Our concern are US reports of clots.” The person living with RA added: “I would be unwilling to switch from Simponi as my family has history of heart attacks and strokes. I have had no clots and it has not been suggested I might get them.”
- **Patient E:** Hopes that new therapy would help control the disease and that the benefits outweigh the costs and possible side effects. It will be ideal if it would help me “provide some independence and normalcy back into my life so I can be more productive and contributing member of society.”

### **Section 7 – Companion Diagnostic Test**

Not applicable to this submission.

### **Section 8 – Biosimilar**

Not applicable to this submission.

### **Section 9 – Anything Else?**

Based on a large body of peer-reviewed evidence, ACE recommends a well-rounded treatment plan for RA that includes education (both disease and self-management), appropriate immunosuppressive medication(s), therapeutic and recreational exercise, appropriate amounts of rest during flares, physical therapy, healthy diet and an overall healthy lifestyle. Paramount among these is the timely initiation of the most suitable medication(s), chosen by the patient in consultation with their rheumatologist. Biologics and targeted small molecule medications are proved to effectively address disease signs and

symptoms – like swelling, pain and fatigue – but also improve mortality and reduce heart disease and other complications of inflammatory arthritis.

In general, we find patients asking the following:

- Is there one or a few advanced therapies that you feel may work the best for me? If yes, why?
- What are the different ways to take the ones you think might work best for me at this point in my disease course?
- What are the most common and the most serious side effects for the advanced therapy you are recommending?
- Do I have to stop what I'm taking now to clear it from my body before starting on the advanced therapy you recommend?
- Can I stop any of the other medications I'm currently taking when I start on the advanced therapy you recommend? If so, when?
- How long do I have to be off one or all my current medications before I can start on the advanced therapy you recommend?
- Can I get pregnant while taking the advance therapy you recommend?
- How quickly do I need to decide?

ACE made minor grammatical corrections to input where needed but in no way altered the meaning or intent of the input.

### **Appendix: Conflict of Interest Declaration**

- 1) Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

This submission was summarized and written solely by the staff of Arthritis Consumer Experts, free from consultation, advice, influence, or financial support from any outside individual, group or company.

- 2) Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No.

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

Arthritis Consumer Experts has not received any grants-in-aid from AbbVie since 2016.

**Company**

**Check Appropriate Dollar Range**

	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Cheryl Koehn

Position: Founder and President

Patient Group: Arthritis Consumer Experts

Date: July 24, 2019

## Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	Upadacitinib for rheumatoid arthritis
Name of the Patient Group	Canadian Arthritis Patient Alliance (CAPA) & The Arthritis Society
Author of the Submission	[REDACTED]
Name of the Primary Contact for This Submission	[REDACTED]
Email	[REDACTED]
Telephone Number	[REDACTED]

### 1. About Your Patient Group

The Canadian Arthritis Patient Alliance (CAPA) is a grass-roots, patient-driven, independent, national education and advocacy organization with members and supporters across Canada. CAPA creates links between Canadians with arthritis to assist them in becoming advocates and to improve their quality of life. CAPA believes the first expert on arthritis is the person who lives with arthritis, and is an organization for patients run by patients. We are a virtual organization with no physical location and communicate with our community primarily through electronic methods, such as our [website](#), quarterly newsletter, e-mail, and social media. CAPA welcomes all Canadians with arthritis, and those who support CAPA's goals, to become members.

The Arthritis Society (AS) has been setting lives in motion for over 70 years. Dedicated to a vision of living in a world where people are free from the devastating affects that arthritis has on the lives of Canadians, the Society is Canada's principal health charity providing education, programs and support to the over 6 million Canadians living with arthritis. Since its founding in 1948, The Society has been the largest non-government funder of arthritis research in Canada, investing more than \$200 million in projects that have led to breakthroughs in the diagnosis, treatment and care of people with arthritis. The Arthritis Society is accredited under Imagine Canada's Standards Program. The website [www.arthritis.ca](http://www.arthritis.ca) provides more detailed information.

### 2. Information Gathering

We developed a survey to hear directly from people living with rheumatoid arthritis (RA) about their experiences with RA and any experiences taking upadacitinib. CAPA and AS collaboratively developed the survey and the design was informed by the lived experiences of the CAPA Board Members who all live with various forms of arthritis. The survey was shared via e-mails and social media (CAPA and AS Facebook and Twitter accounts) through our respective Canadian networks and communities. The survey was open from June 7, 2019 to July 8, 2019.

An AbbVie contact provided us with names and email contact information of the Canadian rheumatologists who had patients enrolled in the upadacitinib clinical trial. CAPA provided a letter to these rheumatologists via email and asked them to pass it on to these clinical trial participants that explained CADTH, the Common Drug Review process, and why their input would be of value. The letter provided a link to the survey as well as contact information for [REDACTED], in case they wanted to be in touch via email or phone. The AbbVie contact also put CAPA in contact with a rheumatology nurse who provided the survey questions to individuals she knew participated in the upadacitinib clinical trial.

Fifty-one online survey responses were received of which no individuals had experience taking upadacitinib, and one set of survey responses was provided directly to CAPA by the rheumatology nurse on behalf of one upadacitinib clinical trial participant. The survey collected demographic data, however not all respondents completed this section. Those who completed demographic data (n=36) represented a range of ages from 8 (survey responses entered by mother on behalf of child) to 77 years old, with about three-quarters of those between 45-75 years old. After the 8-year-old, the next youngest respondent who indicated age was 22 years old. The vast majority of respondents indicated that their RA was moderate in terms of its severity.

### 3. Disease Experience

About 1% of Canadians live with RA, and while both men and women can be diagnosed with RA, it is far more common in women (women are 2-3 times more likely to have RA than men). RA is a chronic autoimmune disease in which the body's immune system attacks and causes inflammation in joints. When uncontrolled, this inflammation results in permanent and irreversible damage to joints that are affected. RA is also a systemic disease meaning that other parts of the body in addition to joints can be affected, including the eyes, lungs, and heart. RA can vary in severity from mild to very severe. A person may experience active periods of disease (commonly known as flares or flare-ups) and times where there is decreased activity or even inactivity (remission). While people who have RA generally live with a number of the same symptoms, how they experience those symptoms and the severity of their RA can be very different from person to person – RA is unique to each person who lives with it. There is currently no cure for RA.

People living with RA who completed the survey made the following comments about the day-to-day effects of their symptoms:

*“The most important to control are Pain [sic], stiffness, swelling, loss of mobility, fatigue. RA affects my every day by limiting what I am able to do, I have to plan out activities so that I only do one or two things a day.”*

*“Morning stiffness makes bathing and dressing very time consuming and dangerous due to increased fall risk. Fatigue makes it difficult to arise [sic] earlier to allow for extra time needed for these activities, a constant vicious circle.”*

*“Stiffness, fatigue and pain.”*

*“Swelling in my feet, hands and knees. I am in constant pain.”*

*“Pain, inflammation and loss of range of motion. Difficulty walking, running, stairs.”*

RA impacts lives in many ways: completing daily tasks that many well individuals take for granted may become difficult or too exhausting to complete; participating in leisure activities can be difficult; caring for or spending time with family members such as children and loved ones, such as spouses / partners also becomes difficult.

*"Fatigue is my biggest concern. It's every day, 365 days a year. By the time 6pm rolls around, I'm exhausted and usually have to take a nap. Evening activities can be difficult.."*

*"It doesn't really effect my work but one [sic] bad days it effects what activities I can do with my kids. Or i [sic] am limited on how much time I can spend doing an activity such as gardening."*

*"Live alone and mornings are so difficult. I have good bra days and bad ones. A good one means I can get a bra on within 15 min. Personal care is hard i.e. putting on deodorant. Getting dishes out of cupboard."*

*"Joint soreness and flare ups, difficulty with activities of daily living."*

*"I struggle to make meals and do fun, physical activities, like kayaking, that I used to enjoy."*

People indicated difficulties in contributing and participating at school or work due to the fatigue, pain, and other symptoms of the disease:

*"I am no longer able to work due to RA. Extreme joint pain, head fog, and just feeling bad many days. If I attempt to work manually I usually pay for it..."*

*"Had to abandon post-graduate work and part-time university employment due to effects of rheumatoid arthritis and side effects of drugs used to treat it."*

*"I do not work I am on CPP Disability."*

*"I cannot work as I used too and it has caused financial stress and a total drain of my resources and savings."*

*"Biologics are incredibly expensive. When I went through a period of unemployment, I had to enroll in pharmacare and pay thousands out of pocket. I'm limited in my job opportunities because of fear of the cost of prescription drugs."*

*"I've had to take a work demotion so I could work from home."*

RA's impacts also extend to others within a person's circle, including caregivers such as spouses / partners and children. Often, these people take on additional chores or tasks such as cooking, cleaning, shopping, etc. to support the person living with RA, roles change as spouses / partners take on more, such as supporting their spouses / partners in getting to and from medical appointments, and RA also affects intimacy.

*“The pain is the worse. It effects dressing myself, walking cooking and intemancy [sic] with my husband. Sex has been one activity I have not been able to do for almost two years the pain stopped me plus my husband found causing me pain a turn off.”*

*“The episodic nature makes planning ahead difficult and uncertain and has an impact on my social life. I cannot entertain my friends at home as I used to as cleaning my house is another very difficult thing to do..”*

*“Fatigue and brain fog affect my work life and joint pain affects my ability to do what enjoy life, i.e. gardening, exercise, house work. I rely greatly on my family to assist me..”*

People living with RA are also at risk for other diseases or conditions, including eye, lung, and heart issues as well as depression and mental health issues. A flare is when someone’s RA is particularly active, and these flares are experienced differently by people depending on their RA - for some people, flares can be incapacitating. Flares are unpredictable: you don’t know when they’ll happen, how bad they will be, or how long they will last. They may last for a few hours, days, weeks or even months. People with RA learn to reactively deal with flares in an attempt to self-manage them. Data from the Canadian Early Rheumatoid Arthritis Cohort indicate that most people try to self-manage their flares until they can no longer manage them, and only then will they seek help from their rheumatologist or other health care provider (See “Self-Management of RA Flares Varies by Severity and Duration: Results from CATCH,” [http://www.earlyarthritis.ca/participants\\_research-year.php?Year=2016](http://www.earlyarthritis.ca/participants_research-year.php?Year=2016)). People must deal with flares reactively and this unpredictable nature of flares and RA generally imposes a feeling of not being able to control one’s RA or even future at times.

*“The pain, because it affects the activities I’m able to do, and my mental health.”*

*“Lung involvement has become a major problem.”*

*“Learnt to live with unpredictability.”*

#### **4. Experiences With Currently Available Treatments**

Current medications for RA aim to control inflammation and minimize disease activity to prevent irreversible joint damage and other subsequent affects, given that there is currently no cure for RA. Many treatments simply help people get through their day. Treatments used to manage RA include non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, sulfasalazine, hydroxychloroquine (also an anti-malarial drug) and various biologic medications (protein-based medicines, rather than small molecules), and small molecules that now target the janus kinase (JAK) pathways. The following provides a general description of the treatments used and their side effects:

- NSAIDs are used to treat inflammation which in turn often also affects (i.e. lessens) pain. The NSAIDS may cause many side effects, from stomach upset to changes in kidney function.
- Corticosteroids are commonly used to control/reduce inflammation and while effective, can produce side effects when taken for longer durations and at higher doses. Corticosteroids can cause short-term effects such as weight gain, acne, excess facial hair, mood swings, high blood

pressure, high blood sugar, increased infection, stomach ulcers, hyperactivity, and increase in appetite. Long-term effects include osteoporosis, glaucoma and cataracts, osteonecrosis, skin changes, heart disease, and stroke.

- DMARDs that are antimalarial medications such as hydroxychloroquine taken in a high dose and over a long period may accumulate in the background of the eye (retina) and cause a loss of vision and in rare cases, blindness. People with RA should have annual eye exams to monitor for this.
- Other DMARDs such as methotrexate and biologic medications may include other side effects. Methotrexate often causes nausea, hair loss, and may cause liver damage. Its nausea effects are sometimes mitigated by also taking folic acid, splitting doses over the course of a few hours, and/or taking subcutaneously rather than orally. Biologic medications may have side effects such as injection reaction irritation, increase risk of upper respiratory infections, pneumonia, urinary tract infections and skin infections.
- Upadacitinib is a JAK inhibitor, meaning that it targets the janus kinase (i.e. "JAK") enzyme family, and it targets the JAK1 protein (there are 2 other JAKs called JAK2 and JAK3. There are currently two other JAK inhibitors available to people who live with RA, tofacitinib (inhibits JAK3, and to a much lesser extent, JAK1 and JAK2) and baricitinib (inhibits JAK1/2). To date, JAK inhibitors have shown side effects that include increased infections (opportunistic infections, viral infections, urinary infections, pneumonia, herpes zoster, cellulitis). Since this class of drugs is fairly new, long-term safety and efficacy data are being collected.

Treatment for RA is based on trial and error for each individual, as well as prescribing according to RA Guidelines that have been developed by professional medical associations such as the Canadian Rheumatology Association (<https://rheum.ca/resources/publications/canadian-recommendations-for-management-of-ra/>). Patients reported that they had tried a number of treatments for RA. Often, currently available treatments can be difficult to tolerate and manage:

*"My current treatment I feel I am at about 80%, I think my fatigue is not being addressed. Other treatments in my past worked better for me. But the effectiveness of the drugs started to wear off after years of being on them"*

*"Have fatigue all the time - even with sleeping 8 hrs a day. I was taken off Arava after being on it for 6 yrs due to head tremors and leg tremors. I travel from PEI to Halifax to see a Rheumatologist as there is no Rheumatologist on the Island. I have been on Humira for 11 yrs and it seems to be working, I could not tolerate Methotrexate after being on it for 4 yrs as I was feeling nauseated all the time and after 4 yrs asked to be put on something else.."*

*"Have been on methotrexate for about 3 years, my rheumatologist thinks I'm in remission. I have blood work done every 3 months, & am doing fine as far a liver results are concerned. I also must take 1000 mcg of folic acid to counter the effects of the medication."*

*"Methotrexate/sulphasalazine, hydroquinine plus this year, Remicade. With the addition of remicade my symptoms appear to be under control.."*

*"The best treatment for me is tofacitinib. I have tried all the other meds or cannot take them (tnf receptors) At the moment I am at 1/2 dose moving slowly to full dose (I was suffering from chronic sinusitis. It is easy to access. I cannot tolerate the stomach problems with mtx [methotrexate], have had serious side effects with the tnf's (neuropathic damage with enbrel) The sinus infections were awful with xeljanz until I underwent IVIG treatments once a month."*

*“I’m in process of switching biologics and last 3 haven’t worked so it’s been difficult past 9 months. On prednisone now and having issues and new med with that. Don’t think this one is working as it’s been 3 months of increasing pain and disability.”*

*“I used injectable methotrexate for a year initially and did not tolerate it well, I would not be able to get up from the bed for 3 days, nausea, hair loss, sun and light sensitivity were all side effects ; some of which I experience till today. It also elevated my liver enzymes. I am sensitive to drugs so have tried and failed sulphasalazine [sic], Arava, litleuomide [sic], all with severe side effects and my own cost .... I have experienced blood in my stool, severe rashes, diarrhoea, migraines, dizziness, vertigo, shortness of breath, stomach ulcers etc. due to side effects“*

*“I’ve tried 2 DMARDS, prednisone & have just started on my 2nd Biologic. My first DMARD (MTX) worked quite well, but due to elevated liver enzymes, I was unable to continue it. Prednisone helped, but only at a higher doses (above 15 mg) & was not an acceptable long term solution (my main side effect was a noticeable increase in appetite). Plaquenil didn’t seem to improve my RA symptoms at all & I had headaches almost daily, which was very uncommon for me.”*

*“I was on methotrexate for decades. It worked at first, but I eventually had to go off due to an immune system failure. I avoided taking it as prescribed when I was a kid because it made me so sick. I have been on biologics for 13 years and they have well managed my active disease. I occasionally take over the counter analgesics for pain, but most do not actually help.”*

Patients may also pursue medical cannabis and/or non-pharmacological approaches to manage RA symptoms , such as physiotherapy, occupational therapy, massage therapy, counselling, or acupuncture. These approaches can often help to address the symptoms of the disease, such as pain and fatigue. However, there are significant unmet patient needs in terms of accessing non-pharmacological treatments, often because they are not reimbursed through provincial health care systems, the treatment options are simply not offered, or there are lengthy waits.

*“Using a TENS devise seems to ease for a short while. Averse [sic] to chemical treatments. Cannabis helps if not overused.”*

## **5. Improved Outcomes**

People living with RA reported that current treatments are difficult to tolerate because of side effects. A variety of side effects are difficult to manage such as those described above. Some of these side effects require treatment with other medications, such as anti-nausea medications. Minimizing these side effects are important outcomes that should be considered when evaluating new therapies.

Even with currently available treatments for RA, patients’ outcomes can vary significantly. Some medications are effective for some people while not effective for others. Some treatments will effectively manage RA for a short period of time before a person’s immune system adapts to a drug’s presence (i.e. becomes non-responsive to it) and they will have to switch to another medication. In some cases, people living with RA may not respond to any of the currently available medications. As a result, patients need a number of medication options to manage their RA throughout their lives. Unfortunately, so little is understood about RA that there is currently no way to predict who will best respond to which medications and/or the best dose of those medications for individuals.

There are outcomes that are important to people living with RA, and these include:

- reduction in pain and fatigue
- reduction in RA complications
- increased mobility
- ability to work and be productive at work
- ability to carry out activities of daily living and social roles
- ability to effectively carry out caregiving and parenting tasks
- decrease in medication side effects.

*“I would want as normal an existence as possible with few side effects.”*

*“I would like a medication with less side effects, I really look in to those now when choosing a treatment! I am looking for something that is easy to use and will improve the pain and stiffness in my joints.”*

*“Will it assist with the fatigue? ... Anything that assists with the fatigue is worth a shot.”*

*“I would hope for remission. No pain or inflammation.”*

## 6. Experience With Drug Under Review

We received responses to the survey questions by one person who participated in the Canadian upadacitinib clinical trial. This person's experiences with upadacitinib are provided as responses to the questions that are shown below.

What positive and negative effects did you experience?

*“I started the trial drug in pill form in May of 2017 and within days I noticed some relief from pain and swelling. My ankle and wrist joints were my biggest problem and after a few weeks I was able to do some yard work like using the lawn mower to cut grass. I don't recall any negative effects at all.”*

Which symptoms does upadacitinib manage better and which ones does it manage less effectively, compared to other medications you have taken?

*“The trial drug definitely managed pain and swelling efficiently which enabled me to get mobile reducing the feeling of uselessness and reliance on others.”*

Does it cause side effects?

*“None that I am aware of at this time.”*

Is it easier to use than other medications you have tried?

*“The pill form was easier to take than the Humira injections that I was switched to.”*

Do you expect it to change your long-term health and well-being? How?

*“I hope that the pain and swelling stays in check and the joint damage is stopped.”*

What impact did the medication have on your quality of life and day-to-day activities?

*“Being on the drug trial has been like a miracle for me I am able to do most of my previous activities.”*

## **6. Companion Diagnostic Test**

Not applicable

## **7. Anything Else?**

No further comments at this time.

## Appendix: Patient Group Conflict of Interest Declaration

### Declaration from CAPA

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

An AbbVie contact provided us with names and email contact information of the rheumatologists in Canada who had patients enrolled in the upadacitinib clinical trial. CAPA provided a letter to these rheumatologists via email and asked them to pass it to these clinical trial participants that explained CADTH, the Common Drug Review process, and why their input would be of value. The letter provided a link to the survey as well as contact information for Dawn Richards, in case they wanted to be in touch via email or phone. The AbbVie contact also put CAPA in contact with a rheumatology nurse who provided the survey questions to individuals she knew who participated in the upadacitinib clinical trial.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No

3. List any companies or organizations that have provided your group with financial payment over the past 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				X
CADTH (travel support for annual symposium)	X			
Janssen		X		
Manulife	X			
Pfizer (including Pfizer Hospira)			X	
Purdue	X			
UCB		X		

4. 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.

D. Richards is a self-employed consultant who, in the last 2 years, has received honoraria, speaking fees

or consulting fees from Innomar, Janssen, Lilly, Manulife, Merck, NovoNordisk.

Name: Dawn Richards  
 Position: 1st Vice-President  
 Patient Group: Canadian Arthritis Patient Alliance  
 Date: July 22, 2019

## Declaration from the Arthritis Society

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.  
 See the section above for which CAPA provided details.
2. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.  
 No
3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Amgen				X
Abbvie				X
Bayer Healthcare				X
BMS			X	
Celgene				X
Eli Lilly				X
Eupraxia Pharmaceuticals	X			
IMC			X	
Janssen				X
Merck				X
Novartis				X
Pfizer				X
Sanofi			X	
UCB				X

5. I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Helen Anderson

Position: Senior Manager, Education Services

Patient Group: The Arthritis Society

Date: July 22, 2019