

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	Dawn Richards
Name of the Primary Contact for This Submission	Dawn Richards (CAPA) & Helen Anderson (TAS)
Email	
Telephone Number	

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 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 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 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). 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 as 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.

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