CADTH

Common Drug Review

Patient Group Input Submissions

sarilumab (Kevzara) for treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more biologic or non-biologic Disease-Modifying Anti-Rheumatic Drugs (DMARDs).

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
Arthritis Consumer Experts (ACE Planning and Consulting, Inc.) — permission granted to post.
Canadian Arthritis Patient Alliance (CAPA), The Arthritis Society — permission granted to post.

CADTH received patient group input for this review on or before November 2, 2016.
CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter’s responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

Arthritis Consumer Experts (ACE Planning and Consulting, Inc.)

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	sarilumab
Name of the patient group	Arthritis Consumer Experts (ACE Planning and Consulting, Inc.)
Name of the primary contact for this submission:	[redacted]
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Permission is granted to post this submission	Yes

1.1 Submitting Organization

Arthritis Consumer Experts (ACE) is a national organization that provides science-based information, education and support programs in both official languages to people with arthritis. ACE serves consumers living with all forms of arthritis by helping them take control of their disease and improve their quality of life.

Arthritis Consumer Experts is committed to the following organizational objectives:

- To inform, educate and empower people with arthritis to help them take control of their disease and improve their quality of life;
- To provide evidence-based information in reader-friendly language to people with arthritis, the public, governments and media;
- To provide research decision-making training to people with arthritis to help them participate meaningfully in research organizations and in consultations with government.

ACE's membership and program subscribers include people with arthritis, their families, their caregivers, rheumatologists, and other health professionals, elected officials, and senior government bureaucrats.

1.2 Conflict of Interest Declarations

a) Regarding corporate members and joint working, sponsorship, or funding arrangements:

Over the past 12 months, ACE have received grants-in-aid or research funding from: AbbVie Corporation, Amgen Canada, Arthritis Research Canada, Canadian Institutes of Health Research, Celgene, Hoffman-La Roche Canada Ltd., Innovative Medicines Canada, Janssen Inc., Eli Lilly Canada, Merck Canada, Novartis, Pfizer Canada, Sanofi Canada, St. Paul's Hospital (Vancouver), UCB Canada, and the University of British Columbia. ACE also receives unsolicited donations from its community members (people with arthritis) across Canada.

b) Regarding those playing a significant role in compiling this submission:

This submission was expressly written by the staff of Arthritis Consumer Experts, free from advice or influence from any outside individual, group or company.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The information was gathered through Arthritis Consumer Experts' (ACE) day-to-day interactions with people living with rheumatoid arthritis, its work with clinical researchers in Canada, and through an iterative process with scientific members of the ACE advisory board.

2.2 Impact of Condition on Patients

Patients' day-to-day lives are affected greatly by their rheumatoid arthritis. Unlike most people who can take their physical/mobility abilities for granted, people living with rheumatoid arthritis must always consider their current disease activity and decide what they can (and cannot) cope with or achieve, how they can go about it, and how much help they may need to engage in activities of daily living, leisure or work.

Patient A has been living with RA for 13 years. She is currently in remission. Before remission, she had to moderate her activity level according to her pain and stiffness during times of flare-ups. She is able to work full time as a physiotherapist and continues to swim, bike, walk and cross-country ski without difficulty. She admits that blood tests and medical appointments are of inconvenience and disrupts her routine, but she is thankful to have good access to excellent care.

Patient B has been living with RA for 6 years. She gets morning stiffness and swelling of hands, feet and knees lasting up to 20 minutes. She also has difficulty using her hands due to loss of range-of-motion. She gets bi-monthly flare ups with flu-like symptoms, including fever, sweating, aching/swelling in joints throughout her body, headaches, fatigue, nausea, and poor sleep pattern.

The tiredness and swelling in her joints impacts her ability to exercise, leading to an increase in weight and decrease in muscle tone.

Patient C experiences joint damage due to her RA. Even though she's had 4 operations on her feet, it is still painful for her to walk and stand in one place for a long time. She also has trouble chopping food and doing gardening work. She is unable to wear nice shoes, like high heels.

Patient D has been living with RA for 28 years. Her disease onset was rapid and severely debilitating, forcing her into a wheelchair at the age of 27 and rendering her unable to work or care for herself for about one year. She recounted how it took her nearly six or seven years to find a combination of medications that helped her get back about 50% of her life. She had to leave full time employment and lost her private health insurance and disability benefits. Her disease “wreaked havoc” on every aspect of her, and her family’s, lives.

2.3 Patients’ Experiences With Current Therapy

Patient A has been in remission with a combination of methotrexate, hydroxychloroquine and NSAIDs. She does not experience any side effects with her current therapy. Besides medication therapy, she believes staying active and having a positive attitude have helped her stay in remission. Having a low stress occupation also helps her in managing her RA.

Patient B has experience using abatacept, methotrexate and Celebrex. Currently, she takes a self-injecting biologic once per week. The medication controls her RA symptoms on a scale of 6/10 most days. Even after taking her medication, she still experiences stiff and swollen joints.

Patient C currently takes a combination of NSAID, methotrexate, Enbrel and Plaquenil for her RA. Previously, she used Humira but the medication loss its efficacy after 8 years. She hates taking methotrexate as it makes her nauseous, tired and gives her headaches. Injecting a biologic always stings for her.

Patient D has been on all conventional DMARDs over the past 28 years, including, gold salts, methotrexate, hydroxychloroquine, and sulfasalazine, as well as two biologic response modifiers. She currently takes methotrexate weekly, golimumab once every four weeks, and daily celecoxib. When she started her first biologic, she experienced a dramatic improvement in her disease and became able to work full time and reintroduced a number of leisure and physical activities her disease forced her to give up for years.

In general, the thousands of RA patients that ACE has interacted with over the past 17 years believe that having a breadth of medication option with unique mechanism of actions to carefully choose from is appropriate, like it is for patients with cancer, HIV and other serious chronic diseases and illnesses. As well, they feel that the best treatment is one that has the fewest adverse effects. Through ACE’s research and education efforts, people with RA who interact with our organization generally understand there is a high degree of variability of disease and that there is a need for increased research activity into the causes and possible cures for the disease.

2.4 Impact on Caregivers

Patient A did not comment about how her RA affects her caregiver(s).

Patient B has a very supportive family but believes they do not understand how RA affects her mood and ability to do the amount and intensity of tasks that she used to do. She has to ask her family for help.

According to Patient C, her husband has to work at a job he did not actually want to stay in because it had benefits. He took care of her after each surgery. He has a less active social life, neglects his own health and has lots of stress.

Patient D attributes her disease as the root cause of her divorce from her husband of 17 years. At her disease onset, she was nearly completely incapacitated by the inflammation and stiffness in 35 or more joints and her husband had to take on all household responsibilities (including meals preparation) while trying to grow his own landscaping business. The family stress as a result of her developing RA was significant. Her immediate family did not understand the nature of autoimmune forms of arthritis, such as RA, and her friends pressured her to try naturopathy and other non-evidence based treatment approaches causing the family financial hardship.

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

The information was gathered through Arthritis Consumer Experts' (ACE) day-to-day interactions with people living with rheumatoid arthritis, its work with clinical researchers in Canada, and through an iterative process with scientific members of the ACE advisory board.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

a) Based on no experience using the drug:
All of the patients interviewed expressed sentiments that if their current therapy works, they do not want to be switched to a new medication. The only reason they should be switched to a new medication is if their current therapy loses its efficacy. Furthermore, they believe that everyone should get equal reimbursement access to medication treatments for RA.

Patient D specifically commented on how having reimbursement access to the full range of the medications with targeted mechanisms of action helped her gain back her life. She and her rheumatologist were able to discuss the choices and together make a decision to first go on a biologic administered intravenously, and when that stopped working, an injectable one. She is aware that there is now a pill form medication available with the same or similar effectiveness as biologics and biosimilars, but is disappointed that it is not yet on her province's drug formulary.

b) Based on patient's experience with the new drug as part of a clinical trial or through a manufacturer's compassionate supply:
None of the patients interviewed for this patient input have had experience with sarilumab for the treatment of RA.

Section 4 — Additional Information

Each person living with RA responds differently to each medication thus, every biologic (originator or biosimilar) and targeted synthetic DMARDs should be added to publicly funded drug plans. In our respondents' opinion, access to sarilumab means a new chance for them to have a treatment that may be effective in managing their disease if another biologic(s) or targeted synthetic DMARD used before it, fails. They also believe that sarilumab might be another good treatment option for people with RA who commonly experience side effects from other RA treatments.

Canadian Arthritis Patient Alliance/The Arthritis Society

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	sarilumab (Rheumatoid Arthritis)
Name of the patient group	Canadian Arthritis Patient Alliance (CAPA) The Arthritis Society
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Permission is granted to post this submission	Yes

1.1 Submitting Organization

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, assists them to become more effective advocates and seeks to improve the quality of life of all people living with the disease. CAPA believes the first expert on arthritis is the individual who has the disease, as theirs is a unique perspective. We assist members to become advocates not only for themselves but all people with arthritis. CAPA welcomes all Canadians with arthritis and those who support CAPA's goals to become members.

The Arthritis Society has been setting lives in motion for over 65 years. Dedicated to a vision of living well while creating a future without arthritis, The Society is Canada's principal health charity providing education, programs and support to the over 4.6 million Canadians living with arthritis. Since it's founding in 1948, The Society has been the largest non-government funder of arthritis research in Canada, investing more than $190 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.

1.2 Conflict of Interest Declarations

a) *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:*

Sources of grants and support received by CAPA in the last year include: AbbVie Canada, Arthritis Alliance of Canada, The Arthritis Society, Canadian Institutes for Health Research Institute of Musculoskeletal Health & Arthritis, Hoffman-LaRoche Canada, Janssen Canada, Novartis Canada, Pfizer/Hospira Canada, Pfizer Canada, Eli Lilly and UCB Pharma. Additionally, CAPA has also received support in the past from: Amgen Canada, Canadian Institutes for Health Research, Canadian Rheumatology Association, Ontario Rheumatology Association, Rx&D, Schering Canada, Scleroderma Society, and STA Communications.

The Arthritis Society does not believe that it or those individuals playing a significant role in compiling this submission have a conflict of interest that influences the information provided in this patient group submission. The Arthritis Society accepts funding from many pharmaceutical companies in order to work towards fulfilling its mission of enabling Canadians with arthritis to live well and be effective self-managers and to lead and support arthritis research and care. In order to be fully transparent and meet the request to disclose pharmaceutical manufacturers who have provided support to the organization please be aware that over the past 12 months The Arthritis Society has accepted funding from the following members of the pharmaceutical industry: Abbvie, Amgen, Bayer, Bristol Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Purdue, Roche, UCB. The vast majority of The Arthritis Society's funding comes from individual donors as personal charitable giving.

b) *We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:*

One of the authors of this submission received honoraria from Sanofi in 2015 in order to provide a presentation of the journey of a person living with inflammatory arthritis.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

One of the authors of this submission was originally diagnosed with Juvenile Idiopathic Arthritis therefore these personal experiences were considered in the development of this submission. More information was obtained through personal experiences of the Board of Directors of the Canadian Arthritis Patient Alliance in living with inflammatory arthritis. The Arthritis Society had contact with one patient facilitated by a rheumatologist involved in the clinical trials. The Arthritis Society used social media to gather patient testimonials.

2.2 Impact of Condition on Patients

Rheumatoid Arthritis (RA) is a serious, disabling auto-immune disease that affects every aspect of a patients' day-to-day life. Patients are typically diagnosed when they are between the ages of 25 and 50. It affects three times more women than men and 1 in 100 Canadians are affected by RA or roughly 300,000 Canadians. There is currently no cure for RA – once a person develops RA, they live with it for the remainder of their life.

The disease is characterized by inflammation in the joints that destroys the lining of the joint and ultimately the surrounding bone resulting in the need for a total joint replacement. Once damage occurs, it is not reversible and can cause significant pain and disability. It is well documented that RA is a systemic disease and can be accompanied by fatigue and numerous co-morbidities, such as cardiovascular disease, osteoporosis and lung disease.

RA is a challenging disease to manage and physicians and patients often have to try different drugs to find something that works well. One patient said, “Finding the best RA treatment is hit and miss. It took quite some time to find a drug that fit my particular needs.” Another patient said, “A lot has happened since I was diagnosed. We have gone through many trial and error paths in order to create a balanced point with my RA.” In addition, a patient’s immune system can adapt to a drug making it necessary to switch to another treatment when one becomes ineffective. As a result, patients require many medication options as treatment response is not possible to predict and changes over time. Research has shown and it is now common knowledge that newly diagnosed patients should be actively treated early in the disease to avoid irreversible joint damage, control pain and improve overall quality of life for the patient.

When the disease is not controlled, patients endure severe inflammation, pain and fatigue. It can be extremely difficult to undertake the following day to day activities:

- self-care
- sleeping
- pursuing post-secondary education
- becoming and staying employed
- walking
- completing housework, grocery shopping and cooking
- maintaining and pursuing relationships
- having and caring for children
- participating in social activities and hobbies.

Patients said:

- “Battling pain causes fatigue. Fatigue means you can't do what you used to or what you want to which means a radical change in habits. I struggled to find a new career where I can be productive and also manage pain and fatigue.”
- “Controlling the deterioration of my feet, knees and hands is important. I still curl, but with a push stick. I still fish, but do not hold the rod long. I try to do everything I use to do, only slower and more carefully.”
- “I have pain, interrupted sleep, low energy and fatigue. I have compromised immunity, so I get sick easily and stay sick longer.”
- “Right now the RA is under control and I am functioning well. When I’m having a flare the usual is- fatigue, swelling and pain in hands, ankles, knees, wrists, all over body sore and swollen.”
- “I would like to be able to maintain a cleaner apartment. I need help completing tasks. I would like to be able to accomplish much more, faster and feel better about myself in the process.”
- “Daily activities are totally dependent on how I feel when I wake up. If I have a good night of uninterrupted sleep (10-12 hours), I am able to do more the following day (housework, grocery shopping, etc are difficult). My quality of life has decreased substantially in the past 10 years. I used

> to lead a very active work/personal life. Now, I expend most of my effort taking care of myself and trying to get well."

Without control of the disease, major joint surgeries such as joint replacement or fusions can be required and possibly lead to multiple procedures throughout a person's life. Because of the extensive damage to their joints, some patients who do not respond to the available treatments might also have to use technical or mobility aids such has bath lifts, canes or wheelchairs, have their house/car adapted and rely on para-transit to do daily activities. One patient said, "I need to depend on aids to assist me."

The disease can also become a serious physical and psychological burden for the person living with arthritis and their families. One patient said, "Dealing with day-to-day issues is challenging, what other people without RA might not find problematic. Also challenging is convincing others, including doctors that I have authentic problems with depression, anxiety & stress." Another patient said, "Trying to get on with life, but finding it hard when feeling so anxious and down."

2.3 Patients' Experiences With Current Therapy

Clinical practice guidelines emphasize early aggressive treatment of RA, which provides the best long-term outcomes for people with RA. A number of treatment approaches are used to manage RA including Non-steroidal anti-inflammatory drugs (NSAIDS), corticosteroids and disease modifying (conventional synthetic and biological) anti-rheumatic drugs (DMARDS) such as Methotrexate, Etanercept and Infliximab. Effective treatments mean that people with RA do not need to live with the permanent damage, high medical costs (e.g. surgery, mobility aids, accessible housing) and disability. Early intervention is an absolute necessity in order to allow people with arthritis the opportunity to fully participate in all aspects of life.

Notwithstanding this fact, patients' responses to medication can vary significantly. Some medications are effective for some people with arthritis while not effective for others. Some treatments will only manage the disease for a short period of time before the patients' immune system adapts to a drug presence (i.e. becomes non-responsive to it) and they will have to switch to another medication. In some cases, patients with RA may not adequately respond to any of the biologics currently available. One patient said, "I had to go through a lot of different drugs first before I was able to go on a biologic. I wish there was some way to tell if a biologic would be effective without having to wait six months for each one. I am now on my 6th biologic." Patients need a number of medication options in order to effectively manage their disease throughout their lives. There are also no specific tests that identify which medication will be effective for a person living with rheumatoid arthritis. This means that a person with the disease will need to go on one or more medications on a trial and error basis in order to find a medication that is effective. Often, the treating physician determines which medication is most appropriate based on a number of factors such as patient preferences, mode of administration, anticipated side effects, etc.

While side effects of existing treatments may vary, they can include: nausea and vomiting, extreme fatigue, decreased immune function (as current medications are immuno-suppressants), injection reactions, and for biologics, auto-immunity is often developed to treatments after prolonged exposure. Some medications can only be administered through an infusion which can cause long-term issues with vein scarring and it can become increasingly difficult to insert the IV. There can be issues with tolerating Methotrexate (the standard of care) as it causes nausea, vomiting and diarrhea for 24 hours (and sometimes longer) after administration. Patients said, "With methotrexate it's very harsh in the stomach, I really dislike taking it." Another patient said, "Oral methotrexate made me sick for 3-4 days per week with nausea, diarrhea, and extreme fatigue. Using the injectable version of methotrexate, I feel nauseous and tired for one day, which is better. When your drugs cause you to feel unwell, it is a lot easier not to take them."

The patient on the clinical trial for Sarilumab said, "My basic treatment is drug control and a massage every three weeks which works great for the joints. Sarilumab has made the biggest difference in my dealing with RA. I have less inflammation and less pain. It is letting me get my strength and mobility back."

2.4 Impact on Caregivers

Depending on a person's ability to perform daily activities and their ability to be employed, caregivers of people living with RA are relied upon in varying capacities. Depending on the extent of disability or if the patient's disease is not well controlled, the spouse and family may need to help patients with RA with day to day activities such as bathing, getting in and out of bed, and getting dressed. Spouses or family members may need to take additional time off work in order to assist the patient in activities of daily living. There may be additional costs to care for the person with arthritis if the spouse or family member is unable to do so (e.g. homecare, attendant care). This places strain on relationships and imposes additional financial hardships on the entire family.

These additional responsibilities have an immense emotional toll on both patients and their families. In some situations, a caregiver may give the patient their injection or need to take over family responsibilities while the person with arthritis is receiving their infusion or when medication side effects are being experienced (e.g. nausea, vomiting). The stress of dealing with uncontrolled disease can also cause additional psychological stress for the spouse, children and extended family. It can be difficult to watch the health of a parent deteriorate and this can cause ongoing stress for the child(ren) even when the parent is well.

Additionally, when patients do not have employer-provided insurance, it places additional stress on the spouse/partner to remain employed to retain drug coverage. The medication costs for RA are significant and these costs remain a constant consideration in managing a family's finances.

It is important to highlight that RA affects patients and caregivers and family members profoundly, in all aspects of their lives – and does so from the time of diagnosis and throughout their lives. New treatment options have the potential to ease the burden on patients' families, caregivers and the healthcare system.

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

The Arthritis Society had contact with one patient facilitated by a rheumatologist involved in the clinical trials.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

The patient on the clinical trial indicated less inflammation, less pain and a better quality of life outcome:

- "The positive is that I can do more things now with Sarilumab then when I was not taking it. Inflammation and pain is down, whether it is Sarilumab or the combination of the drugs I really do not care. Something is working for me. My liver counts are a bit higher, so I am to cut down on Methotrexate, other than that no side effects. The injections every two weeks are not a problem for me so I can feel better. I feel better than I did 5 years ago."
- "Sarilumab has given me higher expectations for a better life. In fact, I can now go down on the floor and play with my grandkids even though it is still difficult to get up. I would not have thought this possible 5 years ago. I do not expect the deforming of my joints to stop, but as long as I can keep doing things my body and mind are content with the future."