CADTH

CADTH COMMON DRUG REVIEW

Patient Group Input Submissions

ETANERCEPT (ERELZI)

(Sandoz Canada Inc.)

Indication:

- Treatment of moderately to severely active rheumatoid arthritis (RA) in adults. Treatment is effective in reducing the signs and symptoms of RA, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function. Erelzi can be initiated in combination with methotrexate (MTX) in adult patients or used alone.
- Reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) in patients aged 4 to 17 years who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs).
- Reducing signs and symptoms of active ankylosing spondylitis (AS).

CADTH

Etanercept (Erelzi) for the treatment of rheumatoid arthritis, ankylosing spondylitis or polyarticular juvenile idiopathic arthritis

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
Arthritis Consumer Experts — permission granted to post.
The Arthritis Society — permission granted to post.
Canadian Arthritis Patient Alliance (CAPA) — permission (three submissions) granted to post.
Canadian Spondylitis Association — permission granted to post.

CADTH received patient group input for this review on or before February 24, 2017.

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

General Information

Name of the drug CADTH is reviewing and indication(s) of interest	etanercept (Sandoz) to etanercept (Enbrel®)
Indication of interest	For the treatment of rheumatoid arthritis, ankylosing spondylitis or polyarticular juvenile idiopathic arthritis
Name of the patient group	Arthritis Consumer Experts
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Permission is granted to post this submission	Yes

How to Complete This Submission Template

Information Gathering

The information was gathered through Arthritis Consumer Experts' (ACE) call for patient input for this specific submission, day-to-day interactions with people living with forms of autoimmune arthritis, its work with clinical researchers in Canada, and through an iterative process with scientific members of the ACE advisory board.

Information About the Submitting Patient Group

Submitting Patient Group

Arthritis Consumer Experts (ACE) is a national arthritis patient 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.

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:

Over the past 12 months, ACE received unrestricted grants-in-aid from: Amgen Canada, Arthritis Research Canada, AstraZeneca Canada, Canadian Institutes of Health Research, Celgene, Hoffman-La Roche Canada Ltd., 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) We have the following declaration(s) of conflict of interest in respect of 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.

Disease/Condition and Current Treatment Information

Impact of Condition on Patients

Patients' day-to-day lives are affected greatly by their rheumatoid arthritis, ankylosing spondylitis and polyarticular juvenile idiopathic arthritis. Unlike most people who can take their physical/mobility abilities for granted, people living with arthritis must always consider the state of their disease and decide what they can (and cannot) cope with or achieve, how they can go about it, and how much help they may need.

Rheumatoid arthritis patient inputs

Patient A experiences common RA symptoms, such as morning stiffness, pain and inflammation in her joints, loss of motion in affected joints and feeling tired all the time.

Patient B has had RA since she was 28 years old. At first, it was not very well managed as she had poor reactions to medications. As a result of her RA, she has an auto-fused wrist, cannot grip anything or walk without orthotics, and experiences pain in her metacarpophalangeal joints. She also has bone degradation in some areas. She is unable to participate in tennis, hike on steep inclines, and ski – all of which she used to do. Patient B is thankful that there is no knee involvement and that she can continue to ride horses at a significantly reduced rate, 1-2 times per week. Her exercise includes walking 15 minutes, 4-5 times a week.

When interviewed about her RA symptoms, Patient C said, "The disease related symptoms that have the biggest effect on me are pain, tiredness, and learning how to do some things without full use of or pain free joints."

Ankylosing spondylitis patient inputs

According to Patient D, chronic pain means "the mind is always focused on something other than the task at hand, which makes working and relationships extra difficult." She describes the impact of AS on her life as follows: "My foot pain was so bad that I would try to not drink any liquids because I stressed about having to get up from my desk at work to go to the bathroom, knowing I had to walk on my sore foot. I used to crawl to the bathroom in the middle of the night and had to use the walls in our hallway as crutches to get my babies in the nights to nurse them. I used to sleep for up to an hour at a time but had to move from bed to a chair and vice versa all night, every night." She also experiences fatigue and had to quit playing sports (baseball, hockey, curling) but continues to cycle and do low impact exercises despite her pain. She believes that "laying idle is way worse on the joints than keeping moving."

Patient E states that stiffness, pain, and spinal deformity has significantly affected their day to day life. Patient E finds it difficult to wear clothes, socks, shoes, undergarments, do daily tasks, stand or sit for too long (while at work or brushing and shaving), and walk without support. Patient E described AS's effect on their sleep: "Sleep is badly disturbed, force to get up during mid of night and sit with the support of 'wedge' and sometime sitting and sleeping. Becoming side sleeper, need support to change sides. i.e. either hold bed side rail or hold the person with whom you are sleeping with." Patient E cannot lift weights and is not able to work. They need various tools to manage their pain, such as transcutaneous electrical nerve stimulation (TENS) therapy, massage therapy, hot towel, and water treatment. Associated diseases such as uveitis and psoriasis adds pressure to their life and causes depression.

Patient F is concerned that, due to the complexity of AS, he is experiencing symptoms of AS without recognizing it. On days where he was not being treated, he could not get out of bed and walk to the kitchen.

According to Patient G, AS causes "severe chronic pain, severe fatigue, loss of functionality, loss of employment". He finds it challenging to maintain relationships and is unable to perform basic tasks and activities due to severe pain and fatigue.

Polyarticular juvenile idiopathic arthritis patient inputs

Patient H has been living with RA for 50 years. It started with a diagnosis of juvenile idiopathic arthritis (JIA) when she was 7 years old; she now lives with JIA and RA. She cannot stay active as much as she would like. Her RA limits her physical activity for fitness. "I have to get help with fitness as well as basic home care things like house cleaning, yard work and daily living activities because of the inflammation, pain and joint damage from my JIA and RA."

Patient I was diagnosed with pJIA when she was 14, with disease activity in 30 joints. Before her diagnosis, she was a competitive dancer and danced 7 days a week. She was told she can't be active and was forced to leave her dance studio. As a teenager, sports and friends were important to her. After her diagnosis, as someone trying to fit in, she experienced social discrimination. Her friends couldn't understand why she was always tired and why she was not going to outings with them. She lived with pain, fatigue, social anxiety, and had physical challenges at school. She was unable to participate in physical education classes. At grade 12, she missed 50 days of school for medical appointments and was concerned about getting into the university she wanted to.

Patients' Experiences with the Current Treatment

Rheumatoid arthritis patient inputs

Patient A is currently using Enbrel and has been for 10 years, with great success in controlling her RA symptoms. Her body seems to be sensitive to minor changes in chemical formulations. She noted that she has had a negative response to generic NSAIDs Feldene but when she was put back on the brand name version of Feldene, the medication controlled her symptoms. After 5 years, Feldene loss its efficacy. Patient A expressed her concerns about a possible switch from Enbrel to biosimilar etanercept: "Enbrel has lasted the longest for me and I am very concerned that if I were forced to use the biosimilar/generic version of Enbrel, that my body's sensitivity to chemical formulations would once again cause a problem. There are not many medication options left for me so I'd prefer to stay with one that works until it stops working and I am forced to switch to something else."

According to Patient B, Enbrel "gave life back to her." When she had her first child, she had to stop nursing at 5 months because her symptoms were so bad. She had to go back to medications she was on pre-pregnancy (Enbrel, HCQ, Immuran). She currently visits a hand therapist and a chiropractor to help her adjust her ribs. Without her private insurance, she would not be able to afford any of her medications.

Patient C is currently using hydroxychloroquine, methotrexate, and Xeljanz. She also uses voltaren as a topical aid. She commented: "I am happy with how things are going. Because all my meds are in pill form and I can get them all from my local pharmacy. I have good access. The drug company gives me a break on the cost of my biologic or I would have difficulty paying for it."

Ankylosing spondylitis patient inputs

Patient D has had 2 biologics before trying Enbrel. When interviewed about her current therapy, she said: "Enbrel has changed my life. The first two biologics I tried helped with the disease but caused allergic reactions in me; I went on 3 months of a "dry out" before starting Enbrel and was reminded how well the biologics work when I could go for a jog 3 weeks after starting it when I could barely

walk during those 3 months. The biologic is tending to my physical and ultimately, my mental health needs because I feel way more in control of my life due to less pain and frustration." The paperwork and drug reimbursement system is hard to navigate without the help of case coordinators, client care workers, patient assistance programs, and her pharmacist. Adverse effects from the first 2 biologics include allergic reactions at the injection sites and constantly feeling full. She would get welts and they would get worse with each injection. "The fullness was a surprising side effect and had more of an impact on my quality of life than I ever expected. I could no longer eat much or often and constantly felt 'unwell'."

Patient E is on Enbrel and mentions that "whatever little I am able to move around is only possible because of Enbrel." However, Enbrel controls the AS symptoms only and does not manage their psoriasis. Patient E also goes to massage and hot water therapy, which "soothes the joints/muscles." Because the treatments are expensive and mostly involve transportation costs, it is more difficult to maintain consistency.

Patient F is currently taking Enbrel and finds it very effective. It allows him to breath normally with no pain to the rib cage during inhalation and exhalation. There is also no pain in his legs or knees. He credits Enbrel for giving him his mobility back. For him, there are no administration costs. His medical coverage covers Enbrel. Another thing he likes about Enbrel is that he can travel with it on short trips.

Patient G has found that NSAIDs and anti-TNF inhibitors are ineffective for him. He used Enbrel before and it caused severe infection and psoriasis. He is currently on Cosentyx and sees little to no improvement in his AS. He indicated that there was a delay of 30 years in getting his AS diagnosis and thinks that this is reason for the medications' inefficacy. Patient G believes there is a need for more effective anti-inflammatory and pain relieving medications as current medications seem to work for some, but not all. His insurance covers the cost of his biologic medications. He also uses cannabis and kratom for pain relief.

Polyarticular juvenile idiopathic arthritis patient inputs

Patient H is taking the pain medication tramadol. She has had serious infection from biologics due to a surgery she undertook. She has tried gold therapy, methotrexate, Orencia, Anakinra, and Humira. She had a lot of failures with biologics as they all loss their efficacy over time. She has difficulty traveling with Enbrel.

Patient I indicates that she has tried almost all the medications available for someone living with pJIA. When discussing with her rheumatologist about treatment therapy options, it was important for her to observe the scientific evidence behind the prescribed medications. She has a positive outlook on life and prefers improved quality of life over any possible long-term effects her medications may have.

Impact on Caregivers

Patient A did not submit input for this section.

According to Patient B, RA impacts her husband. He is required to pick up slack from her inability to care for their child and help with daily household tasks. They also delayed becoming parents due to her RA. Her disease places additional fatigue on the whole family. Because Patient B can only work 3 days per week, there is also a loss of income.

Patient C says the impact of RA is a financial one for her husband because she uses his private insurance policy to gain access to her medications.

Ankylosing spondylitis patient inputs

Patient D believes that "there is not much a support person can do besides be supportive but that must be draining when it's so constant." Her husband has always been encouraging and supportive of her doing whatever she needs to do. They have to juggle between his full-time work, her full-time work, taking care of 3 little kids, and driving 4 hours to her medical appointments. Her husband does all the heavy lifting and carrying. Before she was diagnosed, her husband stressed over the possibility of becoming a single parent.

Patient E says his AS places a lot of pressure on his family and kids. His wife worries about him when he gets up to switch sleeping positions. Due to his AS, he is unable to work. He feels sad because “every member of the family look at you with sympathy and is ready to extend a hand of help but in return, you can’t do the same.”

Patient F does not rely on caregivers. Enbrel allows him to move around and have a very active life. His only physical challenge is not being able to bend his head backwards and look up. After some stretching and exercising, his morning fatigue fades.

Patient G said that there are “many difficulties for my family who must adjust to my lack of functionality and ability, and deal with severe chronic pain with me.”

Polyarticular juvenile idiopathic arthritis patient inputs

Patient H said that her RA has limited the activities that she and her husband can do together. The disease “limits our activity for outside the home. My husband has to do more of the household chores, such as food prep and yard work.”

Patient I is grateful to have the support of her friends, teachers, and family. They helped others understand what she was going through.

Information About the SEB Being Reviewed

What Are Patients’ Expectations for the SEB?

Rheumatoid arthritis patient inputs

Patient A hopes that anyone currently taking Enbrel will not be forced (financially or otherwise) to use the biosimilar version. She concluded: “Trying the biosimilar version first instead of the original on someone who has never used the original would be a good way to reduce health care costs but please take the needs and concerns of existing users, not just new users into the equation when decisions and recommendations are made.”

Patient B hopes that biosimioar etanercept will work as well as Enbrel.

Patient C did not submit input for this section.

Ankylosing spondylitis patient inputs

Patient D expects it will be easier to access biosimilar etanercept. Because of the reduced cost, there should be less paperwork. She is worried that biosimilar etanercept may not be as effective in treating disease progression and pain.

Patient E did not submit input for this section.

Patient F worries that biosimilar etanercept will not be as effective. He prefers to continue his Enbrel treatment until it fails. He concluded: “I pray that in the future there may be a cure and early detection so people do not have to go through the testing and having to wait for actual damage to the skeletal system before being diagnosed.”

Patient G believes that biosimilar etanercept would be less costly and more accessible for patients. Biosimilar etanercept may be more effective for some patients.

Polyarticular juvenile idiopathic arthritis patient inputs

Patient H’s main concern about biosimilar etanercept is “its efficacy; I’ll be concerned about side effects. Mobility, pain management, hand and feet are getting more damage, have to get surgery on my foot, without being on anything that’s immune altering, have been affecting my joints and deteriorating.”

Patient I did not submit input for this section.

Additional Information

ACE supports biosimilar reimbursement policy development and implementation based on scientific based/fact-based information.

CADTH

The Arthritis Society

General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Etanercept
Indication of interest	Polyarticular Juvenile Idiopathic Arthritis (PJIA) (for AS and RA please reference April 2016 input on Etanercept)
Name of the patient group	The Arthritis Society
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
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Address	www.arthritis.ca
Website	Etanercept
Permission is granted to post this submission	Yes

How to Complete This Submission Template

Information Gathering

Information was obtained from the following sources:

- Contact with 25 families caring for a child living with PJIA who responded to request for feedback for CADTH
- 46 people participated in focus groups on biologics and biosimilars conducted in the fall of 2016

Information About the Submitting Patient Group

Submitting Patient Group

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 its 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.

Conflict of Interest Declarations

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, AstraZeneca, Bayer, Celgene, Eli Lilly, GSK, Hospira, Janssen, Merck, Novartis, Pfizer, Purdue, Roche, Takeda, UCB. The vast majority of The Arthritis Society's funding comes from individual donors as personal charitable giving.

The Society abides by all Canada Revenue Agency and Imagine Canada requirements, and has specific guidelines on advocacy relating to pharmaceuticals that are available upon request.

Disease/Condition and Current Treatment Information

Impact of Condition on Patients

What aspects of this disease/condition are more important to control than others?

Polyarticular arthritis affects five or more joints within the first six months of having JIA. It is the second most common type of JIA in children and teenagers. It is more common in girls than boys. There are two types of polyarticular arthritis: the first type has a positive rheumatoid factor (RF) result on a blood test, and the second type has a negative RF result.

PJIA may include a variety of symptoms that can change from day-to-day and not all symptoms are shared by all children with the disease. The effects of PJIA on the child can depend on the severity of her/his symptoms, treatments, and frequency of flare-ups.

Parents caring for a child with PJIA have identified pain, stiffness and swelling of joints and fatigue as key symptoms that impact their child's daily life:

- "I have two daughters with PJIA. The oldest has been affected in almost all her joints. She has daily pain that varies in severity. When the pain is at its worst, it can prevent mobility…The second is affected mostly in her wrists and ankles. Managing pain and the disease is very important to my girls' daily lives, as they can be greatly affected when not under control."
- "Inflammation of joints in fingers is the most important to control. Uncontrolled, she experiences pain in her hands and reduced dexterity."
- "My daughter is in pain most of the time. It varies in intensity, so pain management is our priority as it affects her ability to focus and have enough energy for school and fun activities. She is unable to do most sports due to significant knee pain."
- "Inflammation, pain and mobility are the most important to control because these symptoms mess up his day if not under control."
- "Morning stiffness and pain. Intermittent painful joints that limit or preclude participation in school, physical education and sport teams, in addition to extracurricular activities. Jaw pain that makes chewing some foods difficult. Joint flares that make walking to school impossible and require the use of crutches for mobilization until joint treatment by rheumatologist."
- "It is important to keep our daughter out of pain and stop damage from being done to her joints, ensuring a future free of disability."
- "My daughter has joint pain in both ankles and wrists. PJIA has also affected her jaw, she has small chin. Fatigue and low energy are also related symptoms."
- "Pain, stiffness and swelling of joints; limited mobility and range of motion; decreased energy; decreased physical strength; eye inflammation; glaucoma; missed school days due to treatment; immunosuppression."
- "Pain and swelling most important to control because these significantly impact his day to day abilities and mental health."
- "Previous joint damage and active inflammation can impact daily activities. It is important to control an inflammation flare. My child has osteoporosis due to JIA and as such does not partake in any contact activities."

- “My child’s flexibility is very poor, healing from sports injuries takes much longer, fatigue onset is quicker which impacts all activities in general.”
- “Symptoms of day to day life include joint pain more days than not. If she can get past the pain and over does it, doing something fun for a day, she ends up in bed for 2-3 days in severe pain. At school she can't keep up with the other children and takes a lot of breaks. The pain is the most important symptom to control. My child misses out on a lot of activities due to pain but also a lot because of nausea and vomiting from medications.”

How does this disease/condition affect day-to-day life?

The disease affects the ability of children to participate in school and physical activities. This is what we heard from parents caring for a child with PJIA:

- “My daughter chooses to not participate in activities because she knows it will hurt her. It makes her sad that she can't jump on a trampoline, skip rope and do fun "kid things" due to her knees hurting. She finds it embarrassing that she can't sit still or comfortably in her chair at school. My daughter misses school and gets behind a bit in class. She can't participate in school functions (Jump Rope for Heart, skipping rope with friends on breaks, gym class, school marathons, soccer, and gymnastics).”
- “Before medication, my son could not walk in school or go to gym with his class. He had to be carried or crawled everywhere.”
- “Pain makes writing and doing assignments too difficult. Opening even previously opened water bottles can be very difficult. My second daughter is affected mostly in her wrists and ankles. Daily pain causes difficulty walking up and down stairs etc.”
- “Inflammation impedes her ability to write and self feed.”
- “My daughter has a wombat chair at school & a tilted desk. She also uses a computer for writing assignments. She sometimes sits out of gym activities when ankles get sore or she gets tired. Although she can play soccer she cannot play in an organized league because the kids her age run circles around her. She also has trouble skating. She cannot go on a trampoline. It is hard for her to participate in track & field.”
- “Pain - not being able to do whole gym class and recess with friends. Exhaustion- can't always play with friends when she wants to.”
- “She used to play rep volleyball but has been restricted by her pain.”
- “He is often unable to run so cannot take part in gym class at school and/or go up the stairs.”
- “Restriction in school activities, also in out of school activities (e.g. ice sports and contact sports).”

It is also important to note that PJIA also has a significant impact on the child’s emotional and psychological well-being. PJIA symptoms mean children often limit participation in social activities with family, friends and peers, which can lead to depression. This is what we heard from parents:

- “My son becomes extremely sad and discouraged that he cannot participate in activities like other kids his age such as soccer, basketball, etc.”
- “Depression-stops her from doing things she loves. She stays in her room often and has difficulty going to school.”
- “Off medication - Morale is low.”
- “There are constant infusions, every 2 weeks that have to be done during doctor hours. This impacts school attendance and grades – school grades effect my child’s anxiety – anxiety is linked to depression. Physical limitations disallow high school competitive sports (played basketball from grade 5 to 9 and can no longer play).”

Access to effective therapeutic treatment is essential for children living with PJIA to participate in the same activities of daily living as their peers.

Patients' Experiences with the Current Treatment

What treatments have you used for the condition and how effective were they?

As each child is distinct, it is inevitable that individuals will react differently to treatments. In some cases, the body may develop a resistance to medication. As a result, it is essential for patients to have access to an array of medications including: disease modifying anti-rheumatic drugs (DMARDS), nonsteroidal anti-inflammatory drugs (NSAIDS), biologics and methotrexate; in order to provide options to allow for individualized approaches to disease management. This is what we heard from families:

- "Both my daughters have been on NSAIDs, DMARDs and now combination of biologics. My oldest daughter is on Celebrex and Orencia. She is the best controlled she has been, although she still has active joints. An infusion every four weeks requires time off work and school. While the cost is manageable, due to drug coverage, it still all adds up after sometimes multiple hospital trips a month. My youngest is on Celebrex, Sulfasalizine and adding Enbrel. She still has active arthritis. Both girls were on methotrexate at different times and that was by and far the worst we've had in terms of side effects. My oldest daughter would vomit prior to receiving her injection. Years later she still has triggers (i.e. alcohol swabs) that cause nausea. Naproxen was also bad for her. By the end she was coughing up blood and having severe nose bleeds. She ended up having both nostrils cauterized."
- "Methotrexate had limited effectiveness. The side effects were slight nausea and lethargy during the first two days after dosing, but overall, she tolerated it reasonably well. Enbrel is effective. No observed side effects. Our family's group benefits will expire within the next two months...we're hoping we'll be able to access financial support."
- "Celebrex and Naproxen gave no pain relief. Methotrexate gave no pain relief. Prednisone gave her a brief period of pain relief, but was only given as a temporary plan to give her a break from methotrexate injections. Enbrel was added and made her pain manageable. The methotrexate made her feel a little 'off' so she was weaned off it a few years later. On its own, Enbrel has worked well. We have full insurance coverage. It did take a great deal of time (months) for the Enbrel approval and while we were waiting my daughter was unable to attend school and could barely move for months. It took many phone calls, and tears until they gave us some under their Enliven compassionate care program. Once our insurance company finally approved Embrel, she has been able to get it with no restrictions. Enliven has been very supportive to us over the years."
- "My child has methotrexate injections once weekly, Enbrel injections twice weekly with no visible side effects to speak of."
- "Naprosyn was not effective. Methotrexate was not tolerated post injection and anticipatory nausea was a side effect. Humira was very painful to inject. Sedated cortisone injections provided a short-term effect. Enbrel was very well tolerated by my child, with minimal site reactions as the only side effect. There are no hardships for our family in regards to accessing treatment as we live in a large centre with a great paediatric rheumatology program as well as having excellent health insurance through work. My child's needs are being met with the treatment she is currently receiving. We have not had to access any patient assistance or support programs."
- "Tried methotrexate but did not work. Prednisone helped but not fully. Side effects from prednisone included the puffy face and moodiness. Tried Embrel and it did not work. Embrel was a struggle as needle night was not fun for our family. Lots of tears from our child with JIA and frustration felt by both my husband and I. Tried Humira and it did not work. Worse on needle night as Humira stung more than Embrel. Both times the hospital set us up with assistance programs to access nurses to teach about giving the needle, as well as covering the cost of the drug while we waited for insurance to kick in. Finally moved to Actemra infusions at the hospital combined with methotrexate and prednisone infusion. We go every four weeks to day medicine and he gets two IV's over two hours. We are at the hospital for about four hours from start to finish. This treatment has worked. We have a child that can run, play like every other child. Recently he is now only getting IV of Actemra so three hours at hospital every four weeks. Things that affect us is the time needed and the cost of parking at the hospital starts to add up. No side effects and our child enjoys going to hospital, as the nurses are amazing."
- "My daughter gets two injections per week which she takes easily but sometimes we need to make accommodations to make sure she gets them. Sometimes the needles hurt. We hope that Enbrel will continue to stop any damage to her joints and give her pain relief and a normal life. We are beginning to see signs that Enbrel is becoming less effective and are in discussion with her doctor to switch to Humira."

Do current treatments have adverse effects that are more difficult to tolerate than others?

This is what we heard from parents:

- “She started with prednisone, had some side effects but, she wasn't on it for too long. methotrexate was very effective but would make her nauseous and sick at times. With Humira we’ve seen amazing results, can't believe the change, her pain levels are low and her health has improved.”
- “New biologic will be a home administered injection. All medications are a source of anxiety and are resisted by our child.”
- “Both girls were on methotrexate at different times and by far was the worst we've had in terms of side effects. My oldest would vomit prior to receiving her injection. She still has triggers (i.e. alcohol swabs) years later that cause nausea. Naproxen was also bad for her, by the end she was coughing up blood and having severe nose bleeds. She ended up having both nostrils cauterized.”
- “Not needle pain, but medicine pain upon injection continues to "hurt" physically, and emotionally.”
- “Methotrexate - limited effectiveness. Side effects were slight nausea and lethargy during the first two days after dosing, but overall, she tolerated it reasonably well. Enbrel is effective. No observed side effects.”
- “The side effects of methotrexate are very harsh. Stomach pain, throwing up and lots of anxiety about needles.”
- “Side effects from Prednisone was the puffy face and moodiness. Tried Enbrel and did not work. Enbrel was a struggle as needle night was not fun for our family. Lots of tears from child with JIA and frustration felt by both my husband and I. Tried Humira and again did not work. Worse on needle night as Humira stung more than Enbrel. Finally moved to Actemra infusions at the hospital combined with Methotrexate prednisone also infusion. No side effects and child enjoys going to hospital as the nurses are amazing.”
- “Oral ibuprofen resulted in stomach pain and appearance of scratches/scars on my daughters face. Developed an oral aversion to swallowing pills in general.”
- “Initially when she was diagnosed she was on Naproxen but it was too hard on her stomach and she required an endoscopy. Also she became anaemic during that time. She is currently still on methotrexate but started Humira injections just over two years ago. This has made her arthritis stable. However she complains of terrible burning when the shot is administered.”
- “Remicade infusion time is long and requires premedication to mitigate possible reactions to drug. Humira burns on injection. Enbrel is not as effective for eye inflammation (uveitis).”
- “We are on oral Methotrexate now and it seems to be working, but now have nausea and vomiting.”

Families’ experiences vary but many parents reported challenges in accessing current treatments. There can be a financial impact with the cost of medications. There are also costs associated with travel to treatment, time off of work, costs of physiotherapy, all of which generates financial stress. Families indicate receiving beneficial support from patient support programs offered by manufacturers. Most participants (80%) in the 2016 focus groups on biologics and biosimilars felt that a patient support program was very important or somewhat important. This is what we heard from families living with PJIA:

- “Cost to travel the 430kms to the nearest children's hospital for appointments is a challenge due to out of pocket expenses (gas, time off work, meals, lodging). We are thankful for having professional care and treatment, but it would be nice to have specialists in the field closer to home. Each trip costs us $250-$300, which we do not have. We do take advantage of Fuel the Care and Ronald McDonald House, but these aren't always available or guaranteed. Physiotherapy is not covered under our health plan, so this is very costly out of pocket as well.”
- “An infusion every four weeks requires time off work and school and while the cost is manageable due to drug coverage, it still all adds up after sometimes multiple hospital trips in a month.”
- “Our family's group benefits will expire within the next two months...we're hoping we'll be able to access financial support.”
- “We live in a smaller city and have to travel to Toronto or Mississauga for doctors and any other support. It is very isolating for our family. No peer to peer support unless I, as a parent, start it. We can't seem to control her pain.”
- “We have done physiotherapy in the past but the cost was prohibitive, even with coverage through my workplace it does not cover that many appointments. The cost to me to miss work for his multiple appointments is also significant and has lead to hardship.”

- “Both times hospital set us up with assistance programs to access nurses to teach about giving the needle as well as covering the cost of the drug while waiting for insurance to kick in… No side effects and child enjoys going to hospital as the nurses are amazing.”
- “We have benefits through my husband's place of employment and all medication has been covered 100%.”
- “No hardships for our family in regards to accessing treatment as we live in a large centre with a great paediatric rheumatology program as well as having excellent health insurance through work.”
- “The support program connected to the biologic medication has been very helpful in accessing treatment since our family does not have drug benefit coverage through our employers.”
- “Patient assistance support programs (guidance and financial) are very good, and very appreciated… traveling with drugs requiring refrigeration is a strain, as well as going through airport security with gel packs and syringes.”
- “Patient assistance/support programs have never been offered to us. Many pharmacies/pharmacists are unfamiliar with biologics. Access to treatments takes time (Exceptional Drug Status Approval process in Manitoba).”

Impact on Caregivers

PJIA can have an immense emotional toll on both the child and their families. It is challenging when you feel you have limited control over the health of your child and this can cause ongoing stress, fatigue and anxiety. There is enormous stress for both the child and caregivers when the disease is not well managed. All the care activities around a child living with a chronic disease: medical appointments; administering medication; dealing with side effects; working with the school; balancing parental work obligations and family commitments have an enormous toll. PJIA impacts the whole family. Families have told us:

- “JIA has made a severe impact not only on our seven year old daughter, but our whole family. She has had emotional/psychological side effects, she has felt she does not belong and feels she does not fit in because she can't participate in functions with her friends and be comfortable. This has an emotional impact on both her father and I. She had severe fatigue during the summer months. Coming from a child who dances and sings in her sleep, we went several months without hearing even such a lyric out of her. The first sign of her feeling better, was her dancing! She was limited to what she could do, but swimming and riding bike were her highlights of summer. We have to choose family vacations that don't require a lot of walking. We have even put Disney World off until we have her JIA under control.”
- “It was overwhelming to deal with the PJIA and the emotional effects on my daughter. It's been a long journey to go through physical therapy, doctor visits, medication side effects, emotional effects, etc.”
- “It is hard for my child to understand why she has to get injections and why there are a large number of doctor’s appointments all the time. There are some emotional challenges day to day.”
- “Migrating healthcare from "managed by parent" to "managed by child" as they become teens and young adults is problematic, particularly if a child was diagnosed as a young child. Treatment days are always "dreaded" and stressful. Potential side effects always lurk in the back of a parent's mind, and soon, probably the young adult child. If the child were to quit the medicine regime, the disease(s) return is a very frightening alternative as a parent.”
- “The treatment really doesn't significantly affect us. As long as the PJIA is controlled, it doesn't significantly affect us either.”
- “Limits travel because of medication and appointments. Appointment scheduling around work and other commitments is very stressful. Side effects and symptoms are difficult for us to manage or provide comfort/relief and so everyone is frustrated that there is nothing we can do.”
- “My daughter has an anxiety disorder and OCD. I often wonder how much of her life with pain and arthritis has contributed to the onset of her mental health challenges. It is a financial burden I have to miss work a lot and she misses a lot of school. There is no coordination of community services and health supports. We are often exhausted.”
- “Mainly the effect is needing time off work for treatments and appointments which is difficult for two working parents. More emotional stress at the beginning when could not find a treatment that worked. Me (the mom) cried a lot.”
- “There have been many challenges for our family since our child's diagnosis. It has very difficult for our child to accept her condition and have sought out professional assessment and treatment for mental health issues. Has difficulty understanding the randomness of her illness and often wonders "why her"/did she do something "bad" to deserve the diagnosis. She finds it difficult to cope with "not knowing" when a flare is going to happen which affects her ability to participate in athletic competitions for which

she has trained hard for. A recent trip to New York was affected her ability to walk for long distances which impacted the whole family, including her brother. Even with biologic treatment, she is often in some pain/discomfort. My husband and I worry a great deal about her future health."

- "Having a child with PJIA is very stressful. We never know how it will affect her day. She often feels very defeated and as a result we all take part in therapy to help deal with the disease and help her."
- "We have faced huge emotional challenges as a family. We have attended counselling to deal with behavioural issues of our daughter. Anger, crying, acting out etc. It's a daily struggle. Also the physical challenges...assist her with showering, combing hair although this is getting better the older she gets. Also anytime we travel or visit places, we have to rent a wheelchair as she does not have a lot of endurance. When she first started on Humira she would have massive meltdowns. That has gotten better over time. It has been very draining on the family."
- "Time taken for caregiving, medication administration and planning, physiotherapy, management of side effects all take time away from daily routine and lifestyle that impacts the entire family. Emotional/psychological effects are numerous and constant; worry/stress about flares or acquiring infections due to immunocompromised status; financial implications of costly drugs, lost time off work for appointments, sickness, etc.; not being able to work full-time, etc."
- "Every day is impacted by my son pain, it is an ongoing stress. We never know day-to-day and even hour-to-hour how he is going to be. He misses a lot of school and social activities due to pain and fatigue, and as a result I miss a lot of work. My son has developed stomach pain and GI concerns as a result of long-term anti-inflammatory use."
- "There are SO many challenges that come with the disease for our family and I'm sure many more. Fortunately I am lucky enough to be able to stay home. I don't think working would be an option since diagnosis. Between the rheumatologist, pediatrician, physiotherapist, ophthalmologist, X-rays, MRI, and blood work, it would be near impossible. This on top of regular appointments and everyday life. We also have other children and my husband works 50-60 hours a week. We are not from London, so there is a lot of driving and parking challenges as well. Having a chronically ill child not only takes a toll on your physical but also mental well-being. You are always worrying and wondering, wishing there was a way to take their pain or trade places with them. It's mentally draining to see your child sick, in pain or upset because of their disease. Side effects do create challenges for my child. She feels sick a lot and ends up with every bug going around. I'm sure it's exhausting and feels unfair to her but she knows the medications work and makes the decision to continue with them. These kids who deal with the disease and effects of treatment on a day-to-day basis are some of the strongest most resilient kids I have ever seen. I know a lot of adults who couldn't handle what they do!"
- "The challenges for our family is that we have a child with a chronic illness, diagnosed at 18 months and still in active treatment 13 years later. Even though she is doing well she is not able to partake in all activities; tires easily and does not have the physical endurance of our other children. The older she gets the more she realizes she is different and this comes with its own emotional stress."

Information About the SEB Being Reviewed

What Are Patients' Expectations for the SEB?

Since biosimilars/ subsequent entry biologics are still fairly new in Canada, caregivers are often not aware of their existence. There is also some confusion about what biosimilars are and what they represent as a potential treatment option. The participants in the 2016 focus groups on biologics and biosimilars reported having a poor understanding of biosimilars. A number of the focus group participants reported that they had never heard of biosimilars. What we heard from parents:

- "Enbrel has enabled us to manage her PJIA. The limited side effects are also clear advantage. The cost is a clear disadvantage."
- "I would expect biosimilars to work the EXACT same way that the actual biologic does. My concern is that they will NOT because they are NOT generic replications. These drugs may not be vetted. They are basically "new" drugs, and have no usage history. This needs to be addressed before I would put my child on this type of drug. Of course, less cost to obtain is a perceived advantage. I'm not sure how significant the cost reduction is versus the potential additional risks of the new biosimilar drug. I also don't know if a biosimilar will treat more than one disease which some true biologics currently do."
- "Clear advantage of biosimilars is the financial cost, but the disadvantage is the list of "non-clinically meaningful" ingredients can vary causing possible allergic reactions (e.g. gluten, eggs)."

- “Biosimilars I’m not to sure about them but I’m hoping for companies to find a medication that is not painful and doesn't have so many side effects. These kids go through enough without having side effects and to have to deal with them day to day. Mental health is the main part we need to put more efforts into.”
- “I would like to see our daughter run and play and be as active as any other 11 year old. I do worry about long term effects on her body/system taking Humira and/or a biosimilar.”
- “I am hoping for biosimilars that they are easier to administer (i.e., subcutaneous injection), more cost effective, and effective in treating arthritis and its complications (uveitis).”
- “I have no experience with biosimilars.”
- “Infusion once a month is nice, but a pill may be easier?”
- “I guess my biggest expectation is that biosimilars will completely control my child’s inflammation with no side effects. It's one thing to be concerned with daily or obvious side effects but I also worry about long-term effects. The chance of increased cancer risk is a real concern.”
- “I'm not familiar with the meaning of biosimilars.”

Key Messages

It is The Arthritis Society’s position that:

- biosimilars have a role to play in the care and management of those living with inflammatory arthritis;
- biosimilars will offer more choice for those living with inflammatory arthritis and have the potential to lower health care costs and increase access to treatment;
- biosimilars, while similar to the innovator biologic, are not identical and cannot be considered generic versions of innovator biologics;
- consistent, universal, unique biosimilar naming practices should be implemented to facilitate tracking of what specific medication is received by a patient;
- a process for post-market surveillance must be put in place to track long-term safety and efficacy of biosimilars;
- all producers of biologic medications – whether innovator or biosimilar – should provide a robust program of patient and physician support; and
- until conclusive evidence determines that switching is safe, switching should not be permitted for patients who are stable on an existing course of biologic treatment except at the express discretion of the physician in consultation with their patient/ parent(s)/ legal guardian(s).

Additional Information

Please provide any additional information that would be helpful to CADTH, CDEC, and participating drug plans. This could include suggesting ways to improve the patient input process, indicating whether the questions are clear, etc.

Comments on Potential Ways SEBs Can be Used

CDR reviewers and CDEC members will not review or use information in Section 8; however, drug plans may consider this information in their decision-making.

Briefly provide your comments on the following scenarios or you may wish to provide other comments.

- The SEB will be used instead of the originator (reference/brand name) product with physician approval before patient receives any treatments
- The SEB would be replacing the originator product with physician approval once the patient has been on the originator product for a period of time, i.e. a one time switch
- The SEB will be used instead of the originator product without physician approval before patient receives any treatments
- The SEB would be replacing the originator product without physician approval once the patient has been on the originator product for a period of time
- Back and forth replacement between SEB and originator product without physician consent

The Arthritis Society approved a position paper "Access to Medication: Biosimilars" revised October 2016. Rather than provide comment on the scenarios above please find below excerpts from the paper that deal with the scenarios.

Issues

Therapeutic Substitution

Therapeutic substitution occurs when a pharmacist substitutes a chemically different drug for the drug that the physician actually prescribed. The drug substituted by the pharmacist usually belongs to the same pharmacologic class and or to the same therapeutic class. With respect to biosimilars, this kind of substitution is not currently permitted, and it is the Arthritis Society's position that it should not be permitted. Patients should receive only the specific drug that the physician has prescribed.

Substitution

Substitution or switching occurs when a patient passes from one biologic to a biosimilar drug (e.g.: switching between two different branded versions of infliximab). Since biologics and their counterpart biosimilars may have different chemical structures, it is not yet known what the effects of switching would be. Studies are under way to evaluate the impacts of switching. It is the Arthritis Society's position that until conclusive evidence determines that switching is safe, switching should not be permitted for patients who are stable on an existing course of treatment except at the express discretion of the physician in consultation with their patient.

Interchangeability

Interchangeability is when a pharmacist switches from a prescribed reference medication to a chemically identical generic medication where the indications are identical, where no contrary direction has been provided by the physician, and where the cost of the generic drug is lower. Health Canada has stated that "SEBs [Biosimilars] are not 'generic' biologics and authorization of an SEB [biosimilar] is not a declaration of pharmaceutical or therapeutic equivalence to the reference biologic drug." Health Canada "does not support automatic substitution of a SEB [biosimilar] for its reference biologic drug." This being stated, interchangeability of an innovator biologic drug with a biosimilar lies within the provinces' authorities**.**

Guiding Principles

- Safety is paramount and a patient-centred approach is crucial.
- While waiting for more conclusive evidence about the impact of switching from an innovator biologic drug to a biosimilar, decisions about substitution must be in the hands of people living with arthritis and their physician, not payers or policy makers.
- People living with arthritis and their physicians need access to information to make an informed choice about treatments.

Canadian Arthritis Patient Alliance (CAPA)

General Information

Name of the drug CADTH is reviewing and indication(s) of interest	TBC (Etanercept)
Indication of interest	Ankylosing Spondylitis (AS)
Name of the patient group	Canadian Arthritis Patient Alliance (CAPA)
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	n/a
Patient group's contact information:	
Email	contact@arthritispatient.ca
Telephone	[redacted]
Address	195 St. Patrick St., Unit 508 Toronto, ON M5T 2Y8
Website	www.arthritispatient.ca
Permission is granted to post this submission	Yes

How to Complete This Submission Template

Information Gathering

The information was obtained through personal experiences of the Board of The Canadian Arthritis Patient Alliance in living with inflammatory arthritis, in addition to many years of interfacing with our membership.

Information about the Submitting Patient Group

Submitting Patient Group

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 more effective advocates and to improve their quality of life. We assist members to become advocates not only for themselves but for all people with arthritis. CAPA believes the first expert on arthritis is the person who lives with arthritis - ours is a unique perspective. CAPA welcomes all Canadians with arthritis and those who support CAPA's goals to become members.

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, Amgen Canada, Eli Lilly, Hoffman-La Roche, Janssen, Purdue, Novartis, and UCB Pharma.

Additionally, CAPA has received support in the past from: Arthritis Alliance of Canada, The Arthritis Society, Canadian Institutes for Health Research (Institute for Musculoskeletal Health & Arthritis), Canadian Rheumatology Association, Ontario Rheumatology Association, Pfizer Canada, Rx&D, Schering Canada, the Scleroderma Society, and STA Communications.

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

None to declare.

Disease/Condition and Current Treatment Information

Impact of Condition on Patients

Though not as common as Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS) is another type of inflammatory arthritis that is a serious, debilitating autoimmune disease, affecting every aspect of a person's life. Patients can feel the onset of symptoms in their late teens to early 20s, and often times live for many years in extreme pain without an accurate diagnosis. Most patients have their own stories about their painful and often debilitating journeys to seek a correct diagnosis. Unlike RA, AS affects predominantly men, a pattern that is not well understood. Sometimes the symptoms of AS in women do not match those of their male counterparts, which makes diagnosis in this population even more challenging. As with other forms of inflammatory arthritis, there is currently no cure for AS – only ways to help alleviate symptoms and hopefully slow the progression of disease – it is a chronic illness that one lives for from the onset of symptoms until death.

AS is characterized by inflammation in the joints of the spine. This inflammation can spread to involve other parts of the spine and, in the most severe cases, involves the entire spine. As the inflammation continues and the body attempts to repair itself, new bone forms. This results in bones of the spine growing together (fusing), causing the spine to become very stiff and inflexible. Even though new bone has formed, the existing bone may become thin, increasing the risk of fractures.

AS is a challenging disease to manage and physicians and patients often try different drugs to find something that works well. Currently, there are no methods to assist physicians predict which patients will respond best to which therapies. In addition, a patient's immune system can adapt to a drug making it necessary to switch to another treatment when one becomes ineffective. Thus, patients require many potential medications as treatment response is impossible to predict and changes over time. Additionally, once a person's AS is relatively stable when on a therapy, there may be a real fear of changing medications for any reason.

For those whose AS is not well controlled, everyday activities, such as participating in school, holding a job, taking care of oneself and one's family, and other activities that the healthy general population simply take for granted, become very difficult. For example, one patient with longstanding AS reported having to get up for work 3-4 hours before his work shift in order to ensure he could adequately deal with the morning stiffness and pain of AS.

It is vital that inflammation be controlled early and well so that patients can continue to be productive members of society and of their families. We can imagine that the economic benefits to society of keeping people living with AS in the work force and as productive members of society are greater than those required of the healthcare system if patients do not receive treatments for their disease.

Patients' Experiences with the Current Treatment

While there are both small molecule and biologic disease-modifying anti-rheumatic drugs (DMARDs) available to treat AS, as per the instructions above, we have focussed this section on the originator drug to TBC which is also the molecule etanercept, or known by the trade name Enbrel.

Since the biology of a person's AS response to medications is not well understood currently or able to be predicted, patients with AS undergo a process of trial and error with their physician's intuition guiding them to find the most suitable treatment for their AS. Some patients experience long periods of responding well to a drug (meaning that their symptoms are well-controlled), while others, for reasons unknown, will need to be exposed to many different drugs over their lifetime to achieve the best treatment of their AS. The

originator drug, Enbrel, is no different for patients. While Enbrel works very well (efficaciously and safely) for some, for others it is not as efficacious (sometimes immediately, or sometimes over time as a patient's immune system adapts to it), and as a result, patients and their physicians will have a conversation and decide whether or not to change the patients' pharmaceutical therapy.

For Enbrel (originator drug), the most common adverse reactions are infections, allergic reactions and injection-site reactions. Since TBC is a slightly different version of etanercept than Enbrel, it is safe to assume that TBC's adverse effects will be similar to Enbrel - offering patients this biosimilar will not alleviate typical side effects that are also found with Enbrel.

With the advent of biologics for the treatment of AS, so has the need been created for either infusions or injections. Some patients have scar tissue and site reactions from injections. In the most extreme case, a patient would have been giving themselves injections for 14 years (since biologics were first approved in 2000) – a reality faced by many patients living with AS. If TBC is approved for the formulary, these will remain items that patients are required to deal with to receive treatment.

Biologics are extremely costly for patients – while some patients have extended health insurance, others do not, and either rely on their own resources or those of their provincial Ministries of Health for assistance. Worrying about the cost/access to a medication in addition to trying to manage one's own disease can be very stressful.

Patients rely on support programs provided by the originator company to help them maintain efficient access to receiving their medication and to be informed and properly taught about a medication's administration, assistance with drug cost coverage, and for general questions about their treatment. This patient support program is an important part of a patient receiving the originator drug.

Impact on Caregivers

It is always assumed that medications for people living with AS are a choice made by a patient and their physician. Depending on a person's ability to cope with activities of daily living and their ability to still be employed, caregivers of people living with AS are relied upon in varying capacities. In some cases, caregivers are required to assist with simple tasks such as bathing, getting in and out of bed, getting dressed, even using the toilet. The emotional toll on both patients and caregivers in this type of situation cannot be underscored enough. In other situations, a caregiver's burden may not be as great, perhaps giving the patient their injection or need to take over family responsibilities while the patient is receiving their infusion. Living with a chronic condition as potentially debilitating as AS can affect a person profoundly psychologically – including caregivers. Additionally, when patients do not have drug coverage options, if one's spouse is their caregiver, this adds to the burden of disease in ways nearly unimaginable.

It is important to highlight that AS affects patients and caregivers and family members profoundly, in all aspects of their lives – and does so from before their diagnosis, throughout their lives.

Information About the Biosimilar Being Reviewed

What Are Patients' Expectations for the Biosimilar?

It is always assumed that medications for people living with AS are a choice made by a patient and their physician. Since this is only the second biosimilar for AS under consideration in Canada, there are a number of perceptions in the patient community about these, which include:

- Potentially being more economic than the originator drugs
- Potentially not having well-established patient support programs like the originator therapeutic
- Not having a well-established post-market surveillance program (and associated safety concerns)
- Not having clinical trial size populations that match that of the originator drug (and hence again, safety and efficacy concerns), and feeling like the patient is being placed in a real-life clinical trial without the same safety monitoring that a trial has
- Providing another option for patients who have not responded well to the originator molecule, or whose immune system has adapted to it, although not being sure that since the biosimilar addresses the same pathway as the originator, and is similar enough to the originator that it will not provide much of an advantage

- Potential confusion at the pharmacy and by healthcare providers that since the biosimilar has the identical INN name as the originator drug that there will be inadvertent switching at the pharmacy level, which could potentially result in serious side effects/adverse effects for patients
- Potential to be 'switched' to the biosimilar by one's insurer due to potential cost, and without being able to make an informed and evidence-based choice in partnership with one's healthcare provider.

Overall, access to biosimilar's provides another potential treatment for patients with AS, with significant concerns and perceptions (positive and negative) which are all highlighted above.

Key Messages

Key submission messages include:

- AS is a seriously debilitating chronic illness that affects all aspects of a person's life
- Therapeutic options are required for patients who live with ankylosing spondylitis – biosimilar's are part of that repertoire of therapies, and for which we support as a treatment for patients who are biologic-naïve or who are being switched to another biologic due to response failure after an informed discussion and decision made with their physician
- While biosimilar's are important opportunities for patients as therapies, there are several perceptions and concerns that the patient community has about them, and which we ask CDEC to seriously consider in its review
- This biosimilar molecule has the identical INN to the originator drug – there are significant issues and concerns for patients around this, including being inadvertently exposed to the wrong drug
- Patient support programs are an important part of biologic therapies and are an integral part of a patient's experience with these severely immuno-suppressive medications.

Additional Information

N/A

Comments on Potential Ways Biosimilar's Can be Used

- CAPA is supportive of biosimilars for biologic naive patients, to individuals who are considering a switch and to patients who are fully informed and understands the decision which was made with their physician.
- We are not supportive of patients switching back and forth from the originator drug to the biosimilar, as it can increase a patient's risk of immunogenicity side effects. This is a significant patient safety issue and could potentially affect patient response to even the originator drug. However, if the patient wants to switch from the originator to the biosimilar we are supportive. As mentioned previously, it is our priority that patients are making an informed decision and they are fully aware of the potential consequences.
- Post market safety is still a concern for CAPA because of the naming issue, otherwise the same regulations are in place for biosimilars as all other drugs.
- CAPA supports biosimilar's as options for patients when the biosimilar has undergone rigorous clinical trials for an indication, for biologic-naïve patients, or for patients who are being put on a new biologic because of failure to respond to another. This is only after careful consideration, dialogue, and informed conversation between physician and patient and is a decision that only they should undertake, not one that should be pushed on them in response to cost, etc.

It is unclear why an opinion is even asked on these sections. If the reader of this submission would simply put themselves in a patient's position, and if they too had lived with AS, they would read the above statements and call them all unacceptable, and may even take it so far as to call them unethical. Physicians work with their patients to provide the best medications possible for the patient – it is doubtful that they would also stand for the statements above.

Canadian Spondylitis Association

General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Etanercept (Marketed by Sandoz Canada)
Indication of interest	Ankylosing Spondylitis
Name of the patient group	Canadian Spondylitis Association
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	
Patient group's contact information:	
Email	info@spondylitis.ca
Telephone	(416) 694-5493
Address	18 Long Crescent, Toronto, On. M4E 1N6
Website	www.spondylitis.ca
Permission is granted to post this submission	Yes

How to Complete This Submission Template

Information Gathering

Information was gathered through lived experiences and requests put out by email to our membership (approximately 1,500 members for whom we have email addresses) and through our Facebook group (>800 members). All members were invited to answer the specific questions outlined in this template. The information so gathered (four patients using Enbrel responded; there were no responses from any patients using an etanercept biosimilar) was complemented by information gleaned from our Facebook group discussions and from many conversations amongst Board members (all of whom live with Spondyloarthritis) and patients, particularly at our forums.

Some information was taken from previous requests for patient input on other drugs indicated for ankylosing spondylitis. This information was limited to the lived experience with AS in Sections 4.1 and 4.3

Information About the Submitting Patient Group

Submitting Patient Group

The Canadian Spondylitis Association is an all-volunteer run patient organization to support, educate and advocate for those living with Spondyloarthritis. The aims of the Association are to create awareness of Spondyloarthritis with the objective of reducing the time from onset of disease until diagnosis, to provide information and education (mainly through patient forums with expert speakers) to those living with Spondyloarthritis, including caregivers and family, to enable them to better manage their disease, and to advocate

for equal access to treatment options. The Association also facilitates discussion amongst its members and support for each other through its use of social media.

The Association's membership is comprised of individuals from all Provinces and Territories who live with Axial or Peripheral Spondyloarthritis, which includes Ankylosing Spondylitis and Psoriatic Arthritis.

Since inception in 2006, the Association has grown to a membership of over 1,800.

Conflict of Interest Declarations

The Canadian Spondylitis Association has received restricted educational and developmental grants from AbbVie, Amgen and Janssen, and restricted travel grants from UCB Canada.

The President, Michael Mallinson, has received honoraria from AbbVie (indirectly), Novartis and UCB Canada.

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

Although we have received funding as noted above, we have no conflicts of interest to declare with respect to compiling the information submitted herein.

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

Although we have received funding as noted above, we have no conflicts of interest to declare with respect to compiling the information submitted herein.

Disease/Condition and Current Treatment Information

Impact of Condition on Patients

Ankylosing spondylitis ('AS') is a painful, progressive form of inflammatory arthritis characterized by inflammation of the sacroiliac joints. Symptoms of AS vary greatly from one individual to another. However, common symptoms are inflammatory pain in the spine, neck, hips and legs, with many experiencing pain in the shoulders, eyes, and feet. Stiffness, particularly in the morning, which can take up to an hour to relieve, is universal. Limited motion due to stiffness and fusing of the vertebrae is often reported. Fatigue, depression and anxiety are typical.

Patients report difficulty with completing daily routines and household chores, caring for their family, participating in sports, lifting up children, sleeping, being in bed, standing for long periods, walking, and sitting for long periods. They also report co-morbidities such as uveitis and Inflammatory Bowel Disease, stomach issues possibly caused by medications as well as social isolation brought on by pain and depression.

Many patients report the impact of being hit by this disease when they are young and active. AS typically strikes individuals, men and women, between the ages of 15 and 45. As one patient said "My daily activities went from always on the go to can't get up and go." The impact on work can be significant. Severely affected patients face long-term disability and leave the work force. Several patients reported being on long-term disability, two for eight years, one for seven years, another for five years and one for two years. Others find it difficult to sit at work, concentrate and make it through the day.

For other patients, the impact of the disease means giving up much-loved recreational activities, particularly sports, or struggling to get through daily routines such as dressing and cooking. Women reported difficulties in managing themselves and in caring for their children.

Relationships suffer. Separation and or divorce is reported because of the strains AS put on their marriages by the burden of the disease was too much for the spouses to bear. Others report supportive spouses but worry about how long the relationship will last.

Parents also worry about the effects their disease have on their children, including not being able to play and tussle with them and a general feeling of inadequacy in responding to their needs.

A typical quality of life issue that comes up repeatedly is the ability to function well on one day but feel totally exhausted and incapacitated the next. This is a fact that is not well understood by employers, family and caregivers, nor, indeed, by patients themselves. The inability to fulfill plans because of painful episodes adds to the frustration of living with the disease.

The psychological impact of the disease because of pain, fatigue and the resulting frustration and depression is often cited by patients. One patient spoke of not being able to do the things for her children that other parents can do and her feelings about this.

The most important aspects of the disease to control are inflammation and pain and the ability to have a good night's rest. All responding patients reported interrupted sleep, often having to alternate between bed and sitting because laying down is painful.

A quotation from an AS patient is relevant because it is a common theme: "So no, I'm not on disability, but I changed every aspect of my life to accommodate this condition. I'm just fortunate enough that my husband supported this, what about people that are not in this scenario!?"

Patients' Experiences with the Current Treatment

All respondents to our request for input are on the originator drug and report favourable outcomes, with limitations. Generally the originator biologic allows patients to function day-to-day even if they still experience some pain and stiffness. Some patients experience complete relief except during flare-ups, while for others the originator drug improves their condition, but not wholly, while others experience smaller improvements. A consensus was that without the originator biologic patients would be worse, to the point of not being able to function and having to rely totally on a caregiver. It was notable that three of the respondents had come to the originator etanercept after trying other anti-TNF biologics but failing on them.

One respondent has moved to an IL-17 inhibitor biologic because of lack of efficacy with the originator etanercept. He experienced severe side effects and had no relief from pain with etanercept. His pain has been reduced only by the use of cannabis and kratom.

Patients are generally satisfied with the originator biologics and the array of medications and treatments (physiotherapy, massage therapy, hot water therapy) available to treat their disease and co-morbidities, although there were a couple of comments that more pharmacological treatments for pain are required.. One patient expressed the need for more social contact; all commented on the high cost of the originator drug and non-pharmaceutical treatments.

Patients are aware of the side effects of the originator biologic, particularly injection site reactions, but seem to accept them as part of the risk-reward calculation of being on a biologic. Because the originator drug is effective for them, they worry about eventual loss of efficacy.

All respondents were grateful for their drug and benefit plans from work, including those that apply to long-term disability recipients. With one exception, they did not report any financial hardship related to taking the originator drug.

All spoke very positively about the patient assistance program offered by the manufacturer of the originator biologic, seeing it as an essential service to them because of the continuity of care and records, and the fact that someone is always available to them on call. The lack of such a support program was viewed as very disadvantageous.

Impact on Caregivers

Patients report there are many difficulties for their families, who must adjust to their chronic pain and lack of functionality and ability. This puts tremendous pressure on families, particularly with child-rearing, where patients are acutely aware of their spouses' single parenting instead of dual parenting with them. We note that AS is a young persons' disease, typically starting in the 15-35 years age bracket, which cover the child-bearing ages.

Patients note that while their family and caregivers are supportive, there is not much that they can do to be supportive to them when they are in pain or mental and emotional issues arise. The biggest challenge for caregivers is in understanding the disease, its

manifestations including extra-articular manifestations, and what it can do to people, physically and mentally, and how it can limit them. This in itself is stressful to caregivers, as well as seeing their loved ones suffer. There is a financial burden to parents as they look after their children.

A patient said that when she went on etanercept, her husband said that he had got his wife back, such was the positive effect of the drug. However, although she could now climb stairs unaided for example, the couple still has to divide jobs so that the husband does the carrying and lifting.

Generally, caregivers must cope with a patient who has unpredictable good days and bad, who may need very personal care (dressing, toilet) at times and whose outcomes are not clear over a life time with the disease. It is emotionally draining for them and restricts their own lives when they are tied into caregiver routines.

Information About the SEB Being Reviewed

What Are Patients' Expectations for the SEB?

Patients in general do not know a great deal about biosimilars. They do seem to know that biosimilars are cheaper than the originator biologic, but some worry that a change from an originator drug to its biosimilar may not work for them. Others, not realizing the close similarity in safety and efficacy of biosimilars to the originator drug, feel that biosimilars offer a different course of treatment. This is perhaps due to the initial messaging about biosimilars that they 'were similar to but not identical to the original biologic'.

Other perceived advantages of a biosimilar are its greater accessibility due to lower cost, and perhaps a reduction in paperwork and process to get on the medication.

Patients hope that biosimilars will slow disease progression and reduce pain and will be cheaper than the originator drug.

It is the position of the Canadian Spondylitis Association to welcome biosimilars as a cheaper alternative to the originator biologics. Given the studies now showing that the safety and efficacy of biosimilars is very comparable to the originator drugs, our position is that prescriptions for a biologic therapy should favour the biosimilar.

Key Messages

1. AS is a serious progressive disease marked by inflammation and pain. There is no cure and learning to best manage one's disease is the ultimate objective.
2. Current biologic drugs are a great improvement in treatment options but are not optimal for everyone.
3. The burden of the disease on the individual, their caregivers and society is considerable.
4. Patient support programs offered by the manufacturers of originator biologics are highly regarded and viewed as indispensable.
5. Biosimilars are welcome as a cheaper cost treatment option. Patients in general do not understand what biosimilars are and their safety and efficacy; a lot more education has to be provided to them.

Comments on Potential Ways SEBs Can be Used

CDR reviewers and CDEC members will not review or use information in Section 8; however, drug plans may consider this information in their decision-making.

It is the position of the Canadian Spondylitis Association to welcome biosimilars as a cheaper alternative to the originator biologics to help with making health care systems more sustainable.

Given the studies now showing that the safety and efficacy of biosimilars is very comparable to the originator drugs, our position is that prescriptions for a biologic therapy should favour the biosimilar even in cases where this may mean switching from the originator drug.

Canadian Arthritis Patient Alliance (CAPA)

General Information

Name of the drug CADTH is reviewing and indication(s) of interest	TBC (Etanercept)
Indication of interest	Juvenile Idiopathic Arthritis
Name of the patient group	Canadian Arthritis Patient Alliance (CAPA)
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
Email	[redacted]
Telephone number(s)	705-929-1135
Name of author (if different)	N/A
Patient group's contact information:	
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Telephone	as above
Address	195 St. Patrick St., Unit 508, Toronto, ON M5T 2Y8
Website	www.arthritispatient.ca
Permission is granted to post this submission	Yes

How to Complete This Submission Template

Information Gathering

The information was obtained through personal experiences of the Board of The Canadian Arthritis Patient Alliance in living with inflammatory arthritis, in addition to many years of interfacing with our membership.

Information About the Submitting Patient Group

Submitting Patient Group

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 more effective advocates and to improve their quality of life. We assist members to become advocates not only for themselves but for all people with arthritis. CAPA believes the first expert on arthritis is the person who lives with arthritis - ours is a unique perspective. CAPA welcomes all Canadians with arthritis and those who support CAPA's goals to become members.

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, Amgen Canada, Eli Lilly, Hoffman-La Roche, Janssen, Purdue, Novartis, and UCB Pharma.

Additionally, CAPA has received support in the past from: Arthritis Alliance of Canada, The Arthritis Society, Canadian Institutes for Health Research (Institute for Musculoskeletal Health & Arthritis), Canadian Rheumatology Association, Ontario Rheumatology Association, Pfizer Canada, Rx&D, Schering Canada, the Scleroderma Society, and STA Communications.

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

None to declare.

Disease/Condition and Current Treatment Information

Impact of Condition on Patients

Juvenile idiopathic arthritis (JIA) affects about 1 child in every 1,000. The term *idiopathic* means “of unknown origin.” JIA can affect children at any age, although rarely in the first six months of life and is the most common type of arthritis for people under the age of 17. JIA causes persistent joint pain, swelling and stiffness. Some children may experience symptoms for only a few months, while others have symptoms for the rest of their lives.

Children who experience symptoms for the rest of their lives, often experience functional impairment due to joint and back pain, heel pain, swelling of joints and morning stiffness, contractures, pain, and anterior uveitis leading to blindness. As children who have juvenile arthritis reach adulthood, they face possible continuing disease activity, medication-associated morbidity, and life-long disability and risk for emotional and social dysfunction. Treatment of juvenile rheumatoid arthritis focuses on controlling pain, improving function and preventing joint damage. Growing up with arthritis can be challenging. However, with care from a team of rheumatology professionals, most children with arthritis live full and active lives. There are various types of childhood arthritis, which can last from several months to many years. In every instance, early diagnosis and treatment can help avoid joint damage.

There are six JIA subtypes. Systemic JIA is considered an autoinflammatory disease. The other types are considered autoimmune diseases. A healthy immune system fights invaders, such as viruses and bacteria. In people with autoimmune or inflammatory diseases, the immune system doesn’t work properly. It becomes overactive even when there is no infection to fight, or it mistakenly attacks healthy cells and tissues. The first type is systemic JIA which causes inflammation in one or more joints and is often accompanied by a high spiking fever (103°F or higher) that lasts at least 2 weeks and a skin rash. Another sub-type, is oligoarticular JIA causes arthritis in four or fewer larger joints and is often accompanied by uveitis. While polyarticular JIA, causes inflammation in five or more joints, often the small joints of the fingers and hands, but weight-bearing joints and the jaw can also be affected. The fourth sub-type is juvenile psoriatic arthritis which involves arthritis that usually occurs in combination with psoriasis. The psoriasis may begin many years before any joint symptoms become apparent. There is also enthesitis-related JIA which is characterized by tenderness where the bone meets a tendon, ligament or other connective tissue, and is accompanied by joint inflammation of arthritis. The final sub-type of JIA is undifferentiated arthritis. This type is used to describe a juvenile arthritis that does not fit into any of the above types, or that involves symptoms spanning two or more subtypes.

Researchers are uncertain about what causes JIA. There is no evidence that foods, toxins, allergies or lack of vitamins play a role in developing the disease. Current research indicates that there is a genetic predisposition to JIA. More than a dozen genetic markers have been identified for JIA, and hundreds more are being considered. However, genetic markers alone can’t determine who will get arthritis. Researchers believe that a trigger, like a virus, can start the disease process in those children with the genetic tendency.

JIA is a challenging disease to manage and physicians, patients and parents/ guardian often have to try different drugs to find something that works well – there are currently no methods that help physicians (and patients) predict which patients will respond best to which therapies. 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.

For those whose JIA is not well controlled, day to day activities, such as participating school and extra-curricular activities, walking, cooking, shopping, chores, and social activities can be extremely difficult and in some cases, impossible to undertake. For example, simply getting out of bed could be a monumental challenge, and putting on one's clothes could take multiple times the energy and amount of time compared to someone without JIA. Imagine spending hours in the morning just to get out of bed, bathed and dressed. Tasks that were once a simple part of your day and taken for granted become all energy consuming. For example, some children are unable to do the buttons on their shirt, brush their hair or maintain basic hygienic needs due to pain and lack of range of motion associated with inflammation. It is vital that inflammation be controlled early and well so that patients can continue to be productive members of society.

Patients' Experiences with the Current Treatment

While there are both small molecule and biologic disease-modifying anti-rheumatic drugs (DMARDs) available to treat JIA, as per the instructions above, we have focussed this section on the originator drug to TBC which is also the molecule etanercept, or known by the trade name Enbrel.

Since the biology of a child's response to medications is not currently well understood or able to be predicted, children with JIA must undergo trial and error in finding the most suitable treatment for their disease. Some children respond well to a medication (meaning that their symptoms are well-controlled for long periods of time), while others, for reasons unknown, will need to be try many different drugs over to determine the best combination of medication to control their disease. The originator drug, Enbrel, is no different for patients. While Enbrel works very well (efficaciously and safely) for some, for others it is not as efficacious (sometimes immediately, or sometimes over time as a patient's immune system adapts to it), and thus, patients, parents and their physicians will have a conversation and decide whether to change the patients' pharmaceutical therapy.

For Enbrel (originator drug), the most common adverse reactions are infections, allergic reactions and injection-site reactions. Since TBC is a slightly different version of etanercept than Enbrel, it is safe to assume that TBC's adverse effects will be similar to Enbrel - offering patients this biosimilar will not alleviate typical side effects that are also found with Enbrel.

With the advent of biologics for the treatment of JIA, so has the need been created for either infusions or injections. Some patients have scar tissue and site reactions from injections. In the most extreme case, a patient would have been giving themselves injections for over 10 years (since biologics were first approved in 2000) – a reality faced by many patients living with JIA. If TBC is approved for the formulary, these will remain items that patients are required to deal with to receive treatment.

Biologics are extremely costly for patients and their parents – while some patients have extended health insurance through their parents, others do not, and either rely on their own resources or those of their provincial Ministries of Health for assistance.

Patients rely on support programs provided by the originator company to help them maintain efficient access to receiving their medication and to be informed and properly taught about a medication's administration, assistance with drug cost coverage, and for general questions about their treatment. The patient support program is an important part of a patient receiving the originator drug.

Impact on Caregivers

Individuals who have a child with JIA report significant work-time loss as compared to parents/ guardians without a child living with JIA, particularly during the year following their child's diagnosis. Parents often must miss days of work to care for their sick children. Parents have to bring children to their physician's regular appointments, and additional urgent and emergency room visits during disease flares or infections (since they are often immunocompromised). In addition, parents have to schedule appointments to obtain laboratory tests and for imaging appointments. Parents have to frequently refill one or more medications. These activities can result in significant emotional, financial and logistical burden for the parents.

In some cases, parents/ guardians are required to assist with simple tasks such as bathing, getting in and out of bed, getting dressed, even using the toilet. The emotional toll on both patients and caregivers in this type of situation cannot be underscored enough.

Living with a chronic condition as potentially debilitating as JIA can affect a person profoundly psychologically – including caregivers. Additionally, when patient's parents or guardian do not have drug coverage options, this adds to the burden of disease in ways nearly unimaginable. It is important to highlight that JIA affects patients and caregivers and family members profoundly, in all aspects of their lives – and does so from before their diagnosis, throughout their lives.

Information About the Biosimilar Being Reviewed

What Are Patients' Expectations for the Biosimilar?

It is always assumed that medications for people living with JIA are a choice made by a patient, parent, and their physician Since this is only the second biosimilar for JIA under consideration in Canada, there are several perceptions in the patient community about these, which include:

- Potentially being more economic than the originator drugs
- Potentially not having well-established patient support programs like the originator therapeutic
- Not having a well-established post-market surveillance program (and associated safety concerns)
- Not having clinical trial size populations that match that of the originator drug (and hence again, safety and efficacy concerns), and feeling like the patient is being placed in a real-life clinical trial without the same safety monitoring that a trial has
- Providing another option for patients who have not responded well to the originator molecule, or whose immune system has adapted to it, although not being sure that since the biosimilar addresses the same pathway as the originator, and is similar enough to the originator that it will not provide much of an advantage
- Potential confusion at the pharmacy and by healthcare providers that since the biosimilar has the identical INN name as the originator drug that there will be inadvertent switching at the pharmacy level, which could potentially result in serious side effects/adverse effects for patients
- Potential to be 'switched' to the biosimilar by one's insurer due to potential cost, and without being able to make an informed and evidence-based choice in partnership with one's healthcare provider.

Overall, access to biosimilar's provides another potential treatment for patients with RA, with significant concerns and perceptions (positive and negative) which are all highlighted above.

Key Messages

Key submission messages include:

- JIA is a seriously debilitating chronic illness that affects all aspects of a child's life and requires extensive parental support and assistance.
- Therapeutic options are required for patients who live with JIA – biosimilar's are part of that repertoire of therapies, and for which we support as a treatment for patients who are biologic-naïve or who are being switched to another biologic due to response failure after an informed discussion and decision made with their physician
- While biosimilar's are important opportunities for patients as therapies, there are several perceptions and concerns that the patient community has about them, and which we ask CDEC to seriously consider in its review
- This biosimilar molecule has the identical INN to the originator drug – there are significant issues and concerns for patients around this, including being inadvertently exposed to the wrong drug
- Patient support programs are an important part of biologic therapies and are an integral part of a patient's experience with these severely immuno-suppressive medications.

Additional Information

N/A

Comments on Potential Ways Biosimilar's Can be Used

- CAPA is supportive of biosimilars for biologic naive patients, to individuals who are considering a switch and to patients who are fully informed and understands the decision which was made with their physician.
- We are not supportive of patients switching back and forth from the originator drug to the biosimilar, as it can increase a patient's risk of immunogenicity side effects. This is a significant patient safety issue and could potentially affect patient response to even the originator drug. However, if the patient wants to switch from the originator to the biosimilar we are supportive. As mentioned previously, it is our priority that patients are making an informed decision and they are fully aware of the potential consequences.
- Post market safety is still a concern for CAPA because of the naming issue, otherwise the same regulations are in place for biosimilars as all other drugs.
- CAPA supports biosimilar's as options for patients when the biosimilar has undergone rigorous clinical trials for an indication, for biologic-naïve patients, or for patients who are being put on a new biologic because of failure to respond to another. This is only after careful consideration, dialogue, and informed conversation between physician and patient and is a decision that only they should undertake, not one that should be pushed on them in response to cost, etc.

It is unclear why an opinion is even asked on these sections. If the reader of this submission would simply put themselves in the position of a parent caring for a child living with JIA, if they would read the above statements and call them all unacceptable, and may even take it so far as to call them unethical. Physicians work with their patients to provide the best medications possible for the patient – it is doubtful that they would also stand for the statements above.

CADTH

Canadian Arthritis Patient Alliance (CAPA)

General Information

Name of the drug CADTH is reviewing and indication(s) of interest	TBC (Etanercept)
Indication of interest	Rheumatoid Arthritis
Name of the patient group	Canadian Arthritis Patient Alliance (CAPA)
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	N/A
Patient group's contact information:	
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Telephone	705-929-1135
Address	195 St. Patrick St., Unit 508 Toronto, ON M5T 2Y8
Website	www.arthritispatient.ca
Permission is granted to post this submission	Yes

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

None to declare.

Disease/Condition and Current Treatment Information

Impact of Condition on Patients

Rheumatoid arthritis (RA) is a chronic, painful, disabling inflammatory condition that affects 1% (~350,000) of Canadians, with the incidence being approximately two to three times higher in women than men. The disease is a chronic inflammatory disease that manifests itself in joints throughout the body. The inflammation in a person's joints 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, disability, and reduced quality of life. Additionally, it is well documented that RA can be accompanied by fatigue and numerous co-morbidities, such as cardiovascular disease, osteoporosis and lung disease. RA can even affect a person's eyes. RA causes a significant burden on people and society as many are unable to continue working and participating in social activities at the same level. RA affects every aspect of a person's day-to-day life, often in their most vital years (between the ages of 25 and 50). It also often influences the individual's family members and friends as the person living with RA may require extra support and assistance.

RA is a chronic illness without a cure– once a person develops RA, they live with it for the remainder of their life. However, there are effective drugs that are increasingly becoming available to treat RA and prevent the damage that RA may cause. In addition to medication and surgery, there are many other self-management techniques.

RA disease varies from person to person and even over a person's lifetime. It is a challenging disease to manage and physicians and patients often have to try different drugs to find a medication that works well. Currently there are no methods that help physicians (and patients) predict which patients will respond best to which therapies. In addition, a patient's immune system can adapt to a drug making it necessary to switch to another treatment when one becomes ineffective. Thus, patients require many medication options as treatment response is not possible to predict and may change unpredictably over time.

For those whose RA is not well controlled, day to day activities such as participating in post-secondary education, becoming and staying employed, taking care of oneself, walking, cooking, grocery shopping, house work, being in a relationship, getting married, having and caring for children, and social activities, can be extremely difficult and in some cases, impossible to undertake. For example, simply getting out of bed in the morning may become a monumental challenge, and putting on one's clothes could take multiple times the energy and amount of time compared to someone without RA. Imagine spending hours in the morning just to get out of bed, bathed and dressed. Tasks that were once a simple part of your day and taken for granted become all-energy consuming.

These exacerbations not only impact an individual's physical health it also puts a strain on their mental and spiritual health. It is difficult for an individual goes from being from being independent, active and mobile to having difficulties simply getting out of bed and getting dressed. This often leads to depression, anxiety and fear for their future. This becomes a vicious cycle. As depression and anxiety, can lead to more physical function problems, higher disease activity, poorer health overall

It is also well documented, that if RA is left undiagnosed, within a decade of its onset, about 50% of people with RA are no longer able to work. It is vital that inflammation be controlled early and well so that patients can continue to be productive members of society and of their families. We can imagine that the economic benefits to society of keeping people living with RA in the work force and as productive members of society are greater than those required of the healthcare system if patients do not receive treatments for their disease.

Patients' Experiences with the Current Treatment

While there are both small molecule and biologic disease-modifying anti-rheumatic drugs (DMARDs) available to treat RA, as per the instructions above, we have focussed this section on the originator drug to TBC which is also the molecule etanercept, or known by the trade name Enbrel.

Since the biology of a person's RA response to medications is not currently well understood or able to be predicted, all patients with RA experience trial and error in finding the most suitable treatment for their RA. Some patients experience long periods of responding well to a drug (meaning that their symptoms are well-controlled), while others, for reasons unknown, will need to be exposed to many different drugs over their lifetime to achieve the best treatment of their RA. The originator drug, Enbrel, is no different for patients. While Enbrel works very well (efficaciously and safely) for some, for others it is not as efficacious (sometimes immediately, or sometimes over time as a patient's immune system adapts to it), and as a result, patients and their physicians will have a conversation and decide whether or not to change the patients' pharmaceutical therapy.

For Enbrel (originator drug), the most common adverse reactions are infections, allergic reactions and injection-site reactions. Since TBC is a slightly different version of etanercept than Enbrel, it is safe to assume that TBC's adverse effects will be similar to Enbrel - offering patients this biosimilar will not alleviate typical side effects that are also found with Enbrel.

With the advent of biologics for the treatment of RA, so has the need been created for either infusions or injections. Some patients have scar tissue and site reactions from injections. In the most extreme case, a patient would have been giving themselves injections for 17 years (since biologics were first approved in 2000) – a reality faced by many patients living with RA. If TBC is approved for the formulary, these will remain items that patients are required to deal with to receive treatment.

Biologics are extremely costly for patients – while some patients have extended health insurance, others do not, and either rely on their own resources or those of their provincial Ministries of Health for assistance. Worrying about payment for a treatment or even access to a therapy can be an extremely stressful for a person who lives with RA. Stress can often play a negative role in one's disease.

Patients rely on support programs provided by the originator company to help them maintain efficient access to receiving their medication and to be informed and properly taught about a medication's administration, assistance with drug cost coverage, and for general questions about their treatment. This patient support program is an important part of a patient receiving the originator drug.

Impact on Caregivers

It is always assumed that medications for people living with RA are a choice made by a patient and their physician. Depending on a person's ability to cope with activities of daily living and their ability to still be employed, caregivers of people living with RA are relied upon in varying capacities. In some cases, caregivers are required to assist with simple tasks such as bathing, getting in and out of bed, getting dressed, even using the toilet. The emotional toll on both patients and caregivers in this type of situation cannot be underscored enough. In other situations, a caregiver's burden may not be as great, perhaps giving the patient their injection or need to take over family responsibilities while the patient is receiving their infusion. Living with a chronic condition as potentially debilitating as RA can affect a person profoundly psychologically – including caregivers. Additionally, when patients do not have drug coverage options, if one's spouse is their caregiver, this adds to the burden of disease in ways nearly unimaginable.

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 before their diagnosis, throughout their lives.

Information About the Biosimilar Being Reviewed

What Are Patients' Expectations for the Biosimilar?

It is always assumed that medications for people living with RA are a choice made by a patient and their physician. Since this is only the second biosimilar for RA under consideration in Canada, there are a number of perceptions in the patient community about these, which include:

- Potentially being more economic than the originator drugs
- Potentially not having well-established patient support programs like the originator therapeutic
- Not having a well-established post-market surveillance program (and associated safety concerns)
- Not having clinical trial size populations that match that of the originator drug (and hence again, safety and efficacy concerns), and feeling like the patient is being placed in a real-life clinical trial without the same safety monitoring that a trial has
- Providing another option for patients who have not responded well to the originator molecule, or whose immune system has adapted to it, although not being sure that since the biosimilar addresses the same pathway as the originator, and is similar enough to the originator that it will not provide much of an advantage
- Potential confusion at the pharmacy and by healthcare providers that since the biosimilar has the identical INN name as the originator drug that there will be inadvertent switching at the pharmacy level, which could potentially result in serious side effects/adverse effects for patients
- Potential to be 'switched' to the biosimilar by one's insurer due to potential cost, and without being able to make an informed and evidence-based choice in partnership with one's healthcare provider.

It is important to note that when a person's disease is doing well because of medication, the thought of changing medications for any reason at all is terrifying. There is still significant concern about being pressured to use medications due to economic reasons even when not at a natural point of requiring a change in medication.

Overall, access to biosimilars provide another potential treatment for patients with RA, with significant concerns and perceptions (positive and negative) which are all highlighted above.

Key Messages

Key submission messages include:

- RA is a seriously debilitating chronic illness that affects all aspects of a person's life
- Therapeutic options are required for patients who live with rheumatoid arthritis – biosimilar's are part of that repertoire of therapies, and for which we support as a treatment for patients who are biologic-naïve or who are being switched to another biologic due to response failure after an informed discussion and decision made with their physician
- While biosimilar's are important opportunities for patients as therapies, there are several perceptions and concerns that the patient community has about them, and which we ask CDEC to seriously consider in its review
- This biosimlar molecule has the identical INN to the originator drug – there are significant issues and concerns for patients around this, including being inadvertently exposed to the wrong drug. This is the second biosimilar for etanercept, which means if this medication is placed on the formulary, there will be three different etanercepts on the Canadian market.
- Patient support programs are an important part of biologic therapies and are an integral part of a patient's experience with these severely immuno-suppressive medications.

Additional Information

N/A

Comments on Potential Ways Biosimilars Can be Used

- CAPA is supportive of biosimilars for biologic naive patients, to individuals who are considering a switch and to patients who are fully informed and understands the decision which was made with their physician.
- We are not supportive of patients switching back and forth from the originator drug to the biosimilar, as it can increase a patient's risk of immunogenicity side effects. This is a significant patient safety issue and could potentially affect patient response to even the originator drug. However, if the patient wants to switch from the originator to the biosimilar we are supportive. As mentioned previously, it is our priority that patients are making an informed decision and they are fully aware of the potential consequences.

- Post market safety is still a concern for CAPA because of the naming issue, otherwise the same regulations are in place for biosimilars as all other drugs.
- CAPA supports biosimilar's as options for patients when the biosimilar has undergone rigorous clinical trials for an indication, for biologic-naïve patients, or for patients who are being put on a new biologic because of failure to respond to another. This is only after careful consideration, dialogue, and informed conversation between physician and patient and is a decision that only they should undertake, not one that should be pushed on them in response to cost, etc.

It is unclear why an opinion is even asked on these sections. If the reader of this submission would simply put themselves in a patient's position, and if they too had lived with RA, they would read the above statements and call them all unacceptable, and may even take it so far as to call them unethical. Physicians work with their patients to provide the best medications possible for the patient – it is doubtful that they would also stand for the statements above.