Common Drug Review
Patient Group Input Submissions

etanercept (Brenzys) for treatment of moderately to severely active rheumatoid arthritis in adults(2) Reducing signs and symptoms of active ankylosing spondylitis

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

CADTH received patient group input for this review on or before April 28, 2016

Disclaimer: The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations.

While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

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

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

General Information

Information Gathering

The information was gathered through Arthritis Consumer Experts' (ACE) day-to-day interactions with people living with ankylosing spondylitis, 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

Name of the drug	The name of the subsequent entry biologic (SEB) similar to etanercept (Enbrel®) is not yet confirmed.
Indication of interest	ankylosing spondylitis
Name of the patient group	Arthritis Consumer Experts (ACE Planning and Consulting, Inc.)
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
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Website	www.jointhealth.org
Permission is granted for CADTH to post this submission	Yes

Submitting Patient Group

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Conflict of Interest Declarations

a) Regarding corporate members and joint working, sponsorship, or funding arrangements:
Arthritis Consumer Experts receives unrestricted grants-in-aid from the following private and public sector organizations: AbbVie Corporation, Amgen Canada, Arthritis Research Canada, BIOTECanada, Canadian Institutes of Health Research, Celgene Inc., Eli Lilly Canada Inc., Hoffman-La Roche Canada Ltd., Janssen Inc., Merck & Co., Inc., Pfizer Canada, Sanofi Canada, UCB Canada Inc. and the University of British Columbia. ACE also receives unsolicited donations from its community members (people with arthritis) across Canada.

b) Regarding those playing a significant role in compiling this submission:
This submission was expressly written by the staff and advisory board members 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 ankylosing spondylitis (AS). 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.

Patient A has been living with symptoms of AS since March 2013. His symptoms include having pain and not being able to sit down on a chair for more than 30 minutes. He experiences pain in his lower back, hand, foot, and neck, and stiffness.
A caregiver has submitted to the patient input for ankylosing spondylitis. "By controlling the disease process, pain and fatigue improve and with this comes a more active lifestyle; allowing a person to further improve their condition by exercising, getting restorative sleep, increasing the energy needed to socialize, etc. This creates potential for even greater improvement, therefore, less stress on the healthcare system.

Patient B's symptoms include pain and stiffness in his back, neck, and hips. His experiences gastrointestinal problems and eye pain/itchiness during flare ups. He thinks that "the most important symptom to control is the back, neck, and hip pain since it can cause immobility."

Patient C experiences sore back/hips and major fatigue every day. "These affects my everyday life in many ways – sitting at work, concentrating at work and making it through the day. Bending down to play with my kids or helping them do things."
Patient D has morning stiffness that limits her abilities, such as getting up and being ready on time for work and other engagements. She further explains: "Pain interferes with all aspects of daily life –

can be anywhere from a mild distraction to complete debilitation. Exhaustion caused by the disease is very difficult to manage as it can be unpredictable."

Patients' Experiences With Current Therapy

Patient A has been taking anti-inflammatory drugs until July 2014, along with practicing yoga and swimming. However, his AS was still active. As a result, his rheumatologist put him on Humira. He said: "I started taking Humira in July 2014, together with yoga and swimming and I am feeling better, I started with 2 shots per month and I am currently taking one per month and I am 75% normal".

Patient B is on Enbrel and has been for 7-8 years. Without his Enbrel, it is difficult for him to get out of bed. Once he is up and has had a hot shower and start to move, thing get better slowly to the point where he feels fine. After 5 to 6 hours in from the time he gets up, he starts to feel the pain and needs to rest. With Enbrel, he is able to perform day-to-day activities with very little stiffness and pain. Enbrel is working very well for him. Flare ups do happen, but only as frequent as 2-3 times per year. At times of a bad flare, he has to take more NSAIDs and muscle relaxants and wait for it to pass. He is concerned about the severe side-effects of Enbrel, like cancer, but has not experienced any bad side effects. He has developed seasonal allergies; however, he is uncertain whether this is due to Enbrel, age, and/or environmental factors. At times of a bad flare, he has to take more NSAIDs and muscle relaxants and wait for it to pass. He also visits a registered massage therapist on a monthly basis. His work healthcare plan pays fully for his medications. He is worried that when he retires, he will not be able to afford Enbrel. He also gets coverage through his provincial healthcare plan. Both his insurance and the provincial healthcare plan have made Enbrel more accessible for him.

Patient C is currently using Enbrel, once a week, and arthrotech (NSAID). She also visits a naturopath and have a sugar/wheat free diet. She is sore and very tired most days and thinks that without Enbrel, it could be much worse. The adverse effects she experiences with Enbrel are injection site reactions. "My only complaint is all the paperwork and waiting for benefits, trillium, etc. to approve the drug and payments. This can be very stressful." She adds: "The Enbrel assistance program is amazing. They help so much with approvals through benefits, offset costs and even do bridging boxes which were free to me."

Patient D is currently on Enbrel and finds it very effective. "I personally have experienced a 75-80% reduction in symptoms. Enbrel has some pretty serious risks but I feel they are worth the risk, and the side effects have been fairly minimal for me." She has noticed that Enbrel doesn't really help with fatigue unless the pain is well managed. She also goes to physio therapy. She adds: "Enbrel is covered by my provincial plan, but needed special authority. Enbrel's support program paid my $1400 deductible which was extremely helpful for me."

*Note: The caregiver did not provide feedback on this section.

Impact on Caregivers

According to the caregiver, "any chronic condition effects, not only the person living with it, but always involves their relationship with family and friends. Living with health challenges is full of choices, compromises and problem solving. These involve, and many times affect, family and friends. Their input is invaluable. In the end, it is the individual's choice. We learn many helpful things from family, friends, physicians, pharmacists, and, from the variety of symptoms we live with."

Patient B describes the impact on his family and friends: "Obviously, it's difficult for them to see me in pain when I am. Sometimes, I have to take days off work as well, once for as long as a week, when flare-ups occur." If he is unable to work, he would be in a lot of pain and cause him and his family lots of stress and fatigue. With AS, he carries emotional and psychological baggage that affects his family and friends.

Patient C thinks her AS has a big impact on her family. "It's hard because they don't understand the disease and what it can do to you and how it can limit you. [My AS] makes me very emotional each day because it's frustrating to hurt and be tired all the time. Fatigue is huge – it's hard to work and concentrate all day at work and then come home and do family things and home things."

For Patient D's family and friends, the main challenge is to understand and relate to the disease. Sometimes, she feels she and her loved ones are being judged because she doesn't look sick and yet am taking very serious medications, which has to be injected.

*Note: Patient A did not provide feedback on this section.

Information About the SEB Being Reviewed

What Are Patients' Expectations for the SEB?

The caregiver stated their concern about SEBs, as follow: "Since biologics, such as Enbrel or Humira, are difficult to copy, SEBs would, I presume, conduct similar research before marketing. These are complex drugs and I image any changes in the formula could change the expected results and side-effects. Has sufficient time passed to know the long-term side-effects of innovator biologics?"

Patient B hopes that SEB etanercept will have the same positive effects as Enbrel. "I'm thinking the disadvantages are the same as for Enbrel: possibility of debilitating side-effects and diseases. I'd also hope for a cheaper alternative and one without as many possible side-effects, especially ones like cancer."

Patient C believes the advantage of the SEB is that it will cost less. She expects effects and outcomes to be similar to Enbrel, just more cost effective.

Patient D believes the main advantage of the SEB is that it will be cheaper, which "can benefit everyone, including all taxpayers who currently support the government programs that pay for the drugs." She hopes the SEB etanercept will help eliminate her pain, stiffness, and fatigue.

*Note: Patient A did not provide feedback on this section.

Key Messages

- Arthritis Consumer Experts is focused on connecting with, and helping people who live with various forms of autoimmune arthritis (in addition to osteoporosis and all other forms of arthritis). It is on their behalf that ACE advocates for positive reimbursement recommendations when supported by appropriate levels of research evidence and where the safety and efficacy profile is assured by Health Canada. Doing so appropriately offers more medication options and creates an environment for the physician and patient to practice "personalized medicine" and possibly achieve disease remission. Focusing on remission as the treatment target delivers the

best chance of a person with AS gaining back some semblance of a normal life and maximizing their full potential as human beings and contributing members of society.

- Each person living with AS responds differently to each medication, and no single biologic or subsequent entry biologic therapy is effective in everyone with the disease. Based on in depth discussions with people in the arthritis community, ACE's believes that public reimbursement access to the SEB etanercept will represent an additional option in the treatment armamentarium.

Additional Information

The expressions of concern about SEB safety from people interviewed for this submission highlight the need for evidence/fact-based information delivered in lay-friendly language for AS and other forms of inflammatory arthritis.

Comments on Potential Ways SEBs Can be Used

Arthritis Consumer Experts provides information and education on SEBs consistent with the research literature and best practice clinical guidelines developed by clinical experts in the field of rheumatology. These experts should guide the use of SEBs through informed consultation with their patients and based on their values, preferences and beliefs.

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Information Gathering

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Indication of interest	rheumatoid arthritis
Name of the patient group	Arthritis Consumer Experts (ACE Planning and Consulting, Inc.)
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
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Patient group's contact information: Email	feedback@jointhealth.org
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Disease/Condition and Current Treatment Information

Impact of Condition on Patients

Patients' day-to-day lives are affected greatly by their rheumatoid arthritis (RA). 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.

One patient (patient A) 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."

According to patient B, rheumatoid arthritis caused permanent damage to one of her wrists, which "has auto-fused – I have lost some extension and flexion." Without her medication, the symptoms she feels most often are pain and stiffness.

Patient C, a female who is now 58 years old and has had RA for 15 years, describes RA's impact on her life as follows: "The disease-related symptoms and problems that impact my life on a day to day basis are fatigue, pain, and an overall sadness or decreased mood (maybe some depression at times). I become overwhelmed at times, nauseated and experience a sweep of heat (similar to hot flashes) – sometimes for no apparent reason and sometimes when I'm exhausted."

According to patient D, her day-to-day symptoms include morning stiffness and swelling of her hands, feet, knees lasting up to 20 minutes and difficulty using her hands due to loss of range-of-motion. She also experiences "frequent bi-monthly flare ups with flu-like symptoms – fever,

sweating, aching/swelling in joints throughout my body, headaches, fatigue, nausea, [and] poor sleep pattern. Affects to eyesight – blurred vision. Tiredness and swelling joints impacts [my]ability to exercise, thus weight increase and muscle tone decrease. Decrease in ability to open jars, do up fasteners on clothing, tie shoelaces." Some of the joints on her hands have become "misshapen". She thinks that if she was less stiff and swollen, she'd be able to do more exercise and stay in better shape.

Patient G was diagnosed with RA since late 2011. She was misdiagnosed with tendonitis on her feet and none of the healthcare professional she was seeing at the time suspected it was RA. She is no longer able to work fulltime and works freelance in auto financing and as a temp vacation relief for a document processing service company.

Patient H's RA limits all the activities she partakes in. "Though I have had 4 operations on my feet, it is painful for me to walk, and especially painful to stand in one place, like waiting for a bus, or a bank or grocery line-up. I have trouble chopping food to make meals and often need help to cut my food when eating out or attending a conference. If my initial treatment had been better, I might have a more 'normal' life. If I go to a social event, I need to be sure there will be places to sit. I am embarrassed by the ugly shoes I wear and feel that I am not seen as looking professional. Most aspects of housecleaning take more physical effort than I can expend so I have to live with what I can do, not what I want to do. Taking public transit makes me anxious. If I don't get a seat, I run the risk of falling and upsetting my carefully balanced life."

Patient I has difficulty dressing herself, doing buttons, pulling on pants, doing up zippers, doing her hair, walking long distances (require walking aids), getting up off of low chairs on toilets, getting in and out of cars, holding anything, lifting cups/glasses/cutlery to mouth, dropping and picking up items, not able to lift a large towel, and getting out of bed independently.

Patient J said that before taking any medications, she experienced flares that were so bad that she lost the use of one of her wrist (leading to 4 months' disability from work), unbearable pain in wrist and neck areas, migraines, and depression. After taking medications, she is able to go back to work, run, and drive standard again.

*Note: Patients E, F, and K did not provide feedback on this section.

Patients' Experiences with Current Treatment

Patient A has been waiting for the approval of Enbrel for over 2 months. She is currently just taking the pain medication tramadol. She has not been on any biologics since April 2011 as she has had serious infection from other biologics due to a surgery she undertook. She went back to gold therapy. Other treatments include methotrexate (which made her sick), Orencia, Anakinara (Kineret), and Humira. She had a lot of failures with biologics as they all lost efficacy over time. She has difficulty with traveling with Enbrel.

Patient B, in talking about her current treatment with Enbrel, summarized: "I have been taking Enbrel since 2001. It has given my life back! My most recent x-rays have shown improvement in the RA affected joints of my hands and feet. I feel that my symptoms of pain and stiffness have been eliminated since I have been taking Enbrel. I have taken up horseback riding and jumping and am

continuing to enjoy twice weekly rides. Also, in the past three years, I have been able to reduce the dosage of Enbrel from 50 mg/ml weekly to 50 mg/ml bi-weekly."

Patient C is also using Enbrel. "I manage my disease very well with the drugs I am on. Enbrel was a life changer. I've been on it for approximately 12 years. I found relief within the first few days after my initial shot. I still require 15 mg of methotrexate weekly and 400 mg of Celebrex daily to manage my symptoms as well as antidepressants, anti-anxiety and sleeping pills. As well as the drugs I manage my disease by exercising, meditation and pacing myself."

Patient D did not specify which medications she uses but mention that "after trying many medications and using the last available self-injecting biologic once per week, the medications control her RA symptoms on a scale of 6/10 most days."

As of May 18, 2005, patient E was no longer able to tolerate methotrexate 4 times a day. She used Humira for 2 years but it lost its efficacy. She then switched to Enbrel but had to stop taking Enbrel in 2015 as it, too, became ineffective. As of June 25, 2015, she is on Xeljanz. In her words, it is a "Miracle: No more salazopyrin. No more cortisone…This is really miraculous and paid by the RAMQ in Quebec."

Patient F, a male patient who has been living with RA for 15 years have been on Enbrel for the last 8 years. He uses one other medication – leflunomide 10 mg. He can self-administer his medications.

Patient G is currently on Plaquenil, a low dose methotrexate, and Actemra. The medications have improved her life; however, she continues to get occasional flare ups. She thinks she her RA is 85% controlled. Actemra is the first biologic she's ever been on and she is worried that she may not get the same efficacy if she switches biologics. Adverse effects she experiences due to her current treatment therapy include mouth ulcers, long healing time for a simple scratch of the skin, and fatigue. She does not have difficulty accessing her current treatments and finds the Actemra Support Program (Joint Effort) and her case manager there responsive and helpful.
Patient H shared her treatment history with us: "I am now using Enbrel since my first anti-TNF drug was not holding my RA back. My doctor and I decided that Humira was less effective after 8 years of working pretty well and I changed about 6 months ago. My disease has always "smoldered" just as my first rheumatologist predicted. There are always some symptoms despite treatments. I take an NSAID, methotrexate, Enbrel and Plaquenil. I always have fatigue and pain in my joints. I have developed Sjögren's syndrome in addition to RA, and this has added another whole layer of treatments and care. Taking care of RA and Sjögren's syndrome takes as much time as a part time job would." Her desire is to have no joint damage and to be able to live a full, normal and well-rounded life. She only has enough energy to be successful in one area so both her work and personal life suffers. She is forced to run errands on the weekend because of the constant need for rest. She adds: "I hate taking methotrexate. I know all there is to know about dealing with it effectively and it still makes me nauseous, tired, and headachy every week. Injecting a biologic always stings. I worry a lot about taking NSAIDs and my CV risks. I have to take Losec or I get heartburn and gerd. Even paying 10% of the cost of my biologic took a big bite out of my budget. I was offered patient support for the first year of Humira and while I started on the Enbrel. That helped me to access the treatment.

Patient I have taken Enbrel on 2 occasions; first time was for 4 years, and the second time around, for 2.5 years; however, Enbrel has recently stopped working again. She is currently taking Plaquenil

and Prednisone. When Enbrel did work, it helped her become more independent in personal care, reducing the amount of assistance she needed from friends and family. She is concerned about having allergies to other medications and cannot switch to another biologic because of her allergy to the preservative agent Polysorbate 80. She has had anaphylactic shock before due possibly to preservatives in her current treatment therapy. She has no difficulty accessing current treatment because she has a good medical plan and can administer her old medication.

Patient J is currently on Enbrel and have been for 2 years, along with methotrexate. She is also taking medications to treat her depression. Previously, she's had allergic reactions to Plaquenil. Enbrel helps her with flare ups, inflammation, control damage to the joints, and manage pain. As a result of her medications, she is anemic, gets very tired, and have localized swelling in injection area. In regards to accessing current treatment, it was a "rollercoaster ride. My rheum had to fight with BC PharmaCare back and forth as they wouldn't approve Enbrel because I haven't tried 2 DMARDs together. The drug company ended up supporting me while negotiation was going on with PharmaCare. Luckily, my work insurance pays for 80%, while the drug company pays for 20%. I have an accessible nurse through Enliven."

Patient K started with Prednisone at 10 mg per day in April, 2004. After her diagnosis, she underwent various blood tests and x-rays of the feet, hands, and neck. From May to November 2014, she took methotrexate, folic acid, Prednisone, Plaquenil, Apo-Hydroxyquine, Celebrex and Depo-medrol. In November 2004, she received her first prescription of Enbrel after RAMQ approves her rheumatologist's request for authorization to prescribe Enbrel. By February 2015, she was only taking Apo-Hydroxyquine, methotrexate, folic acid, and Enbrel. From August 2005 to May 2014, she experienced a series of viral infections (sinus infections, rhinitis, pneumonia) – tests reveal that these symptoms may be due to her sleep apnea. Because of some complications to her lungs, she consulted a lung specialist in July 2015. After further tests, it was found that Enbrel was responsible for her symptoms – she stopped Enbrel in July 2015. Her rheumatologist continues to monitor the changes that may be present due to stopping Enbrel and increased her dosage of methotrexate and made arrangements so that Orencia will be quickly available should severe pain returns. She now takes Tylenol or Celebrex if needed.

Impact on Caregivers

Patient A 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 a lot more of the household chores, such as food prep and yard work."

When asked about her RA's impact on her caregivers, patient C said: "No caregivers, but loved ones – who sometimes bear the brunt of my frustration with RA."

In her input, patient D said: "My family help me, but they don't understand how the disease affects my moods and my ability to do the amount and intensity of tasks I used to do. They try to understand how my stiffness and pain can limit how much I can physically accomplish some days. They get frustrated and then I feel guilty for not being able to do what I used and have to ask them to help me."

Patient G lives alone but her mother does visit to help her with house chores. "They feel terrible and helpless when I'm having a bad day; however, they have become more understanding and let me

rest at home when I need. I find it very helpful to have a sister who is a licensed practical nurse as she would explain disease symptoms and processes to our mom," she explains.

Patient H's husband had to stick with a job he didn't like because of its benefits to him and his family. Though her husband does not consider himself to be a caregiver, he took care of her after each of her 9 surgeries. Because of her RA, her husband has a less active social life, neglects his own health and experiences a lot of stress.

Patient J has no caregiver but she finds that she has a tendency to not commit to and withdraw from things due to pain that limits her ability to participate in social activities.

*Note: Patients B, E, F, I, and K did not provide feedback on this section.

Information About the SEB Being Reviewed

What Are Patients' Expectations for the SEB?

Patient A's main concern about the SEB 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 B shared her thoughts on SEB, as follows: "I am afraid that an SEB is going to take away the many benefits and gains I have made with taking Enbrel. I don't want to take the chance of changing drugs or being forced to use an SEB instead of Enbrel, to find it is not as effective."

Patient C shared the same concerns: "I expect the SEB to be helpful for some patients, but I don't expect them to replace the biologics. Since they are expensive, I expect they will eventually be used as a first line treatment before reaching for a biologic; however, I don't expect the patients that have found relief after years of searching to forgo the biologics and try an SEB. Very difficult chronic illness and once relief is found, it must be respected."

Patient D does not know what to expect but is under the impression that SEB is only prescribed after the use of an innovator medication is found to be ineffective.

Patient F is concerned whether the SEB will work the same as the innovator biologic and believes that an SEB should undergo the same test and same procedure of any other medications in obtaining an approval from Health Canada.

Patient G had similar concerns: "I don't have any expectations but do expect it to be less expensive. They should not switch people where meds are currently working just because the option is there. I'd hate to see someone taken off a current therapy that works, like how PharmaCare did to me. I don't want someone dictating my treatment. I want full control of my own treatment."

Similarly, patient H said: "I can see that the SEB is desirable because of the lower cost – we need a sustainable healthcare system. Hopefully, this saving will mean more people will get access to better treatment. On the other hand, if I am taking a treatment that works, I would not want to switch drugs."

Patient J is concerned that she would have to go through the same process (4 months of monitoring before any approval), which caused her a lot of anxiety and fear. She also questions whether the side effects will be the same and would the SEB etanercept be as effective.

*Note: Patients E, I, and K did not provide feedback on this section.

Key Messages

Patient D does not know what to expect but is under the impression that SEB is only prescribed after the use of an innovator medication is found to be ineffective.

Patient F is concerned whether the SEB will work the same as the innovator biologic and believes that an SEB should undergo the same test and same procedure of any other medications in obtaining an approval from Health Canada.

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The expressions of concern about SEB safety from people interviewed for this submission highlight the need for evidence/fact-based information delivered in lay-friendly language for RA and other forms of inflammatory arthritis.

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General Information

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. While we tried to reach out to get quotations from actual patients who were in a clinical trial for TBC, we were told that no clinical trials were done in Canada, and by the time we were connected with a key opinion leader who could link us to some global clinical trial sites, it was too late to continue to seek input this way.

Information about the Submitting Patient Group

Name of the drug	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)	
Patient group's contact information: Email	[redacted]
Telephone	[redacted]
Address	204 Gerrard Street East, Unit 3, Toronto, Ontario, M5A 2E6
Website	www.arthritispatient.ca
Permission is granted for CADTH to post this submission	Yes

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, 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

Though not as common as Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS) is another type of inflammatory arthritis that is a serious, debilitating auto-immune 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. 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, which increases the risk of fractures.

AS is a challenging disease to manage and physicians and patients often have to try different drugs to find something that works well – there are currently no methods that help 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. As a result, patients require many potential medications as treatment response is impossible to predict and changes over time.

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 reporting to work 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. 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 Current Therapy

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. We have been informed by the distributor of TBC, Merck Canada, that there were no clinical trials of TBC in Canada, so we have not been able to collect input or responses from Canadian patients with experience with TBC.

Since the biology of a person's AS response to medications is not currently well understood or able to be predicted, patients with AS undergo trial and error in finding 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 SEB 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.

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

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 SEB Being Reviewed

What Are Patients' Expectations for the SEB?

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 SEB 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 SEB 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 SEB 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 SEB 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 SEBs 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 – SEBs 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 SEBs 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 SEB 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.

Comments on Potential Ways SEBs Can be Used

Each point in the template's box is addressed in the following:

- The SEB will be used instead of the originator (reference/brand name) product with physician approval before patient receives any treatments – Unacceptable. This should be a patient/physician joint decision and discussion.
- 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 – Unacceptable. There is no way to predict how a patient with AS will respond to a new medication. This is putting the patient in an unnecessarily risky situation, and does not take in to account what may occur is this is done – e.g. serious adverse event, significant side effects due to a switch, unnecessary immunogenic reaction to new medication. This will only cost the patient and the healthcare system valuable time and resources that would have been prevented by not undertaking a switch in the first place if a patient is doing well on the originator medication.
- The SEB will be used instead of the originator product without physician approval before patient receives any treatments – Unacceptable – as per the first point, only the physician and patient together can decide the best, agreed-upon course of treatment for the patient.
- 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. Unacceptable – only the physician and patient together can decide the best, agreed-upon course of treatment for the patient.
- Back and forth replacement between SEB and originator product without physician consent- Unacceptable- only the physician and patient together can decide the best, agreed-upon course of treatment for the patient.
- There is a real concern about switching patients back and forth from the originator drug to the SEB, 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.
- CAPA supports SEBs as options for patients when the SEB 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 Arthritis Patient Alliance (CAPA)

General Information

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. While we tried to reach out to get quotations from actual patients who were in a clinical trial for TBC, we were told that no clinical trials were done in Canada, and by the time we were connected with a key opinion leader who could link us to some global clinical trial sites, it was too late to continue to seek input this way.

Information about the Submitting Patient Group

Name of the drug	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)	
Patient group's contact information: Email	[redacted]
Telephone	[redacted]
Address	204 Gerrard Street East, Unit 3, Toronto, Ontario, M5A 2E6
Website	www.arthritispatient.ca
Permission is granted for CADTH to post this submission	Yes

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

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Sources of grants and support received by CAPA in the last year include: AbbVie, Amgen Canada, Eli Lilly, Hoffman-La Roche, Janssen, 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

Rheumatoid Arthritis (RA) is a serious, debilitating autoimmune disease that affects every aspect of a person's day-to-day life, and often also those of their family members and friends. Patients are typically diagnosed between the ages of 25 and 50 – their most productive years in life in terms of their families and careers. RA affects three times more women than men and 1 in 100 Canadians are affected by RA (~350,000 Canadians). RA is a chronic illness without a cure for RA – once a person develops RA, they live with it for the remainder of their life. The disease is notably variable from person to person and even over a person's lifetime.

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

RA is a challenging disease to manage and physicians and patients 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 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 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 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. 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. 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 Current Therapy

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. We have been informed by the distributor of TBC, Merck Canada, that there were no clinical trials of TBC in Canada, so we have not been able to collect input or responses from Canadian patients with experience with TBC.

Since the biology of a person's RA response to medications is not currently well understood or able to be predicted, patients with RA undergo 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 SEB 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 14 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.

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 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 SEB Being Reviewed

What Are Patients' Expectations for the SEB?

Since this is only the second SEB 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 SEB 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 SEB 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 SEB 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 SEBs 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:

- 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 – SEBs 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 SEBs 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 SEB 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.

Comments on Potential Ways SEBs Can be Used

Each point in the template's box is addressed in the following:

- The SEB will be used instead of the originator (reference/brand name) product with physician approval before patient receives any treatments – Unacceptable. This should be a patient/physician joint decision and discussion.
- 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 – Unacceptable. There is no way to predict how a patient with RA will respond to a new medication, whether it has a similar mode of action to another drug. This is putting the patient in an unnecessarily risky situation, and does not take in to account what may occur is this is done – e.g. serious adverse event, significant side effects due to a switch, unnecessary immunogenic reaction to new medication. This will only cost the patient and the healthcare system valuable time and resources that would have been prevented by not undertaking a switch in the first place if a patient is doing well on the originator medication.
- The SEB will be used instead of the originator product without physician approval before patient receives any treatments – Unacceptable – as per the first point, only the physician and patient together can decide the best, agreed-upon course of treatment for the patient.
- 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. Unacceptable – only the physician and patient together can decide the best, agreed-upon course of treatment for the patient.
- Back and forth replacement between SEB and originator product without physician consent- Unacceptable- only the physician and patient together can decide the best, agreed-upon course of treatment for the patient.
- There is a real concern about switching patients back and forth from the originator drug to the SEB, 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.
- CAPA supports SEBs as options for patients when the SEB 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.

Canadian Spondylitis Association

General Information

Information Gathering

Information was gathered through lived experiences and requests put out through our Facebook group (over 630 members). All members were invited to answer the specific questions outlined in this template. The information so gathered (four patients using Enbrel responded) was complemented by information gleaned from our Facebook group discussions and from many conversations amongst the Board members (all of whom live with Spondyloarthritis) with patients, particularly at our forums.

Some information was gleaned from recent requests for patient feedback to input on other drugs indicated for ankylosing spondylitis. This information was limited to the lived experience with AS in Sections 3.1 and 3.3.

Information about the Submitting Patient Group

Name of the drug	SEB ETANERCEPT
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 for CADTH to post this submission	Yes

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 ten years ago, the Association has grown to a membership of over 1,600.

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.

[redacted], has received honoraria from AbbVie (indirectly) and Novartis.

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. One patient reported being on long-term disability for seven 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 caring for their children.

Relationships suffer. Two patients reported being separating from their spouses because the strains put on their marriages by the burden of the disease was too much for the spouses to bear.

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.

Patients' Experiences With Current Therapy

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 by "75%-80%" while others experience smaller improvements. One comment was "I am sore most days and very tired'. 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.

Patients are generally satisfied with the originator biologics and the array of medications and treatments (physiotherapy, massage therapy) available to treat their disease and co-morbidities and did not express any unmet needs in this area. One patient expressed the need for a personal support worker and more social contact.

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. Two respondents expressed concerns about the possibility of cancers caused by the originator drug.

All respondents were grateful for their drug and benefit plans from work, including those that apply to long-term disability recipients. 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

The biggest challenge for caregivers is in understanding the disease and what it can do to people and how it can limit them. This in itself is stressful to them, as well as seeing their loved ones suffer. There is a financial burden to parents as they look after their children. One respondent relies very heavily on her father, who also cares for his parents, to come to her home every day to help get her daughter ready for school and to drop her off there. She also relies on her father, an elderly individual himself, for household chores that she cannot do, some grocery shopping and for picking up her daughter from school. It is physically wearing on him and involves financial costs to him. This is a typical story of people with severe disease.

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 have some knowledge of what a SEB is and have the expectation that it will work as well for them as the originator drug, in terms of both efficacy and safety. Some patients hope that the SEB may be safer, and have fewer side effects, than the originator drug. All patients were aware that the SEB should be cheaper than the originator drug and welcomed this savings to both their private payer drug plans, meaning a reduction or at least a slowing down of the increase in premiums, and, as tax-payers, to the public drug plans.

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. SEBs are welcome as a cheaper cost treatment option provided they are as safe and efficacious as the originator drug.

Comments on Potential Ways SEBs Can be Used

It is the position of the Canadian Spondylitis Association that SEBs are a welcome addition to treatment options for Ankylosing Spondylitis provided that there is no forced switching of a patient from an originator drug to a SEB if the patient is doing well and is stable on the originator drug. Such switching between an originator drug and a SEB should only be made by a physician with the consent of the patient. Drug plans and pharmacists should not be able to force the switch.

The Arthritis Society

General Information

Information Gathering

Information was obtained from the following sources:

- Contact with seven people living with AS who responded to request for feedback for CADTH.
- The Subsequent Entry Biologics and Inflammatory Arthritis Survey November 2015: the Society polled relevant stakeholders, including people living with inflammatory arthritis and their caregivers to better understand their needs. More than 700 people from across Canada contributed to the survey.
- One-on-one e-conversations with five individuals living with AS about their experiences through The Arthritis Society's engagement on social media.

Information about the Submitting Patient Group

Name of the drug	Etanercept
Indication of interest	Ankylosing Spondylitis (AS)
Name of the patient group	The Arthritis Society
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@arthritis.ca
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Website	www.arthritis.ca
Permission is granted for CADTH to post this submission	Yes

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 pharmaceutical companies in order to work towards fulfilling its mission of enabling Canadians with arthritis to live well and be effective self managers and to lead and support arthritis research and care. In order to be fully transparent and meet the request to disclose pharmaceutical manufacturers who have provided support to the organization please be aware that over the past 12 months The Arthritis Society has accepted funding from the following members of the pharmaceutical industry: Abbvie, Amgen, Bayer, Bristol Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Purdue, Roche, UCB. The vast majority of The Arthritis Society's funding comes from individual donors as personal charitable giving.

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?

The main condition-related symptoms that patients indicated as having the greatest impact on their day to day life included pain, fatigue and stiffness:

- A person with AS said, "The most important symptoms to control are: 1) pain 2) stiffness 3) fatigue. When these symptoms are not controlled it can be totally debilitating, to the point of not being able to work or play with my kids."
- Another person living with AS said "Fatigue and morning stiffness are the two symptoms that have the greatest impact on my day-to-day life and quality of life. I think that it's important to control the fatigue that arthritis sufferers feel, because it drains us of our energy. Sometimes I have difficulty getting out of bed or staying out of bed for long because the fatigue is too overwhelming, and I cannot get through a day without a nap. It affects all aspects of life, but most importantly, being able to work. There are days that I cannot work because I am just too tired."
- A female living with AS stated, "Exhaustion from simply doing nothing. Permanent stiffness and not being flexible in my whole body that affects everything from breathing to even moving. Pain 24/7. Feels like you're trapped in your own body."
- Another individual with AS said, "Overall levels of pain, stiffness and fatigue have the most impact. AS is a constant physical and mental drain on my body and mind. Thanks to the enormous amount of medication and an exercise regime I am able to do most of my daily activities, both family and work. During flares there are days when I must take it easy. Without the medication I simply cannot imagine how I would lead any kind of life."
- Another woman living with AS said "I am never free of pain. The fatigue of AS can be disabling all on its own. Both pain and fatigue together can leave me bedridden."
- One man living with AS said, "The fatigue... I can never plan ahead too much because I don't know if I will be up to the activity planned. I gave up going to the theatre, the gym and night classes all because I needed to save all my energy for work."
- One woman living with AS identified "Fatigue, tightness and pain. I'm not able to stand for more than 30 minutes at a time without pain. Pain radiates down my leg, pain in my lower and middle back as well as in my neck, hands, knees and feet. Challenges getting a good night's rest, not enough

rest and restless sleep." She also said, "Pain does not let up, even with painkillers. I wake up very stiff in the mornings and that stiffness does not ease until the afternoon; then fatigue sets in."

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

- One man living with AS said, "My symptoms include neck and back pain. I get stiff easily and am unable to perform heavy lifting at my job. I am unable to play sports, like soccer, with my child. Controlling the inflammation and pain is most important. Without a biologic I am unable to work, and even everyday tasks like showering and climbing stairs becomes difficult."
- One woman living with AS said, "I cannot clean, go out for hikes or participate in a lot of activities I use to enjoy, such as bike riding or bowling. Even grocery shopping is exhausting. I had to change my work schedule so I could work from home every other day to help deal with my condition."
- An individual living with AS said, "It even impedes social activities, as I sometimes have to turn down plans (or alter plans) because my fatigue or pain and stiffness is too high. Similarly, there are a lot of activities that I am unable to do now as a result of my AS. My physical activity level has greatly declined, as many activities are too hard on my joints now."
- A person living with AS said, "I am unable to stand or sit or lay down for extended periods. I'm unable to lift heavy things. The pain in my neck, lower back and hips is sometimes so bad I can't stand straight."
- Another person living with AS said "I was unable to work 4-5 days a month as I could not get out of bed without help due to joint pain, also had uveitis 3-4 times per year to the point I could not drive for days at a time."
- One woman with AS said, "I stopped working downtown; I now work from home. Less travelling because it is too hard."
- One person with AS stated, "I need to pace myself and exercise is a priority for me."

Patients' Experiences With Current Therapy

As each person is distinct, it is inevitable that individuals will react differently to treatments options. We believe it is essential to have access to a range of Disease Modifying Anti-Rheumatic Drugs (DMARDS), including biologics and Methotrexate, so that there are options to allow for individualized approaches to disease management. Patients often need to use a variety of drugs to control and self-manage their arthritis, some in combination with NSAIDS, DMARDS, biologics, corticosteroids, and natural health products.

Unfortunately, there are many adverse effects that can be present with the pharmaceutical treatment of AS including fever, night sweats, weight loss, tiredness, stomach pain, easy bruising or bleeding, pale skin, feeling light-headed or short of breath, rapid heart rate, nausea, itching, loss of appetite, dark urine, lowered ability to fight infection, allergic reactions etc. Those side effects also demonstrate the importance of having different treatment options as patients can react differently to a medication.

Patients identify cost of medication as an access to treatment challenge. The cost of some medications used in the treatment of AS are high and require private insurance coverage through work or a family member. Without insurance options some individuals or family members take on extra work to pay for medications. The requirements to be approved for medications are onerous on the patient. Many provincial drug plans require significant paperwork and constant checking in to see of the patient requires the medication. Manufacturer compassionate programs provide assistance to patients in financial need who meet their eligibility requirements.

People living with AS have stated:

- "I would say that my AS is being moderately managed with currently available treatments. I was on Enbrel for about 15 or 16 months, but I had to switch to Humira as I was developing stomach symptoms and had developed uveitis and was in a flare with my back. My doctor felt that the entire range of AS symptoms (including joint pain, stomach issues, eye issues, etc) would be better managed with Humira. I only recently switched (a few weeks ago) so it is too early to tell if the Humira is working. Up until my back flare and other symptoms developed, the Enbrel was working for me and I was able to work more regularly and I was able to engage in far more activities. I am also taking an NSAID daily for my pain. I was taking it twice daily, but I ended up having to reduce my dosage, as I was developing great stomach pain as a result of the NSAID (despite it containing a stomach guard). I would say that this was a side effect that was difficult to tolerate. I would say that there are hardships in accessing current treatments. I am lucky to have personal benefits through my husband, but because I cannot work regularly, I personally do not have benefits. My biologic medication is nearly $2000 a month, and with even a 10% co-pay, I would be unable to afford this medication if the drug company did not offer financial assistance. Many people, however, are unable to afford the medication that they need because they do not have additional benefits. I would say that patient assistance programs are a great benefit to being able to access the treatment that we need."
- "With treatment, I am able to participate in a daily routine for a manageable and happy life, with a few restrictions here and there. Side effects are few and manageable at this time with no undue challenges.
- "I am currently taking: Enbrel, Celebrex, and Methotrexate. My current biologic, Enbrel, has lost considerable amount of efficacy. I get about 1.5 days of some symptom control followed by 1 day of almost no control. There needs to be better biologics with symptom control that lasts longer. The frequency that I have to take Enbrel isn't ideal. It would be better if there was an effective biologic that was able to be taken less frequently. I am lucky that between Pharmacare and my extended health my medication is covered. Patient assistance program is very helpful at the beginning of treatment. Help with getting Pharmacare and dealing with private insurers is very valuable."
- "I am using a biologic Enbrel. I ended up with pneumonia within the first month. I still need pain medications when I do too much. Sulfasalazine bothered my stomach with horrible acid reflux, Methotrexate bothered my stomach and I lost hair. Another medication affected my eyesight. I have double vision from dry eyes from AS."
- "My biologic is instrumental in assisting me to function on a basic level so I can work well, work out, stretch (which benefits me even more), and pursue enjoyable recreational activities. It helps me to be a father, husband, co-worker and friend. Most side effects are easily manageable. Fair PharmaCare, my work insurance plan, and drug manufacturer co-pay assist help to cover the cost of the medication, thankfully. I feel well taken care of and motivated to give back."

Impact on Caregivers

People living with AS have told us:

- "I am lucky that I have such a wonderful and supportive family, but my disease does not come without its difficulties. My husband is very supportive, but it is stressful not being able to work regularly. That means that we are relying primarily on one income, which does put a lot of financial strain on our family. Also, being limited by fatigue, pain and stiffness means that he sometimes has to do more around the house (has to take on extra responsibilities), which can be difficult for him, as he is tired from working full time. It also affects my friendships, as I am sometimes forced to turn

down plans or alter plans because of my disease. I would not say necessarily that the side effects of treatment create any challenges for my family and friends, but my disease activity level does."

- "The constant up and down of pain levels definitely affects my family and friends. There are the changes in my emotional state, when the pain is greater my temper is shorter, and it is much harder to deal with things with my kids. These are just the normal interactions of any family but they become very difficult as the pain level rises."
- "My husband has to look after me if I have a bad flare, he rushes home to ensure I eat, makes sure I don't bath unless he is there to help me out. He worries about me, so does my mom and son. They have to tend to me; they fear I may not recover this time. They have to do the heavy lifting."

Information About the SEB Being Reviewed

What Are Patients' Expectations for the SEB?

Since subsequent entry biologics/ biosimilars are still fairly new in Canada, patients are often not aware of their existence. In the November 2015 survey on the topic, at the question "As it relates to treatment options for arthritis, have you ever heard of "subsequent entry biologics (SEB)" or "biosimilars"?", 28% (202) of the respondents answered "Yes" and 72% (517) "No".

What we heard from patients:

- "I would expect that the treatment would at least be able to treat what is currently being "treated" by biologic medications that are readily available on the market. I would like to see fatigue, joint pain and morning stiffness addressed by new treatment, but I feel that these are symptoms that are currently being treated by those medications already on the market."
- "More pain and joint stiffness relief."
- "What I am looking for is a better response, so simply it working better at controlling pain and stiffness and lasting longer than Enbrel. I have tried the 50mg Enbrel and it controlled symptoms for about 3.5 days. A big advantage I anticipate is a more consistent effectiveness between doses and actual lot numbers. With Enbrel I have found the effectiveness can be different between different lots. Some lots work great, and some lots are less effective. I assume with a newer biologic that this would be more consistent."
- "Less side effects and less frequent treatment."
- "If a new treatment was even better and cured completely or erased current symptoms still not completely removed by current treatments I would consider changing, but my fears would be that it would be the same or not as good as current treatments. Then going back to the old treatments would be unviable and rendered ineffective."

Key Messages

- SEBs/biosimilars have a role to play in the care and management of those living with certain types of arthritis, and that SEBs/biosimilars will offer more choice for those living with certain forms of arthritis and have the potential to lower health care costs and increase access.
- SEBs/biosimilars may be a natural option for patients who have not yet been on a biologic, or who are on a biologic and no longer responding appropriately (as determined by the patient and their physician) to that biologic.
- SEBs/biosimilars, while similar to the innovator biologic are not identical and cannot be considered generic versions of innovator biologics.

- Implementation of consistent, universal, unique SEBs/biosimilar naming practices will facilitate straightforward traceability in the affected patient population.
- Implementation of a policy that does not allow therapeutic substitution of SEBs/biosimilars and biologics is critical.
- Implementation of a policy that does not allow automatic interchangeability of innovator biologics and SEBs/biosimilars is critical.
- A process for post-market surveillance must be put in place to track long-term safety and efficacy.
- The Arthritis Society is supportive of robust patient assistance / support programs and would expect to see quality patient programs from new SEB entrants to the market.

Comments on Potential Ways SEBs Can be Used

The Arthritis Society approved a position paper "Access to Medication: Biosimilars" revised February 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 belongs to the same pharmacologic class and or to the same therapeutic class. With respect to biosimilars therapeutic substitution would allow a pharmacist to dispense any biologic medication for the same indication rather than the specific medication that was prescribed. Since biologics and their counterpart biosimilars have slightly different chemical structures, evidence will need to be gathered on how or if therapeutic substitution affects patients as there is currently very little available.

Interchangeability

- Interchangeability is different from therapeutic substitution. Generic medicines, which are designated by Health Canada as bioequivalent, are interchangeable with their reference product and often automatically interchanged by pharmacists. Health Canada has stated, "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.
- Decisions about the use of a biosimilar or biologic innovator drug must be in the hands of people living with arthritis and their physician, not payers or policy makers.
- SEBs/biosimilars have a role to play in the care and management of those living with certain types of arthritis, and that SEBs/biosimilars will offer more choice for those living with certain forms of arthritis and have the potential to lower health care costs and increase access.
- SEBs/biosimilars may be a natural option for patients who have not yet been on a biologic, or who are on a biologic and no longer responding appropriately (as determined by the patient and their physician) to that biologic.

- SEBs/biosimilars, while similar to the innovator biologic are not identical and cannot be considered generic versions of innovator biologics.
- Implementation of consistent, universal, unique SEBs/biosimilar naming practices will facilitate straightforward traceability in the affected patient population.
- Implementation of a policy that does not allow therapeutic substitution of SEBs/biosimilars and biologics is critical.
- Implementation of a policy that does not allow automatic interchangeability of innovator biologics and SEBs/biosimilars is critical.
- A process for post-market surveillance must be put in place to track long-term safety and efficacy.

The Arthritis Society

General Information

Information Gathering

Information was obtained from the following sources:

- Contact with 54 people living with RA who responded to request for feedback for CADTH.
- The Subsequent Entry Biologics and Inflammatory Arthritis Survey November 2015: the Society polled relevant stakeholders, including people living with inflammatory arthritis and their caregivers to better understand their needs. More than 700 people from across Canada contributed to the survey.

Information About the Submitting Patient Group

Name of the drug	Etanercept
Indication of interest	Rheumatoid Arthritis (RA)
Name of the patient group	The Arthritis Society
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@arthritis.ca
Telephone	416-979-7228
Address	393 University Ave., Suite 1700, Toronto, ON, M5G 1E6
Website	www.arthritis.ca
Permission is granted for CADTH to post this submission	Yes

Submitting Patient Group

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Disease/Condition and Current Treatment Information

Impact of Condition on Patients

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

This is what we heard from people living with RA:

- "Mobility and functionality are most important to control including minimizing joint damage. After that pain control is important. Lack of proper mobility and movement on my hands makes it difficult to do simple tasks like type on a laptop, use a smartphone etc. My hands tire quickly so that can limit how much typing I can do at one time."
- "Swelling of the joints and fatigue effect me most. Controlling those two items is most important. Right now, I struggle to lift and hold my children. Trying to find work that I can do will be difficult as my RA has progressed since I have had my children. Typing for extended periods of time and manipulating things with my hands is difficult. Lifting weight and doing physical labour is also a significant challenge with my RA."
- "Limits my ability to walk distances. I cannot sleep more than 3 hours at a time due to pain. Fatigue and tiredness make tasks harder. I work from home now full-time because of mobility issues and to save energy from travel. I get my family to shop for me. I do not go out for more than one hour as it wears me out."
- "Day to day pain levels, and affected areas vary greatly with my RA. Joint pain and fatigue are my greatest battles. I had to give up sports and most physical activities due to the disease. I cannot bike, run or get on the floor to play with my kids and long walks with my husband are rare."
- "Morning stiffness that last six hours, pain, fatigue. Had to go on disability. In bed most of the day or then using wheelchair. Need home support worker now just to get dressed."
- "Pain, stiffness, weakness (especially in hands), brain fog, hearing loss, dry eyes, sinusitis. The most important part is to control pain and increase strength. It makes my day hard if I have a lot of tasks to be done, I get fatigued easily. I am limited with physical activity and RA makes my hobbies hard to do (horse riding, dog showing, etc)."
- "Fatigue, joint pain... Both of these have affected my ability to work. Joint pain affects my day to day life in that I may be unable to do a certain task- such as typing, writing with a pen, opening a pill bottle. On days when my hand joints really hurt my fine motor skills are poor. On days when my foot joints really hurt my mobility is poor."

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

This is what we heard from people living with RA:

- "I struggle with all daily living tasks such as dressing, hygiene, and cooking as well as cleaning and caring for myself. My condition changes rapidly and sometimes I am bed bound and completely unable to do much of anything including being able to sit up or turn over unaided. It affects all of my joints and has done from the age of 9 years old."
- "I am constantly tired, no matter how many hours of sleep I get. Makes it hard to plan anything. I can't play any sports anymore & working out is almost impossible."
- "Fever, chills and flu like symptoms affect me daily. Swollen joints make it hard to dress and do my hair and makeup."
- "Flare ups in multiple joints for days/weeks on end. I can no longer work because of RA. The fatigue from being in constant pain. Can't sleep at night because of pain. Some joints so swollen and stiff they actually seize up. I no longer work, run, take ballet class, golf or play slow pitch. This disease has brought my full, productive life to almost a complete halt. When I was first diagnosed I was almost totally incapacitated. I couldn't cook, clean house, dress or groom myself. Lots of days I couldn't walk or go to the bathroom myself. RA made my life a living hell!"
- "Fatigue, pain in feet and hands. Losing my career as a musician. Not being able to write, craft, open bottles, wash my hair. Not being to walk for very long."
- "Without my biologics I would be in so much pain in all my joints I would not be able to work. Even then, I can't run or do too much physical work without paying for it the next day. I'm still tired a lot and don't do as much physical activity that I'd like. My grip strength is also like an 80 years old when I'm just reaching 50 later this year. So it's frustrating trying to do some of the little things around the house."
- Limits my ability to walk distances. I cannot sleep more than three hours at a time due to pain. Fatigue and tiredness make task harder. I work from home now full time because of my mobility issues and to save energy from travel. I get my family to shop for me. I do not go out more than one hour as it wears me out.

It is also important to note that RA also has a significant impact on the patients' emotional and psychological wellbeing. The condition is often misunderstood by others. RA symptoms mean individuals often limit participation in social activities with family and friends which can lead to social isolation. This is what we heard from people living with RA:

- "I barely have any friends any more, and the only people who try to understand are my parents. Not even my brother. Having an invisible illness makes people think that I am faking it. I'm tired, emotionally and physically. My boyfriend left me when I first got sick because he didn't want to deal with it. That can really screw with your head."
- "Unable to work contributes nothing to the family, can't shake the feeling of like a failure. Depression is slowly creeping up with my RA as well."
- "It has greatly impacted my life. The impact has been less in the last three months now that the side effects are better managed. I have lost friends, almost lost my job due to sick time and am doubted as I have an invisible illness."
- "Everyone outside of it (inner circle) doesn't understand and gives me a hard time about it. I've had to step away from volunteering at my daughters sporting events and have received criticism about it because no one understands why I look able to do something and I really cannot."
- "I don't go out as much with my daughter because I'm in pain or tired. She has learned to be sedentary. I don't have many friends."
- "I used to have a ton of friends I did activities with, but since I can't do all those things anymore those friends have drifted away. I feel pretty isolated and depressed a lot of the time."

- "The emotional stress and anxiety are overwhelming. Fighting off depression while you are constantly in pain, unable to do the simplest thing and constantly needing to sleep is very hard. It is hard to make long term plans because you don't know how you will feel. I was constantly cancelling on friends and family. People that were not close to me would judge me a lot and say well you look ok, everyone gets a few aches and pains. This adds to your depression and anxiety and you start to think that maybe you are just a wimp."

Patients' Experiences with Current Therapy

As each person 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), biologics and Methotrexate; in order to provide options to allow for individualized approaches to disease management. This is what we heard from people living with RA:

- "Enbrel It is very effective in managing my RA. Enbrel along with significant dietary changes have reduced and almost eliminated swelling in my hands."
- "I have used Enbrel and Humira with excellent RA control for a combined total of 8-9 years. Remicade was my first and was very successful. I used Remicade for about a year until I developed sensitivity to it and changed to Enbrel."
- "I've tried Enbrel, Humira and Orencia biologics. Enbrel worked for a year and put me in remission. However, the insurance plan updated their computer systems and my special approval for Enbrel got deleted. It took three weeks to sort out and by the time it was fixed and my insurance began covering it again (I couldn't afford to pay out of pocket so did not get my weekly doses at this time) the Enbrel had lost its effectiveness and I went into a terrible flare. My doctor then prescribed Humira which just didn't work at all. I then went to the IV infusion of Orencia which has been working for the past three years very well."
- "I am using Enbrel for my RA. This treatment used to control all my symptoms. I have been taking this for 5 years now, and the past year it hasn't been working as well."
- "I am using a biologic and it is highly effective. Most, if not all, of my symptoms are under control today due to my medication."
- "I am currently using Actemra which I inject weekly at home. It took about a year to start working initially by infusion then switched to self injections later after problems with IVs. I found I had greater relief with my first biologic, Enbrel (while it worked)."

Do current treatments have adverse effects that are more difficult to tolerate than others? This is what we heard from people living with RA:

- "When I took Enbrel it shot my liver numbers through the roof and I was taken off all medication until it came back down to normal. I also took Cimzia which started to work well but I couldn't continue."
- "I am using Enbrel. For eight years it controls/manages my symptoms to a certain amount. I take Methotrexate one day and injectable Enbrel within 24hrs. The medications cause fatigue, so it slows me down. Medications suppress symptoms so helps with overall disease. Helps me to function without any major mobility aids now. Still walking and managing. Nausea is major side effect. Believe it is from Methotrexate. FATIGUE is major and I get dizziness at times. Sometimes I have a swollen red area after injecting."
- "I was on Enbrel and loved it. Called it the miracle drug, but after 4 years on it I was diagnosed with MS because of it."

- "Enbrel, I would say it's fairly effective though I still have flare ups (although less intense and less often). I do have daily pain to cope with and fatigue. The worst side effect is the sinusitis, it's really affecting my quality of life I have constant sinus infections it's disgusting, embarrassing and uncomfortable. I am covered by insurance for now for Enbrel, but am scared of when I run out of coverage."

Do patients have difficulty accessing current treatments because of the costs? This is what we heard from people living with RA:

- "I'm on weekly injections of Enbrel and Methotrexate. If I didn't have insurance through work, I'd have to pay the entire $1,700 monthly bill for the Enbrel. Even paying the 20% each month until I reach my Pharmacare deductible is rough on a full time salary. I worry about the long term side effects. Increasing the risk of cancer scares me the most, but without the injections my life would be a daily nightmare."
- "Costs for Enbrel are absurd, but it has been the most effective treatment for me. I do not receive patient assistance but my workplace group insurance covers a good portion of the costs."
- "I receive 100% coverage through my husband's benefits. However we have difficulty as we have to pay up front on the plan before being reimbursed. $1800 is a lot of money to front every month and then waiting two weeks for payment. Also, the biologics are the only drugs that have completely gotten rid of my pain and inflammation. I can only afford them because my husband has benefits. I am working a part time job, hoping to get full time and my own benefits soon. However, if my husband loses his job and benefits, I would not be able to afford my Orencia. If I was not taking my Orencia, I wouldn't be able to work as I'd be in so much pain in almost all my joints. If I don't work, I won't be able to get my own benefits. It's a terrible cycle."
- "I take Enbrel and Methotextrate for my RA. Before beginning the biologic, I had a hard time keeping my RA under control. I had a lot of flares and was unable to get off of prednisone. The biologic has helped my disease be symptom free at times or have low activity of symptoms. These drugs have given me the ability to participate in life again, to continue to work and to be independent. The cost of the biologics is a hardship. My drug is currently being partially covered by my insurance company. However it is up for review again in two months time and is not guaranteed to be renewed. It was a long process to get approved (many months) of confusing back and forth of paperwork and then of doctors calling in and pharmacists. It causes a lot of anxiety while waiting for approval. Now reapplying I am worried about what I will do if I am not approved again. Finding a good drug combination that is successful is very difficult and takes many months."
- "Going to see my doctor I have to drive almost two hours which means more time off of work and the cost of gas. I spend around $200.00 a month on my Enbrel. And that is more than a day's wages at work."
- "I take Plaquenil and supplements. It only gets me through the day. I use to take a lot more. I also use to take a biologic. I don't have insurance because I work on contract."
- "The patient assistance program is so important I couldn't afford it otherwise."
- "The cost is the most significant issue when accessing these drugs. I was able to receive the medication on a compassionate card basis as I had participated in a drug study for the company. I had a lot of support from my doctor and the company. It was awesome to have such great people to talk with through the whole process."
- "The only concern is costs. Currently the government is paying the majority for my medications because I am a university graduate student. I am worried about affording these once I graduate."
- "Worked diligently with my doctor to get coverage, but had to go through eight different drugs to prove they did not work before the OK for Enbrel. It should not be. If your doctor knows a certain

drug like Enbrel WORKS, then the doctor should be trusted and the patient should not have to go through all these other drugs to prove it is the correct one."

- "The cost of the biological is a hardship. My drug is currently being partially covered by my insurance company. However it is up for review again in two months time and is not guaranteed to be renewed. It was a long process to get approved (many months) of confusing back and forth of paperwork and then of doctors calling in and pharmacists. It causes a lot of anxiety while waiting for approval, and now replying to this review, I am worried of what I will do if I am not approved again. Finding a good drug combination that is successful is very difficult and takes many months."
- "Currently the biologic company I have dealt with had a patient care coordinator; they were able to work with my Insurance provider to discuss financial coverage, etc. I had no issues with the process, but I believe if I were to do this on my own, it would have been far more complicated and less efficient."

Impact on Caregivers

People living with RA have told us:

- "Before I began the biological, my husband had to help dress me as I could not do up buttons, zippers, snaps or tie laces. I could not open shampoo bottles or shaving cream or hold the razor to shave my legs. My husband had to assist me in this daily as well. I didn't have the strength to carry the laundry baskets down to the washing machine or open bottles or cans for cooking. My husband and kids had to assist in many daily chores I did on my own everyday. This was a difficult adjustment for everyone. For me, it caused constant pain and it was very upsetting because I was losing all my independence. I was only 42 and couldn't believe I would have to rely on someone to do almost everything for me for the rest of my life. I was constantly fatigued and tired and unable to drive kids to activities and struggled to stay positive and make it through a day of work. The emotional stress and anxiety are overwhelming. Fighting off depression while you are constantly in pain unable to do the simplest thing and constantly needing to sleep is very hard. It is hard to make long term plans because you don't know how you will feel and I feel like I constantly was cancelling on friends and family. People that were not close to me would judge me a lot and say well you look ok, everyone gets a few aches and pains. This adds to your depression and anxiety and you start to think that maybe You are just a whimp."
- "Initially RA prevented me from participating in a lot of activities I did with my friends and family, but mostly affected my children. Some days I couldn't even drive them to their activities. It is very frustrating to not be able to participate in activities you used to. Every day presents challenges. I can't open a jar or bottle so our dinner plans must change because I can't complete the prep. Every day is emotionally and physically draining. Fortunately after 20 years my family and friends know my limitations, see my pain and frustration and assist me when they can."
- "I am unable to participate in several activities with my two year old daughter, like parent and tot classes. I struggle to lift her. My husband helps me to move my three month old when I breast feed as I struggle. My employment opportunities are far more limited, as I am unable to complete jobs that require physical labour. The cost of my medications adds to our financial burden."
- "It really affects the relationship with my husband. I am irritable and in pain constantly. No sex drive. I often can't do the things socially I would like to do. I can't go to a gym or run or stay out and eat with friends. I can't do a lot of things and people don't understand."
- "My husband is very stressed because we rely on his benefits. He hates his job but is afraid to leave because he doesn't know if he can find another employer whose benefits will cover the cost of $20,000 a year for my medication. He also works in a factory where the job security is not the best, he lives in constant fear of being let go. If that happens not only would we lose his income but mine

as well. I would become too sick to work without my medication and be forced to quit my job. I work part time and do not receive any long term disability if I become too ill to work."

- "Initially it prevented me from a lot of activities I did with my friends and family, but mostly affected my children. Some days I couldn't even drive them to their activities. It is very frustrating to not be able to participate in activities you used to. Every day presents challenges. I can't open a jar or bottle, so our dinner plans must change because I can't complete the prep. Every day is emotionally and physically draining...Luckily my family and friends support me no matter where I am in my journey."
- "I have no social life and I find it extremely hard going out. It obviously impacts on my family as they have to care more for me and I am unable to do the simple things people take for granted like going to the shop for milk etc. I have two young children and it impacts greatly on them. I am unable to take my children places or simply play with them because of the pain and limitations with joint movement etc."

Information About the SEB Being Reviewed

What Are Patients' Expectations for the SEB?

Since subsequent entry biologics/ biosimilars are still fairly new in Canada, patients are often not aware of their existence. In the November 2015 survey on the topic, at the question "As it relates to treatment options for arthritis, have you ever heard of "subsequent entry biologics (SEB)" or "biosimilars"?", 28% (202) of the respondents answered "Yes" and 72% (517) "No".

What we heard from patients:

- "I hope that it would work better but with less risk of infections. That it's less painful to take (injection) that it controls pain better, and that it lasts longer."
- "Well it has been a really slow process (4 years) before I had any noticeable improvement in my flare ups, swelling and pain. So my hope for a new biologic treatment would be quicker relief and easier access (as in cost) and delivery of medications for patients."
- "I would like fewer side effects to worry about. I don't mind the needles! I would expect one to be easier on my body, easy to administer, less side effects. I hope it addresses the fatigue and help me do some activities like I once did."
- "I would hope new biologics would address the extreme fatigue that comes with RA. Nothing seems to help it this far. Additionally, I would hope that any new subcutaneous biologics would be latex free. I have a latex allergy and am therefore limited to IV infusions due to the current subcutaneous options containing latex."
- "I hope that a new biologic would last more than four years before it stopped working. I also wish on the administrative side that they would help with private insurance companies to get these drugs paid for."

Key Messages

- SEBs/biosimilars have a role to play in the care and management of those living with certain types of arthritis, and that SEBs/biosimilars will offer more choice for those living with certain forms of arthritis and have the potential to lower health care costs and increase access.
- SEBs/biosimilars may be a natural option for patients who have not yet been on a biologic, or who are on a biologic and no longer responding appropriately (as determined by the patient and their physician) to that biologic.

- SEBs/biosimilars, while similar to the innovator biologic are not identical and cannot be considered generic versions of innovator biologics.
- Implementation of consistent, universal, unique SEBs/biosimilar naming practices will facilitate straightforward traceability in the affected patient population.
- Implementation of a policy that does not allow therapeutic substitution of SEBs/biosimilars and biologics is critical.
- Implementation of a policy that does not allow automatic interchangeability of innovator biologics and SEBs/biosimilars is critical.
- A process for post-market surveillance must be put in place to track long-term safety and efficacy.
- The Arthritis Society is supportive of robust patient assistance / support programs and would expect to see quality patient programs from new SEB entrants to the market.

Comments on Potential Ways SEBs Can be Used

The Arthritis Society approved a position paper "Access to Medication: Biosimilars" revised March 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 belongs to the same pharmacologic class and or to the same therapeutic class. With respect to biosimilars therapeutic substitution would allow a pharmacist to dispense any biologic medication for the same indication rather than the specific medication that was prescribed. Since biologics and their counterpart biosimilars have slightly different chemical structures, evidence will need to be gathered on how or if therapeutic substitution affects patients as there is currently very little available.

Interchangeability

- Interchangeability is different from therapeutic substitution. Generic medicines, which are designated by Health Canada as bioequivalent, are interchangeable with their reference product and often automatically interchanged by pharmacists. Health Canada has stated, "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.
- Decisions about the use of a biosimilar or biologic innovator drug must be in the hands of people living with arthritis and their physician, not payers or policy makers.
- SEBs/biosimilars have a role to play in the care and management of those living with certain types of arthritis, and that SEBs/biosimilars will offer more choice for those living with certain forms of arthritis and have the potential to lower health care costs and increase access.

- SEBs/biosimilars may be a natural option for patients who have not yet been on a biologic, or who are on a biologic and no longer responding appropriately (as determined by the patient and their physician) to that biologic.
- SEBs/biosimilars, while similar to the innovator biologic are not identical and cannot be considered generic versions of innovator biologics.
- Implementation of consistent, universal, unique SEBs/biosimilar naming practices will facilitate straightforward traceability in the affected patient population.
- Implementation of a policy that does not allow therapeutic substitution of SEBs/biosimilars and biologics is critical.
- Implementation of a policy that does not allow automatic interchangeability of innovator biologics and SEBs/biosimilars is critical.
- A process for post-market surveillance must be put in place to track long-term safety and efficacy.