Subsequent Entry Biologic Template for Submitting Patient Group Input to the CADTH Common Drug Review

Section 1 — General Information

Section 2 — How to Complete This Submission Template

2.1 General Information

2.2 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.

2.3 Providing Experiential Information

None to suggest- prompts which are in this template are very useful.

Section 3 — 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:	Dawn Richards
Position or title with patient group	Vice President
Email	
Telephone number(s)	
Name of author (if different)	N/A
Patient group's contact information: Email	
Telephone	
Address	
Website	www.arthritispatient.ca
Permission is granted for CADTH to post this submission	X Yes ☐ No

3.1 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.

3.2 Conflict of Interest Declarations

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

Sources of grants and support received by CAPA in the last year include: AbbVie, 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.

Section 4 — Disease/Condition and Current Treatment Information

4.1 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.

4.2 Patients' Experiences with the Current Treatment

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

4.3 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.

Section 5 — Information About the SEB Being Reviewed

5.1 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.

Section 6 — 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.***

Section 7 — Additional Information

N/A

Section 8 — 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.