Common Drug Review
Patient Group Input Submissions

infliximab (Inflectra) for ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, rheumatoid arthritis

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

CADTH received patient group input for this review on or before October 1, 2014

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

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

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

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

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.

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra®, the subsequent entry biologic similar to infliximab
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]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	[redacted]
Patient group's contact information: Email	info@jointhealth.org
Telephone	606-974-1366
Address	200A - 1228 Hamilton Street
Website	www.jointhealth.org
Permission is granted for CADTH to post this submission	Yes

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

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

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

1.2 Conflict of Interest Declarations

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

Arthritis Consumer Experts receives unrestricted grants-in-aid from the following private and public sector organizations: AbbVie Corporation, Amgen Canada, Arthritis Research Centre of Canada, BIOTECanada, Bristol-Myers Squibb Canada, the Canadian Rheumatology Research Consortium, Canadian Institutes of Health Research, Celgene Inc., GlaxoSmithKline, Hoffman-La Roche Canada Ltd., Janssen Inc., Pfizer Canada, Purdue Pharma L.P., St. Paul's Hospital, 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 is not applicable, as it was solely the staff and advisory board of Arthritis Consumer Experts that aided in the compilation of this information.

Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

Patients' day-to-day lives are affected greatly by their ankylosing spondylitis. 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.

Examples of activities that those living with ankylosing spondylitis have difficulty with, include:

- **Getting out of bed in the morning.** Morning stiffness, particularly of the spine, can sometimes mean a patient must factor that it may take from a few minutes to more than an hour for their joints and back to "loosen up" enough for them to begin their day.
- **Getting in and out of a bathtub** usually requires assistive devices or the help of another person.
- **Driving.** Some patients have difficulty getting in and out of a car on their own and some cannot cope with sitting for very long, so are unable to drive when a long commute is involved.
- **Working.** Between the general fatigue, pain, and malaise that is the norm with AS and the unpredictable nature of the disease (some days the pain is more extreme than others), going to work is not always possible. In cases where the disease is more advanced (for example when the hip is damaged to the point that it needs to be replaced), people are forced to leave the workforce altogether and live on the limited income of a disability pension.
- **Cooking.** Lifting heavy pots, bending to retrieve dishes, and standing while preparing meals are often physically impossible without assistive devices and other accommodations in the kitchen.
- **Exercise.** Most people's only barrier to exercise is the will to do so. For those living with AS, the barriers include the typical daily back and joint stiffness, pain, and fatigue, in addition to flares of the disease that cause body aches and inflammation, which can often raise the patient's pain rating (on a scale of one to ten) from around a five or six up to nine or ten. Exercise is crucial to reducing the stiffness associated with AS and for overall health and wellbeing, but people living with the effects of the disease are often precluded from participating in this basic necessity.
- **Sitting.** Regularly sitting for long periods is generally bad, so for everyone it is advisable to get up often to move around. For a person living with AS, frequently getting up to move around is not only more important, it's far more difficult.
- **Walking.** Walking is the most basic physical activity that most people take for granted; yet people living with AS sometimes have such limited range of motion that even walking is a challenge.

- **Relationships and intimacy.** Spending time with friends and family can be limited for a person living with AS due to fatigue, back stiffness, and pain. Social activities such as camping, air travel, excursions that involve getting in and out of a car, sitting in a movie theatre, staying up late, etc. are limited for those who live with AS. Physical intimacy can be hampered by reduced mobility, pain, depression, and discomfort.
- **Sleeping.** Many people living with AS experience pain at night that prevents sleeping soundly and can even cause the patient to wake up several times, adding to the fatigue already associated with the disease.
- **Parenting.** Mothers with RA have identified physical limitations caring for young children, such as bathing and carrying children and manipulating small items like buttons or hair ribbons when helping their children dress. And fatigue affects a parent's ability to participate in family activities.

2.2 Patients' Experiences with the Current Treatment

In general, of the patients ACE has spoken with about their experiences of managing their RA with currently available treatments (including Remicade® infliximab), their comments included:

- Intolerance of methotrexate in combination with the originator and other biologic therapies, including side effects such as stomach problems and nausea.
- Preferred route of administration (IV over self-injection).
- Significant disease improvement while on the originator product.
- Lack of efficacy. This is indicative of the high variability of medication effectiveness at the outset from patient to patient in this disease state and is reflected in the research literature.
- Loss of efficacy, including biologics. For example, a particular biologic worked well for a few years, but then stopped working. (This is indicative of the variability of medication effectiveness over time from patient to patient in this disease state and is reflected in the research literature.)

It should be noted that the CDR process, including patient input processes, were not in place at the time Remicade® infliximab was approved by Health Canada and placed on public formularies.

In general, the patients that ACE has interacted with over the past 15 years believe that the more options there are, the better. Having more options could mean having reimbursement access to medications, thus providing a backup plan in case the current treatment stops working or is no longer covered under an insurance plan. As well, the general agreement was that the best treatment is one that has the fewest adverse effects. Through ACE's research and education efforts, people with AS who interact with our organization generally understand there is a high degree of variability of disease and the need for increased research activity into the causes and possible cures for the disease.

In support of research, ACE recently conducted a survey with people living with arthritis. Patients ranked "being able to function and live a normal life" and "having affordable and accessible treatment options" as the top two priorities for them. ACE believes additional medication options will allow patients to consider their unique situation when deciding (alongside their doctor) which medication to take for their disease.

2.3 Impact on Caregivers

Generally, a caregiver's experience depends on whether the patient is a spouse or parent, and the degree to which the patient is debilitated by their disease. For example, if a patient is doing well physically and is for the most part independent, the caregiver may have few difficulties. However, if the patient is experiencing extreme pain, fatigue, or depression, especially on a regular basis, then it may be

necessary for the caregiver to not only help the patient more with day-to-day activities, but also take over their patient's usual household/financial responsibilities. Additionally, a caregiver may have to take time off work to care for their patient.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

ACE conducted three regional surveys in Canada to ascertain what their membership thinks about SEBs in general. Their feedback is as follows:

Survey respondents reported:

- Concern that clinical trials for SEBs are not as scientifically rigorous as they are for the originator product.
- Concern about the possibility that a medication may be switched for a SEB without consent from the patient or his/her physician.
- Fear about safety and lack of patient support while on a SEB.
- Uncertainty whether SEBs would work as well for their disease compared to the originator biologic.
- Concern that SEBs were not being reviewed by Health Canada for safety and efficacy the way other medications were.
- They want SEBs to only be prescribed by a physician upon discussion and mutual agreement with the patient.

Section 4 — 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 osteoarthritis). It is on their behalf that ACE advocates for positive reimbursement recommendations for all possible gold standard treatments. 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 arthritis 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 ankylosing spondylitis responds differently to each medication, and no single 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 Inflectra® may possibly represent an additional option in the treatment arsenal.
- It should not be assumed that Inflectra® will act in the body the same as its originator biologic, infliximab, because the complexity of manufacturing large molecule compounds leads to subtle variations between the two medications. They are not identical, so should be treated as distinct treatments in the review process as well as on the payer or pharmacy level.
- In ACE's opinion, and that of the arthritis community, Inflectra® should be treated as an additional option and not as a replacement for its originator biologic, infliximab for the above reason, but also because of the unknown effects on patients of switching between a SEB and its originator product. For these reasons, ACE urges that the Common Drug Review's recommendations include advice that would help prevent public payers from being able to decide whether a SEB can be covered as though it were interchangeable with its originator.

Section 5 — Additional Information

The current consensus in rheumatology is that ankylosing spondylitis is one of two types of axial spondyloarthritis (axSpA). The other is non-radiographic axial spondylitis (nr-axSpA). The latter disease is considered to be an earlier form of AS (even though it may not become AS later) before structural changes to the sacroiliac joints show up on an X-ray. Otherwise, the signs and symptoms of the two diseases are similar. Medication recommendations should reflect this new understanding.

The first two SEBs to be approved in Canada are similar to infliximab (Remicade®). Arthritis consumer and health professional groups, and other disease organizations, called for distinct generic and brand naming for any and all SEBs entering the Canadian marketplace. They did so because of the need to remove confusion about which medication was being prescribed or taken on the part of prescriber and consumer/patient, and equally important, to accurately track adverse events once they came into wide use.

Proposed drug name reviews and approvals worldwide fall under the jurisdiction of the World Health Organization (WHO). Alarmingly, the first two SEBs to be approved by Health Canada carried the same generic name as infliximab (Remicade®), and similar brand names (Inflectra® and Inflectra®), rendering post-marketing surveillance impossible, and possibly presenting brand name confusion in the marketplace.

At the request of a number of regulatory jurisdictions, the WHO is working to address the issue of generic naming and is close to issuing a draft generic naming framework. To our knowledge, no action has been taken to address the brand name similarities.

Section 6 — Comments on Potential Ways SEBs Can be Used

The information below was provided to CADTH in ACE's June 6, 2014 submission on their proposed SEB Patient Input Form consultation process:

First, CADTH openly states that it has no jurisdiction (expertise?) to make statements about interchangeability, substitutability or switching. The logical conclusion therefore is that any commentary provided by patient organizations on CADTH's interpretation on interchangeability, substitutability or switching is irrelevant.

Second, collecting information from patient organizations on issues/concerns relating to interchangeability, substitutability or switching and then providing it to CADTH participating drug plans when they have no jurisdiction to make recommendations is an inefficient use of resources and may preempt the direct dialogue patient organizations should have with federal and provincial drug plans.

A number of drug plans have patient input mechanisms to which patient organizations should provide their views on interchangeability, substitutability or switching. For those provinces still sadly lacking patient input mechanisms, patient organizations should make their views on the subject known to the Minister of Health and the senior bureaucrat in charge of the provincial drug reimbursement plan.

Third, the decision to take, or not take, a medication should be made by the patient with careful consideration and in discussion with their specialist physician. Elected officials, policy makers and pharmacists do not have the right to interfere with this complex, often life-changing decision.

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

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

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra®, the subsequent entry biologic similar to infliximab
Indication of interest	Psoriatic arthritis (PsA)
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]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	[redacted]
Patient group's contact information: Email	info@jointhealth.org
Teleph	606-974-1366
Address	200A - 1228 Hamilton Street Vancouver, BC V6B 6L2
Websit	www.jointhealth.org
Permission is granted for CADTH to post this submission	Yes

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

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

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

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

This is not applicable, as it was solely the staff and advisory board of Arthritis Consumer Experts that aided in the compilation of this information.

Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

Patients' day-to-day lives are affected greatly by their psoriatic arthritis. Unlike most people who can take their physical/mobility abilities for granted, people living with psoriatic 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.

Examples of activities that those living with psoriatic arthritis have difficulty with, include:

- **Getting out of bed in the morning.** Morning stiffness—a hallmark symptom of psoriatic arthritis, along with pain and swelling in the joints, tendons, and ligaments of fingers and toes—can sometimes mean a patient must factor that it may take from a few minutes to more than an hour for their joints to "loosen up" enough for them to begin their day.
- **Getting in and out of a bathtub.** This basic hygiene activity usually requires assistive devices or the help of another person. When disease flares are bad, lifting their arms up and holding their hands over their heads to wash their own hair can be difficult, if not impossible.
- **Getting dressed.** Many of those living with PsA that ACE has spoken with have difficulty getting dressed due to reduced range of motion and in some cases so have a hard time tying shoelaces and using buttons, for example, due to "sausage fingers". Only certain shoes can be worn: heels, flip-flops, and shoes that lack support are usually out of the question. Clothing choices are limited as a result.
- **Driving.** Some patients have difficulty getting in and out of a car on their own, while others may not have the hand strength or wrist mobility to change gears. Still others cannot cope with sitting for very long, so are unable to drive when a long commute is involved.
- **Working.** Between the general fatigue, pain, and malaise that is the norm with PsA and the unpredictable nature of the disease (some days the pain is more extreme than others), going to work is not always possible. In cases where the disease is more advanced, people are forced to leave the workforce altogether and live on the limited income of a disability pension.
- **Cooking.** Lifting heavy pots, chopping vegetables, opening jars, bending to retrieve dishes, and standing while preparing meals are often physically impossible without assistive devices and other accommodations in the kitchen.

- **Exercise.** Most people's only barrier to exercise is the will to do so. For those living with PsA, the barriers include the typical daily stiffness, pain, joint swelling, and fatigue, in addition to flares of the disease that cause body aches and inflammation, which can often raise the patient's pain rating (on a scale of one to ten) from around a five or six up to nine or ten. Exercise is crucial to reducing the stiffness associated with PsA and for overall health and wellbeing, but people living with the effects of the disease are often precluded from participating in this basic necessity.
- **Sitting.** Regularly sitting for long periods is generally bad, so for everyone it is advisable to get up often to move around. For a person living with PsA, frequently getting up to move around is not only more important, it's far more difficult.
- **Walking.** Walking is the most basic physical activity that most people take for granted; yet people living with PsA sometimes have such limited range of motion that even walking is a challenge. In some cases, when the feet are affected, patients are rendered unable to walk at all.
- **Relationships and intimacy.** Spending time with friends and family can be limited for a person living with PsA due to fatigue, joint stiffness and swelling, and pain. Social activities such as camping, air travel, excursions that involve getting in and out of a car, sitting in a movie theatre, staying up late, etc. are limited for those who live with PsA. Physical intimacy can be hampered by reduced mobility, pain, depression, and discomfort.
- **Sleeping.** Many people living with PsA experience pain at night that prevents sleeping soundly and can even cause the patient to wake up several times, adding to the fatigue already associated with the disease.
- **Parenting.** Mothers with PsA have identified physical limitations caring for young children, such as bathing and carrying children and manipulating small items like buttons or hair ribbons when helping their children dress. And fatigue affects a parent's ability to participate in family activities.

2.2 Patients' Experiences with the Current Treatment

In general, of the patients ACE has spoken with about their experiences of managing their RA with currently available treatments (including Remicade® infliximab), their comments included:

- Intolerance of methotrexate in combination with the originator and other biologic therapies, including side effects such as stomach problems and nausea.
- Preferred route of administration (IV over self-injection).
- Significant disease improvement while on the originator product.
- Lack of efficacy. This is indicative of the high variability of medication effectiveness at the outset from patient to patient in this disease state and is reflected in the research literature.
- Loss of efficacy, including biologics. For example, a particular biologic worked well for a few years, but then stopped working. (This is indicative of the variability of medication effectiveness over time from patient to patient in this disease state and is reflected in the research literature.)

It should be noted that the CDR process, including patient input processes, were not in place at the time Remicade® infliximab was approved by Health Canada and placed on public formularies.
In general, the patients that ACE has interacted with over the past 15 years believe that having a breadth of medication options to carefully choose from is appropriate, like it is for patients with cancer, HIV and other serious chronic diseases and illnesses. As well, they feel that the best treatment is one that has the fewest adverse effects. Through ACE's research and education efforts, people with PsA who interact with our organization generally understand there is a high degree of variability of disease and that there is a need for increased research activity into the causes and possible cures for the disease.

2.3 Impact on Caregivers

Generally, a caregiver's experience depends on whether the patient is a child, spouse, or parent, and the degree to which the patient is debilitated by their disease. For example, if a patient is doing well physically and is for the most part independent, the caregiver may have few difficulties. However, if the patient is experiencing extreme pain, fatigue, or depression, especially on a regular basis, then it may be necessary for the caregiver to not only help the patient more with day-to-day activities, but also take over their patient's usual household/financial responsibilities. Additionally, a caregiver may have to take time off work to care for their patient.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

ACE conducted three regional surveys in Canada to ascertain what their membership thinks about SEBs in general. Their feedback is as follows:

Survey respondents reported:

- Concern that clinical trials for SEBs are not as scientifically rigorous as they are for the originator product.
- Concern about the possibility that a medication may be switched for a SEB without consent from the patient or his/her physician.
- Fear about safety and lack of patient support while on a SEB.
- Uncertainty whether SEBs would work as well for their disease compared to the originator biologic.
- Concern that SEBs were not being reviewed by Health Canada for safety and efficacy the way other medications were.
- They want SEBs to only be prescribed by a physician upon discussion and mutual agreement with the patient.

Section 4 — Key Messages

- Arthritis Consumer Experts is focused on connecting with, and helping people who live with various forms of autoimmune arthritis. It is on their behalf that ACE advocates for positive reimbursement recommendations for all evidence-based treatments. 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 arthritis 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 psoriatic arthritis responds differently to each medication they take, and no single biologic therapy is effective in everyone with the disease. Based on in depth discussions with people in the arthritis community, ACE believes that public reimbursement access to Inflectra® may possibly represent an additional option in the treatment arsenal, but based on the information available to Health Canada, our organization has serious concerns about Inflectra's® short- and long-term safety and efficacy.
- It should not be assumed that Inflectra® will act in the body the same as its originator biologic (Remicade infliximab), because the complexity of manufacturing large molecule compounds leads to variations between the two medications. They are not identical, so should be treated as distinct treatments in the review process as well as on the payer or pharmacy level.

- In ACE's opinion, Inflectra® should be treated as an additional option, not a replacement, for its originator biologic (Remicade® infliximab) for the above reason, but also because of the unknown effects on patients of switching between a SEB and its originator.
- For these reasons, ACE urges that the Common Drug Review's recommendations include advising against public payers listing Inflectra as being interchangeable with its originator.
- Some working for public drug plans have hinted at mandating the use of a SEB for all patients with PsA being prescribed a biologic for the first time. For many reasons, primarily scientific and medical, ACE is vehemently opposed to this suggested "triage" approach to formulary management.

Section 5 — Additional Information

The first two SEBs to be approved in Canada are similar to infliximab (Remicade®). Arthritis consumer and health professional groups, and other disease organizations, called for distinct generic and brand naming for any and all SEBs entering the Canadian marketplace. They did so because of the need to remove confusion about which medication was being prescribed or taken on the part of prescriber and consumer/patient, and equally important, to accurately track adverse events once they came into wide use.

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Third, the decision to take, or not take, a medication should be made by the patient with careful consideration and in discussion with their specialist physician. Elected officials, policy makers and pharmacists do not have the right to interfere with this complex, often life-changing decision.

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

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

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra®, the subsequent entry biologic similar to infliximab
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]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	[redacted]
Patient group's contact information:	[redacted]
Telephon	606-974-1366
Address	200A - 1228 Hamilton Street Vancouver, BC V6B 6L2
Website	www.jointhealth.org
Permission is granted for CADTH to post this submission	Yes

1.1 Submitting Patient Group

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

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

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b) Regarding those playing a significant role in compiling this submission:
This is not applicable, as it was solely the staff and advisory board of Arthritis Consumer Experts that aided in the compilation of this information.

Section 3 — Disease/Condition and Current Treatment Information

3.1 Impact of Condition on Patients

Patients' day-to-day lives are affected greatly by their rheumatoid arthritis. Unlike most people who can take their physical/mobility abilities for granted, people living with rheumatoid arthritis must always consider 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.

Examples of activities that those living with rheumatoid arthritis have difficulty with, include:

- **Getting out of bed in the morning.** Morning stiffness—perhaps the hallmark symptom of rheumatoid arthritis—can sometimes mean a patient must factor that it may take from a few minutes to more than an hour for their joints to "loosen up" enough for them to begin their day.
- **Getting in and out of a bathtub.** This basic hygiene activity usually requires assistive devices or the help of another person. When disease flares are bad, lifting their arms up and holding their hands over their heads to wash their own hair can be difficult, if not impossible.
- **Getting dressed.** Many of those living with RA that ACE has spoken with have difficulty tying shoelaces and using buttons, for example. Only certain shoes can be worn: heels, flip-flops, and shoes that lack support are usually out of the question. Clothing choices are limited as a result.
- **Driving.** Some patients have difficulty getting in and out of a car on their own, while others may not have the hand strength to change gears. Still others cannot cope with sitting for very long, so are unable to drive when a long commute is involved.
- **Working.** Between the general fatigue, pain, and malaise that is the norm with RA and the unpredictable nature of the disease (some days the pain is more extreme than others), going to work is not always possible. In cases where the disease is more advanced, people are forced to leave the workforce altogether and live on the limited income of a disability pension.
- **Cooking.** Lifting heavy pots, chopping vegetables, opening jars, bending to retrieve dishes, and standing while preparing meals are often physically impossible without assistive devices and other accommodations in the kitchen.
- **Exercise.** Most people's only barrier to exercise is the will to do so. For those living with RA, the barriers include the typical daily stiffness, pain, and fatigue, in addition to flares of the disease that cause body aches and inflammation, which can often raise the patient's pain rating (on a scale of one to ten) from around a five or six up to nine or ten. Exercise is crucial to reducing the stiffness associated with RA and for overall health and wellbeing, but people living with the effects of the disease are often precluded from participating in this basic necessity.

- **Sitting.** Regularly sitting for long periods is generally bad, so for everyone it is advisable to get up often to move around. For a person living with RA, frequently getting up to move around is not only more important, it's far more difficult.
- **Walking.** Walking is the most basic physical activity that most people take for granted; yet people living with RA sometimes have such limited range of motion that even walking is a challenge. In many cases ACE has come across patients who have experienced joint pain in their hands and feet, plus shoulders, hips, knees, ankles, and neck, rendering them unable to move around within their homes, let alone go for long walks.
- **Relationships and intimacy.** Spending time with friends and family can be limited for a person living with RA due to fatigue, joint stiffness, and pain. Social activities such as camping, air travel, excursions that involve getting in and out of a car, sitting in a movie theatre, staying up late, etc. are limited for those who live with RA. Physical intimacy can be hampered by reduced mobility, pain, depression, and discomfort.
- **Sleeping.** Many people living with RA experience pain at night that prevents sleeping soundly and can even cause the patient to wake up several times, adding to the fatigue already associated with the disease.
- **Parenting.** Mothers with RA have identified physical limitations caring for young children, such as bathing and carrying children and manipulating small items like buttons or hair ribbons when helping their children dress. And fatigue affects a parent's ability to participate in family activities. In addition, fertility issues and managing RA when contemplating having a child and medicating during pregnancy are also issues both women and men living with the disease.

3.2 Patients' Experiences with the Current Treatment

- Intolerance of methotrexate in combination with the originator and other biologic therapies, including side effects such as stomach problems and nausea.
- Preferred route of administration (IV over self-injection).
- Significant disease improvement while on the originator product.
- Lack of efficacy. This is indicative of the high variability of medication effectiveness at the outset from patient to patient in this disease state and is reflected in the research literature.
- Loss of efficacy, including biologics. For example, a particular biologic worked well for a few years, but then stopped working. (This is indicative of the variability of medication effectiveness over time from patient to patient in this disease state and is reflected in the research literature.)

It should be noted that the CDR process, including patient input processes, were not in place at the time Remicade® infliximab was approved by Health Canada and placed on public formularies.

In general, the patients that ACE has interacted with over the past 15 years believe that having a breadth of medication options to carefully choose from is appropriate, like it is for patients with cancer, HIV and other serious chronic diseases and illnesses. As well, they feel that the best treatment is one that has the fewest adverse effects. Through ACE's research and education efforts, people with RA who interact with our organization generally understand there is a high degree of variability of disease and that there is a need for increased research activity into the causes and possible cures for the disease.

3.3 Impact on Caregivers

Caregiver experience included sadness and frustration upon watching the progression of their daughter's rheumatoid arthritis symptoms, which over time led toward increased debility. More generally, a caregiver's experience depends on whether the patient is a child, spouse, or parent, and the degree to which the patient is debilitated by their disease. For example, if a patient is doing well physically and is for the most part independent, the caregiver may have few difficulties. However, if the patient is experiencing extreme pain, fatigue, or depression, especially on a regular basis, then it may be necessary for the caregiver to not only help the patient more with day-to-day activities, but also take over their patient's usual household/financial responsibilities. Additionally, a caregiver may have to take time off work to care for their patient.

Section 4 — Information About the SEB Being Reviewed

4.1 What Are Patients' Expectations for the SEB?

ACE conducted three regional surveys in Canada to ascertain what their membership thinks about SEBs in general. Their feedback is as follows:

Survey respondents reported:

- Concern that clinical trials for SEBs are not as scientifically rigorous as they are for the originator product.
- Concern about the possibility that a medication may be switched for a SEB without consent from the patient or his/her physician.
- Fear about safety and lack of patient support while on a SEB.
- Uncertainty whether SEBs would work as well for their disease compared to the originator biologic.
- Concern that SEBs were not being reviewed by Health Canada for safety and efficacy the way other medications were.
- They want SEBs to only be prescribed by a physician upon discussion and mutual agreement with the patient.

Section 5 — Key Messages

- Arthritis Consumer Experts is focused on connecting with, and helping people who live with various forms of autoimmune arthritis. It is on their behalf that ACE advocates for positive reimbursement recommendations for all evidence-based treatments. 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 arthritis 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 rheumatoid arthritis responds differently to each medication they take, and no single biologic therapy is effective in everyone with the disease. Based on in depth discussions with people in the arthritis community, ACE believes that public reimbursement access to Inflectra® may possibly represent an additional option in the treatment arsenal, but based on the information available to Health Canada, our organization has serious concerns about Inflectra's® short- and long-term safety and efficacy.
- It should not be assumed that Inflectra® will act in the body the same as its originator biologic (Remicade infliximab), because the complexity of manufacturing large molecule compounds leads to

variations between the two medications. They are not identical, so should be treated as distinct treatments in the review process as well as on the payer or pharmacy level.

- In ACE's opinion, Inflectra® should be treated as an additional option, not a replacement, for its originator biologic (Remicade® infliximab) for the above reason, but also because of the unknown effects on patients of switching between a SEB and its originator.
- For these reasons, ACE urges that the Common Drug Review's recommendations include advising against public payers listing Inflectra as being interchangeable with its originator.
- Some working for public drug plans have hinted at mandating the use of a SEB for all patients with RA being prescribed a biologic for the first time. For many reasons, primarily scientific and medical, ACE is vehemently opposed to this suggested "triage" approach to formulary management.

Section 6 — Additional Information

The first two SEBs to be approved in Canada are similar to infliximab (Remicade®). Arthritis consumer and health professional groups, and other disease organizations, called for distinct generic and brand naming for any and all SEBs entering the Canadian marketplace. They did so because of the need to remove confusion about which medication was being prescribed or taken on the part of prescriber and consumer/patient, and equally important, to accurately track adverse events once they came into wide use.

Proposed drug name reviews and approvals worldwide fall under the jurisdiction of the World Health Organization (WHO). Alarmingly, the first two SEBs to be approved by Health Canada carried the same generic name as infliximab (Remicade®), and similar brand names (Inflectra® and Inflectra®), rendering post-marketing surveillance impossible, and possibly presenting brand name confusion in the marketplace.

At the request of a number of regulatory jurisdictions, the WHO is working to address the issue of generic naming and is close to issuing a draft generic naming framework. To our knowledge, no action has been taken to address the brand name similarities.

Section 7 — Comments on Potential Ways SEBs Can be Used

The information below was provided to CADTH in ACE's June 6, 2014 submission on their proposed SEB Patient Input Form consultation process:

First, CADTH openly states that it has no jurisdiction (expertise?) to make statements about interchangeability, substitutability or switching. The logical conclusion therefore is that any commentary provided by patient organizations on CADTH's interpretation on interchangeability, substitutability or switching is irrelevant.

Second, collecting information from patient organizations on issues/concerns relating to interchangeability, substitutability or switching and then providing it to CADTH participating drug plans when they have no jurisdiction to make recommendations is an inefficient use of resources and may preempt the direct dialogue patient organizations should have with federal and provincial drug plans.

A number of drug plans have patient input mechanisms to which patient organizations should provide their views on interchangeability, substitutability or switching. For those provinces still sadly lacking

patient input mechanisms, patient organizations should make their views on the subject known to the Minister of Health and the senior bureaucrat in charge of the provincial drug reimbursement plan.

Third, the decision to take, or not take, a medication should be made by the patient with careful consideration and in discussion with their specialist physician. Elected officials, policy makers and pharmacists do not have the right to interfere with this complex, often life-changing decision.

Canadian Arthritis Patient Alliance (CAPA)

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.

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra (Infliximab)
Indication of interest	Ankylosing Spondylitis
Name of the patient group	Canadian Arthritis Patient Alliance (CAPA)
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	N/A
Patient group's contact information: Email	[redacted]
Telephone	[redacted]
Address	[redacted]
Website	www.arthritispatient.ca
Permission is granted for CADTH to post this submission	Yes

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

1.2 Conflict of Interest Declarations
a) *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:*
Sources of grants and support received by CAPA in the last year include: AbbVie, Amgen Canada, Arthritis Alliance of Canada, The Arthritis Society, Canadian Rheumatology Association, Janssen, Novartis, Ontario Rheumatology Association, and UCB Pharma.
Additionally, CAPA has also received support in the past from: Canadian Institutes for Health Research, Hoffman-La Roche, Pfizer Canada, Rx&D, Schering Canada, 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 patient's day-to-day 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. 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.

The disease 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 medication options as treatment response is not possible to predict and changes over time.

For those whose AS is not well controlled, day to day activities, such as participating in post-secondary education, becoming and staying employed, taking care of oneself and one's family, and other activities that the healthy general population simply take for granted, become very difficult. 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 with the same INN as Inflectra called infliximab or via the trade name of Remicade. Since Hospice Healthcare was provided its Notice of Compliance by Health Canada for use of Inflectra for AS in June 2014, most people with AS who utilize infliximab to control their AS are utilizing the Remicade brand.

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, Remicade, is no different for patients. While it 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 Remicade (originator drug), the most common adverse reactions are infections, allergic reactions and infusion-related reactions. The Product Monograph for Inflectra indicates that the types of adverse reactions are similar to Remicade- offering patients this SEB will not alleviate typical side effects that are also found with Remicade.

With the advent of biologics for the treatment of AS, so has the need been created for either infusions or injections. Some patients have vein scarring and scar tissue from numerous infusions and injections. In the most extreme case, a patient would have been giving themselves injections or receiving infusions for over a decade (since biologics were first approved in 2000) – a reality faced by many patients living with AS. Patients may also face scheduling issues for infusions and need to take time off work or find someone to deal with family commitments (e.g. babysitting young children). However, if Inflectra is approved, this will not alleviate these requirements for patients – 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?

Since SEBs are new 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 AS – 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

It is unclear to CAPA why CADTH has allowed SEBs to 'jump the queue' for review by CDEC while new innovator drugs that target new pathways for the same diseases are waiting to be reviewed, and whose review timeline appears to be impacted by this 'queue-jumping' phenomenom.

It would be useful for CADTH and CDEC to also consider one Patient Input Submission for all indications for which the SEB is under review. The template form can be broken down to specifically address certain conditions, and in cases where there is significant similarity/overlap between concerns/comments for the same indications, it would save significant time for patients and patient organizations that provide such submissions.

Section 8 — Comments on Potential Ways SEBs Can be Used

Each point in the 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 AS or know someone who does, 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)

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.

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra (Infliximab)
Indication of interest	Psoriatic Arthritis
Name of the patient group	Canadian Arthritis Patient Alliance (CAPA)
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	N/A
Patient group's contact information: Email	[redacted]
Telephone	[redacted]
Address	[redacted]
Website	www.arthritispatient.ca
Permission is granted for CADTH to post this submission	Yes

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

1.2 Conflict of Interest Declarations
a. We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:
Sources of grants and support received by CAPA in the last year include: AbbVie, Amgen Canada, Arthritis Alliance of Canada, The Arthritis Society, Canadian Rheumatology Association, Janssen, Novartis, Ontario Rheumatology Association, and UCB Pharma.

Additionally, CAPA has also received support in the past from: Canadian Institutes for Health Research, Hoffman-La Roche, Pfizer Canada, Rx&D, Schering Canada, 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 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

Psoriatic Arthritis (PsA) is a type of inflammatory arthritis that is a serious, debilitating auto-immune disease, affecting every aspect of a patient's day-to-day life. Patients often experience psoriasis first, and then experience the onset of PsA symptoms usually between the ages of 20-50. PsA affects men and women relatively equally and as with other forms of inflammatory arthritis, there is currently no cure for PsA – only ways to help alleviate symptoms and hopefully slow the progression of disease. PsA is a chronic illness that one lives for from the onset of symptoms until death.

The disease is characterized by inflammation in the joints that destroys the lining of the joint and ultimately the surrounding bone resulting in the need for a total joint replacement. Once damage occurs, it is not reversible and can cause significant pain and disability. There are 5 well-documented patterns of PsA as well, and it can be very different from person to person.

PsA is a challenging disease to manage. Physicians and patients work together to suggest and try different drugs to find something that works well for each patient and their PsA – there are currently no methods that help physicians predict which patients will respond best to which therapies. In addition, a patient's immune system may adapt to a drug, requiring them to then switch to another treatment when one becomes ineffective based on their immune system's adaptation. As a result, patients require many medication options, as they may change medications a number of times during their lifetime.

For those whose PsA is not well-controlled, day to day activities, such as participating in post-secondary education, becoming and staying employed, taking care of oneself (bathing, dressing, activities of daily living) and one's family, and other activities that the healthy general population simply take for granted, become very difficult. 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 PsA 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.

2.2 Patients' Experiences with the Current Treatment

Both small molecule and biologic disease-modifying anti-rheumatic drugs (DMARDs) are available to treat PsA, so as per the instructions provided above, we focus this section on the originator drug with the same INN as Inflectra called infliximab or via the trade name of Remicade. Since Hospice Healthcare was provided a Notice of Compliance for use of Inflectra for PsA by Health Canada in June, 2014, all people who utilize infliximab to control their PsA are utilizing the Remicade brand.

The biology of a one's response to PsA medications is not currently well understood or predicted, causing patients with PsA to undertake a blind trial and error approach to find the most suitable treatment for their PsA, and with minimal side effects. Some patients experience long periods of

responding well to a drug, while for unknown reasons, others will need to be exposed to many different drugs before finding the best treatment for their PsA. The originator drug, Remicade, is no different for patients. While it works very well (efficaciously and safely) for some, for others it is not as efficacious and they then require a different treatment option.

For Remicade (originator drug), the most common adverse reactions are infections, allergic reactions and infusion-related reactions. The Product Monograph for Inflectra does not indicate its types of potential side effects or adverse reactions since Inflectra is being extrapolated for use in PsA and has not undergone clinical trials to evaluate its response and effectiveness for PsA.

PsA biologic treatments require injections or infusions and some patients have vein scarring and scar tissue from repeated infusions and injections. In the most extreme case, a patient would have been giving themselves injections or receiving infusions for over a decade (since biologics were first approved in 2000) – a reality faced by many patients living with PsA. Patients may also time issues associated with going to an infusion clinic for treatment and the need to take time off work or find someone to deal with family commitments while they do so. If Inflectra were to be utilized, it would not alleviate these requirements for patients since its delivery mechanism is the same as Remicade.

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 also rely on support programs provided by the originator company to help them maintain efficient ways to receive their medication and to be kept 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.

2.3 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 PsA 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 PsA 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 PsA 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 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

Since SEBs are new 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
- Disadvantage of being extrapolated for PsA based on rheumatoid arthritis phase I and phase 3 studies – Inflectra has not undergone a clinical trial in patients with PsA – this is an extreme concern for the patient community which sets a precedent that no other drug has been allowed. CDEC reviews on an evidence-base, and if no evidence exists for Inflectra with respect to PsA, it is unclear as to how it can be approved for use in this indication.
- Not having a post-market surveillance program (and associated safety concerns)
- As to a point above, patients have the perception that those with PsA who are put on Inflectra are being placed in a real-life clinical trial without the same safety monitoring that a trial has
- 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 PsA, with significant concerns and perceptions (positive and negative) that are all highlighted above.

Section 4 — Key Messages

Key submission messages include:

- PsA is a seriously debilitating chronic autoimmune disease that affects all aspects of a person's life
- Therapeutic options are required for patients who live with PsA – SEBs are part of that repertoire of therapies however only when they have undergone the clinical trials required for all other 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 5 — Additional Information

It is unclear to CAPA why CADTH has allowed SEBs to 'jump the queue' for review by CDEC while new innovator drugs that target new pathways for the same diseases are waiting to be reviewed, and whose review timeline appears to be impacted by this 'queue-jumping' phenomenon.

It would be useful for CADTH and CDEC to also consider one Patient Input Submission for all indications for which the SEB is under review. The template form can be broken down to specifically address certain conditions, and in cases where there is significant similarity/overlap between concerns/comments for the same indications, it would save significant time for patients and patient organizations that provide such submissions.

Section 6 — Comments on Potential Ways SEBs Can be Used

To re-iterate a comment before – it is simply unacceptable and unethical for CDEC to approve Inflectra for the indication of PsA without this SEB having a requirement to have undergone a clinical trial for this indication. It is unacceptable to extrapolate from the indication of RA to PsA, no matter how 'alike' the diseases may be. This is not allowed for any other drug, and should not be allowed/acceptable for SEBs. Patients are being placed in a position of undo and unnecessary risk because of this.

Each point in the box above 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 PsA or know someone who does, 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)

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.

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra (Infliximab)
Indication of interest	Rheumatoid Arthritis
Name of the patient group	Canadian Arthritis Patient Alliance (CAPA)
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	N/A
Patient group's contact information: Email	[redacted]
Telephone	[redacted]
Address	[redacted]
Website	www.arthritispatient.ca
Permission is granted for CADTH to post this submission	Yes

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

1.2 Conflict of Interest Declarations
a. *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:*
Sources of grants and support received by CAPA in the last year include: AbbVie, Amgen Canada, Arthritis Alliance of Canada, The Arthritis Society, Canadian Rheumatology Association, Janssen, Novartis, Ontario Rheumatology Association, and UCB Pharma.

Additionally, CAPA has also received support in the past from: Canadian Institutes for Health Research, Hoffman-La Roche, Pfizer Canada, Rx&D, Schering Canada, 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 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

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

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

RA is a challenging disease to manage and physicians and patients often have to try different drugs to find something that works well – 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 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. It is also well documented, that if RA is left undiagnosed, within a decade of its onset, 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.

2.2 Patients' Experiences with the Current Treatment

While there are both small molecule and biologic disease-modifying anti-rheumatic drugs (DMARDs) available to treat RA, as per the instructions above, we have focussed this section on the originator drug with the same INN as Inflectra called infliximab or via the trade name of Remicade. Since Hospice Healthcare was provided a Notice of Compliance by Health Canada for use of Inflectra for RA in June 2014, most people with RA who utilize infliximab to control their RA are utilizing the Remicade brand.

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, Remicade, is no different for patients. While it 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 Remicade (originator drug), the most common adverse reactions are infections, allergic reactions and infusion-related reactions. The Product Monograph for Inflectra indicates that the types of adverse reactions are similar to Remicade- offering patients this SEB will not alleviate typical side effects that are also found with Remicade.

With the advent of biologics for the treatment of RA, so has the need been created for either infusions or injections. Some patients have vein scarring and scar tissue from numerous infusions and injections. In the most extreme case, a patient would have been giving themselves injections or receiving infusions for 14 years (since biologics were first approved in 2000) – a reality faced by many patients living with RA. Patients may also face scheduling issues for infusions and need to take time off work or find someone to deal with family commitments (e.g. babysitting young children). However, if Inflectra is approved, this will not alleviate these requirements for patients – 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.

2.3 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 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.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

Since SEBs are new 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.

Section 4 — 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.

Section 5 — Additional Information

It is unclear to CAPA why CADTH has allowed SEBs to 'jump the queue' for review by CDEC while new innovator drugs that target new pathways for the same diseases are waiting to be reviewed, and whose review timeline appears to be impacted by this 'queue-jumping' phenomenom.

It would be useful for CADTH and CDEC to also consider one Patient Input Submission for all indications for which the SEB is under review. The template form can be broken down to specifically address certain conditions, and in cases where there is significant similarity/overlap between concerns/comments for

the same indications, it would save significant time for patients and patient organizations that provide such submissions.

Section 6 — Comments on Potential Ways SEBs Can be Used

Each point in the template 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 immunogenetic 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.
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- 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

Information Gathering
Information was gathered from our general membership and from the Board of Directors. We interact frequently with our membership through patient forums, newsletters, our website and our Facebook pages, which are in both English and French. Our Directors all have AS and speak with many years of experience with different treatments.

Section 1 — Information About the Submitting Patient Group

Name of the drug		Inflectra (Infliximab)
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

1.1 Submitting Patient Group
The Canadian Spondylitis Association was formed in 2006 as a volunteer-run patient support and advocacy association for those living with Spondyloarthritis, a group of related diseases that includes Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA).
The aims of the Association are:

- To promote the growth of CSA membership in Canada
- To be a voice for advocacy for SpA patients across Canada nationally and provincially.
- To support and advocate for research into SpA in Canada.
- To provide a national resource centre for information relevant to the SpA community.
- To provide a national forum for partnerships between the medical and patient communities to further research into the causes and management of SpA.
- To facilitate a pool of willing volunteer patients who may make themselves available for professional training programs such as medical student undergraduate teaching, post-graduate training programs.
- To participate in the international SpA community.
- To promote public awareness of SpA through the media, public forums and other means.

Our membership is comprised of individuals, the majority of whom have Ankylosing Spondylitis but also including individuals with other forms of Spondyloarthritis, and some of their family members.

1.2 Conflict of Interest Declarations

a. *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:*
The Canadian Spondylitis Association receives both unrestricted and restricted grants from pharmaceutical industry partners. We have received funding from Abbvie (unrestricted and restricted grants), Janssen (restricted educational grants) and UCB Canada (restricted travel grant).

b. *We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:*
No conflicts. All Directors are volunteers.

Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

The onset of Ankylosing Spondylitis is often in the teenage years or early 20s. Onset after the age of 45 is unusual. There is no cure and while people experience different levels of severity, the symptoms of the disease are generally pain in the sacroiliac joints, hips, lower back spreading up to and including the neck, morning stiffness, fatigue and depression. Progression of the disease causes fusion in the vertebra and spinal deformity. Other joints such as the knees, ankles and wrists can become involved. Iritis and uveitis are frequently experienced.
The chronic pain of Ankylosing Spondylitis together with fatigue and depression significantly reduces the quality of life for patients, making work or study difficult or impossible. Individuals find that normal activities such as carrying one's baby, walking, participating in athletic and recreational activities, even sitting and driving, become limited.
It is devastating for young individuals to find themselves diagnosed with AS. They become struck down in the prime of life and also suffer because of the lack of awareness and understanding of AS, even though it is almost as common as Rheumatoid Arthritis.

2.2 Patients' Experiences with the Current Treatment

Existing therapies include NSAIDs, analgesics, DMARDs, biologics and exercise. Many patients with milder disease will do well on NSAIDs and appropriate exercise. DMARDs are effective only with peripheral, not axial, disease. For patients with more severe disease, biologics have proved to be very effective in many cases. Many patients are on the biologics approved for AS, Remicade (Infliximab), Enbrel (Entanercept), Humira (Adalimumab) and Simponi (Golimumab).

Some patients have used or are using Remicade, the originator biologic. Some of these patients do very well on it and report almost immediate life-changing effects including lack of pain, stiffness and fatigue. Others find little or no effect. It is often reported that there is a wearing off of the efficacy of the drug in the week prior to the next infusion. In addition, the efficacy of Remicade for a patient may wear off, resulting in the need to switch to another biologic. This points to the fact that existing biologics do not work for everyone and that it is important to have as large an arsenal of biological drugs as possible for AS patients because of the failure rates after starting on biologics.

Side effects reported for Remicade are most commonly allergic reactions, infections and cold-like symptoms. Many patients worry, fear in fact in some cases, going on biologics including Remicade because of possible side-effects which include, rarely, a risk of lymphoma. On balance, the positive effects of Remicade outweigh the side effects for those patients for whom Remicade is effective.

There are hardships, not all cost related, in accessing current biological therapies. Aside from the need to first fail on NSAIDs, we note that the need for infusion treatments for Remicade is disruptive and time-consuming, requiring travel to an infusion site. The cost of a biologic drug therapy is expensive and for those patients without a health insurance plan or one that only partially covers drug costs, or only access to their provincial health insurance, the cost can be demanding, not only on their own financial resources but in some cases, on the resources of their caregiver also.

We note another hardship is how the drug plan may tie someone to an employer. As people increasingly move jobs, the fact that a present employer has an attractive drug plan whereas another potential employer does not, may make moving jobs for career betterment undesirable or very expensive.

We have concerns that the manufacturer of Inflectra will not have the same support program in place for users of the drug as the programs offered by the manufacturer of the originator biologics. These programs are an important source of support and information to patients, including how to finance the costs of the drug and subsidizing the cost as well.

2.3 Impact on Caregivers

AS is an insidious, life-long disease. The long time to diagnosis can be very demanding for both the patient and their caregiver. Patients can feel that along with the pain, fatigue and depression, they are losing their minds. Caregivers find it hard to understand what is happening when faced with someone who looks healthy but has unexplained health issues, who can be normal and active one day and the next sleep all day. This is also true of patients on biologics. It is a common story that the effect of the drug wears off prior to the next infusion or injection, leading to pain, stiffness and fatigue and leaving caregivers wondering what happened.

Because AS commonly appears in the teenage years or 20s, the onset places a physical and mental burden on parents and caregivers. A great deal of patience is required in dealing with young AS patients because of the ups and downs of their disease and their inability to maintain activities in which they were involved. The symptoms of the disease have an adverse effect on their social, educational and business lives, all things that the caregiver will concern themselves with too. The caregiver, if a parent or spouse/partner of the patient, may also find an economic burden in helping to meet treatment costs.

Biologics offer not only relief and slowing of disease progression for those with AS, but relieve the mental anguish and physical burden of caregivers.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

It is clearly the case that patients on biologics that work for them are productive members of society. They are in the work force, paying taxes and living a life of quality. On the other hand, there are those patients who are revolving through different biologics trying to find one that works for them (and their co-morbidities because AS patients can also suffer from Inflammatory Bowel Disease and other forms of Spondyloarthritis). The choice is limited. Additional choices are welcome and desirable.

The perceived advantages of the SEB are:
- Potentially lower costs.
- Potential efficacy where other biologics have failed.

The perceived disadvantages are:
- There being no cost advantage.
- Physician and consumer confusion over the naming of the SEB.
- No changes in possible side effects.
- Safety concerns both in the manufacturing process and in small clinical trials without an understanding of long-term consequences.
- The loss of biological function with stopping and starting biological medications.
- The question of substitutability. Some health plans only pay for 'generic' drugs whereas the decision to use a SEB rather than an originator drug should be the decision of the patient and their physician.

Section 4 — Key Messages

- SEBs offer another biologic drug therapy, not identical to the originator drug, for AS and PsA patients, that may be effective for patients, including those who have failed on one or more biologic, and possibly at lower cost.
- SEBs should not have brand names close to the originator brand names and should have a different INN than the originator drug to avoid stakeholder confusion.
- There should be no interchangeability or substitutability between originator biologics and SEBs at the pharmacy or payer levels. This decision should be made only by the physician and patient. The patient has both a right and responsibility to be informed as to the suitability of both originator drugs and SEBs.
- We have concerns about the manufacturing process and quality control of SEBs. Lack of quality oversight and minor variances in manufacturing can result in inconsistencies in SEBs and this may be harmful to consumers.
- The manufacturers of originator drugs offer substantive patient support programs. It is not clear that the manufacturer of this drug will offer the same type of program.

Section 6 — Comments on Potential Ways SEBs Can be Used

- *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 the decision of the patient and their physician.

- *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. If the patient is stable on a biologic then **no** change should be made (in any direction) unless or until efficacy fades.
- *The SEB will be used instead of the originator product without physician approval before patient receives any treatments*
  Unacceptable and should not even be considered. This should be the decision of the patient and their physician.
- *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*
  Totally unacceptable. This should be the decision of the patient and their physician.

Back and forth replacement between SEB and originator product without physician consent
Totally unacceptable and potentially harmful. This should be the decision of the patient and their physician.

Canadian Spondylitis Association

Information Gathering
Information was gathered from our general membership and from the Board of Directors. We interact frequently with our membership through patient forums, newsletters, our website and our Facebook pages, which are in both English and French. Our Directors all have AS and one with PsA and speak with many years of experience with different treatments.

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra (Infliximab)
Indication of interest	Psoriatic Arthritis
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	[redacted]
Address	[redacted]
Website	www.spondylitis.ca
Permission is granted for CADTH to post this submission	Yes

1.1 Submitting Patient Group
The Canadian Spondylitis Association was formed in 2006 as a volunteer-run patient support and advocacy association for those living with Spondyloarthritis, a group of related diseases that includes Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA).
The aims of the Association are:

- To promote the growth of CSA membership in Canada
- To be a voice for advocacy for SpA patients across Canada nationally and provincially.
- To support and advocate for research into SpA in Canada.
- To provide a national resource centre for information relevant to the SpA community.
- To provide a national forum for partnerships between the medical and patient communities to further research into the causes and management of SpA.
- To facilitate a pool of willing volunteer patients who may make themselves available for professional training programs such as medical student undergraduate teaching, post-graduate training programs.
- To participate in the international SpA community.
- To promote public awareness of SpA through the media, public forums and other means.

Our membership is comprised of individuals, the majority of whom have Ankylosing Spondylitis but also including individuals with other forms of Spondyloarthritis including Psoriatic Arthritis, and some of their family members.

1.2 Conflict of Interest Declarations

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The Canadian Spondylitis Association receives both unrestricted and restricted grants from pharmaceutical industry partners. We have received funding from Abbvie (unrestricted and restricted grants), Janssen (restricted educational grants) and UCB Canada (restricted travel grant).

b. *We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:*
No conflicts. All Directors are volunteers.

Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

The onset of Psoriatic Arthritis, PsA, is often in the teenage years or early 20s and is often preceded by Psoriasis (30% of patients with Psoriasis develop PsA). There is no cure and while people experience different levels of severity, the symptoms of the disease are generally pain and swelling in the peripheral joints, particularly the fingers and toes, but including the knees, ankles and lower back pain, pitted and discoloured fingernails and toenails, discoloured and scaly skin, and extreme fatigue. Iritis and uveitis are frequently experienced.

The chronic pain of PsA together with fatigue and depression significantly reduces the quality of life for patients, making work or study difficult or impossible. Individuals find that normal activities such as carrying one's baby, walking, participating in athletic and recreational activities, even sitting and driving, become limited.

It is devastating for young individuals to find themselves diagnosed with PsA. They become struck down in the prime of life and also suffer because of the lack of awareness and understanding of PsA, a not uncommon disease.

2.2 Patients' Experiences with the Current Treatment

Existing therapies include NSAIDs, analgesics, DMARDs, biologics and exercise. Many patients with milder disease will do well on NSAIDs and appropriate exercise. DMARDs are effective with peripheral disease. For patients with more severe disease, biologics have proved to be very effective in many cases. Many patients are on the biologics approved for AS, Remicade (Infliximab), Enbrel (Entanercept), Humira (Adalimumab) and Simponi (Golimumab).

Some patients have used or are using Remicade, the originator biologic. Some of these patients do very well on it and report almost immediate life-changing effects including lack of pain, stiffness and fatigue. Others find little or no effect. It is often reported that there is a wearing off of the efficacy of the drug in the week prior to the next infusion. In addition, the efficacy of Remicade for a patient may wear off, resulting in the need to switch to another biologic. This points to the fact that existing biologics do not work for everyone and that it is important to have as large an arsenal of biological drugs as possible for AS patients because of the failure rates after starting on biologics.

Side effects reported for Remicade are most commonly allergic reactions, infections and cold-like symptoms. Many patients worry, fear in fact in some cases, going on biologics including Remicade

because of possible side-effects which include, rarely, a risk of lymphoma. On balance, the positive effects of Remicade outweigh the side effects for those patients for whom Remicade is effective.

There are hardships, not all cost related, in accessing current biological therapies. Aside from the need to first fail on NSAIDs, we note that the need for infusion treatments for Remicade is disruptive and time-consuming, requiring travel to an infusion site. The cost of a biologic drug therapy is expensive and for those patients without a health insurance plan or one that only partially covers drug costs, or only access to their provincial health insurance, the cost can be demanding, not only on their own financial resources but in some cases, on the resources of their caregiver also.

We note another hardship is how the drug plan may tie someone to an employer. As people increasingly move jobs, the fact that a present employer has an attractive drug plan whereas another potential employer does not, may make moving jobs for career betterment undesirable or very expensive.

We have concerns that the manufacturer of Inflectra will not have the same support program in place for users of the drug as the programs offered by the manufacturer of the originator biologics. These programs are an important source of support and information to patients, including how to finance the costs of the drug and subsidizing the cost as well.

2.3 Impact on Caregivers

PsA is an insidious, life-long disease. The long time to diagnosis because the disease mimics other conditions can be very demanding for both the patient and their caregiver. Patients can feel that along with the pain, fatigue and depression, they are losing their minds. Caregivers find it hard to understand what is happening when faced with someone who has unexplained health issues, who can be normal and active one day and the next sleep all day. This is also true of patients on biologics. It is a common story that the effect of the drug wears off prior to the next infusion or injection, leading to pain, stiffness and fatigue and leaving caregivers wondering what happened.

Because PsA can appear in the teenage years or 20s, the onset places a physical and mental burden on parents and caregivers. A great deal of patience is required in dealing with young PsA patients because of the ups and downs of their disease and their inability to maintain activities in which they were involved. The symptoms of the disease have an adverse effect on their social, educational and business lives, all things that the caregiver will concern themselves with too. The caregiver, if a parent or spouse/partner of the patient, may also find an economic burden in helping to meet treatment costs.

Biologics offer not only relief and slowing of disease progression for those with PsA, but relieve the mental anguish and physical burden of caregivers.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

It is clearly the case that patients on biologics that work for them are productive members of society. They are in the work force, paying taxes and living a life of quality. On the other hand, there are those patients who are revolving through different biologics trying to find one that works for them (and their co-morbidities because PsA patients can also suffer from Psoriasis, Ankylosing Spondylitis, Inflammatory Bowel Disease and other forms of Spondyloarthritis). The choice is limited. Additional choices are welcome and desirable.

The perceived advantages of the SEB are:
Potentially lower costs.
Potential efficacy where other biologics have failed.

The perceived disadvantages are:
There being no cost advantage.
Physician and consumer confusion over the naming of the SEB.
No changes in possible side effects.
Safety concerns both in the manufacturing process and in small clinical trials without an understanding of long-term consequences.
The loss of biological function with stopping and starting biological medications.
The question of substitutability. Some health plans only pay for 'generic' drugs whereas the decision to use a SEB rather than an originator drug should be the decision of the patient and their physician.

Section 4 — Key Messages

- SEBs offer another biologic drug therapy, not identical to the originator drug, for AS and PsA patients, that may be effective for patients, including those who have failed on one or more biologic, and possibly at lower cost.
- SEBs should not have brand names close to the originator brand names and should have a different INN than the originator drug to avoid stakeholder confusion.
- There should be no interchangeability or substitutability between originator biologics and SEBs at the pharmacy or payer levels. This decision should be made only by the physician and patient. The patient has both a right and responsibility to be informed as to the suitability of both originator drugs and SEBs.
- We have concerns about the manufacturing process and quality control of SEBs. Lack of quality oversight and minor variances in manufacturing can result in inconsistencies in SEBs and this may be harmful to consumers.
- The manufacturers of originator drugs offer substantive patient support programs. It is not clear that the manufacturer of this drug will offer the same type of program.

Section 6 — Comments on Potential Ways SEBs Can be Used

- 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 the decision of the patient and their physician.
- 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. If the patient is stable on a biologic then **no** change should be made (in any direction) unless or until efficacy fades.
- The SEB will be used instead of the originator product without physician approval before patient receives any treatments
  Unacceptable and should not even be considered. This should be the decision of the patient and their physician.
- 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
  Totally unacceptable. This should be the decision of the patient and their physician.

Back and forth replacement between SEB and originator product without physician consent
Totally unacceptable and potentially harmful. This should be the decision of the patient and their physician.

Consumer Advocare Network (Advocare)

Information Gathering
Information for this submission was collected primarily from a survey posted on Survey Monkey. Potential respondents were contacted through two methods: (1) direct individual email request to patients and patient groups that have participated in or consented to receive information about Advocare activities, and (2) notification of the survey posted by the primary author through the social media, namely Twitter and Facebook. In both the email request and the Twitter/Facebook posting, the participants requested were identified as those with inflammatory conditions and specifically rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and/or plaque psoriasis.

Patients and patient groups affected by arthritis and other autoimmune diseases have been active in Advocare sponsored workshops, and, therefore, are known to us as we are known to them. Given the very short time period between our receiving the notice of Patient Input and the deadline for submission, the direct email was only sent out once, but the social media postings were made several times. Snowballing technique was also used in that recipients were asked to forward the survey to other patients and caregivers who fit the criteria.

There were 76 respondents who completed the survey between August 3 and August 19, 2014. Of these, 26% self-identified their primary condition as rheumatoid arthritis, 16% had ankylosing spondylitis, 5% psoriatic arthritis, and 11% plaque arthritis, with another 5% having another primary diagnosis. About 11% identified as caregivers and 26% as members of a related support group. More than half of the respondents were under 40 years of age, with one-tenth under the age of 18 (survey filled out by self or by parent). Only about 12% were over the age of 60.

Section 1 — Information About the Submitting Patient Group

Name of the drug CADTH is reviewing and indication(s) of interest		Infliximab (Inflectra, Remsima)
Name of the patient group		Consumer Advocare Network (Advocare)
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@optimizinghealth.org
	Telephone	416-969-7431
	Address	151 Bloor Street West, Suite 600, Toronto, Ontario M5S 1S4
	Website	www.consumeradvocare.org
Permission is granted to post this submission		Yes

1.1 Submitting Patient Group
The Consumer Advocare Network is a registered not-for-profit organization set up in 1999 to provide education and support to patient groups to promote engagement in healthcare policy and decision-making. Advocare provides regular training and produces education materials for use by patient groups

and also provides input to health policy makers and healthcare providers. In 2012, Advocare created the Canadian Expert Patients in Health Technology, a network of individuals committed to promoting informed patient engagement at all levels of health policy and decision-making.

1.2 Conflict of Interest Declarations

With reference to this submission, the Consumer Advocare Network has received unrestricted educational grants over the past 5 years to develop materials and workshops on subsequent-entry biologics from BIOTECanada, Janssen-Ortho, Amgen, Sanofi, and Wyatt Health Management, as well as funding support from Health Canada to participate in workshops and consultations on SEBs

Durhane Wong-Rieger is a volunteer with the Consumer Advocare Network; she is paid by the Canadian Organization for Rare Disorders and the Institute for Optimizing Health Outcomes, both of which also receive unrestricted funding from these entities for other programmes. She has no conflict of interest to declare in the preparation of this submission.

Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

Symptoms and Impact. Overall, patients described similar symptoms and problems with daily living, regardless of their specific diagnosis. Because the numbers are small and the differences across patient groups are not systematic, this summary will speak to commonalities with specific conditions highlighted where appropriate.

Two issues stand out. First, most patients reported they experienced swelling, stiffness, and pain in the joints (from fingers, to hands to hips and spine), all of which led to decreased mobility, lack of dexterity, weakness, sprains and broken bones. Patients with psoriatic arthritis or plaque psoriasis also reported scaly patches not just on the surface skin but in places such as the mouth or genital area, which interferes with all aspects of daily living. Some with ankylosing spondylitis spoke of symptoms starting after a fall or accident and experiencing severe pain that would not go away and severe enough to put them in hospital or in bed. As a result, their symptoms were attributed to their injury, and it was often years of continued pain and suffering before they could get the “right” diagnosis. Disregard of symptoms and years of delay also seemed to be common experiences for those with plaque psoriasis. The severity of the physical symptoms for all of these conditions varied from being “tolerable” and “occasional flares” to “constant and unrelenting”; for example, from “the moment I wake and right through the night.” For most patients, the symptoms never totally subside and even in their best periods, there was the constant fear of flares (inflammation, stiffness) and pain.

The second issue, and the most difficult, is pain, described as “debilitating”, “sharp, like a knife cutting through your back”, “so bad I can’t sleep at night”, and “so awful that I would rather be dead.” The experience of treatments that can alleviate the muscle/joint symptoms and the pain is described as “euphoric”, “like I got my life back”, and “relief to turn over in bed without pain.” However, even with treatment, the pain and/or the fear of the pain never completely go away. Often, the pain leads to depression, which, in some cases, is serious enough to require medication.

Affect on Day-to-Day Life. Because the survey was targeted at those with knowledge or experience of infliximab, the respondents, overall, consisted of those with moderate to severe disease. Not surprisingly, the impact on daily living and quality of life was significant.

Most indicated they had been diagnosed or suffering from their condition for more than 10 years. Almost all of the respondents not diagnosed with RA reported that getting an accurate diagnosis had been challenging. Many had symptoms and significant pain for years, but they reported that their symptoms were dismissed by their GP or misdiagnosed as something else (including psychological disorders). Moreover, they reported that the years spent trying to get a diagnosis had significantly impacted their physical and psychological health (especially among those with ankylosing spondylitis). Some reported that getting a diagnosis, however devastating the disorder, was a relief.

Patients reported that their condition has totally disrupted their day-to-day lives. Only a small percentage of those who had been working were able to continue with to their previous employment (even with treatment). Some reported that they were now working part-time or had taken considerably different (lower paying, less responsible) jobs or were doing volunteer work.

In terms of daily lives, almost half report that they rely on assistance from family or other caregivers to carry out daily activities, especially those who have diminished mobility or severe pain. Many, however, report that they have been able to carry out many of their daily activities with adaptations, either through physical modifications of living space, use of technology, and/or change in routine.

Activities Unable to Do. The impact on patient capabilities depends on the severity of the condition, effectiveness of treatment, and willingness to adapt, as noted in the answer above.

2.2 Patients' Experiences with the Current Treatment

Participants were asked open-ended questions about the effectiveness of current treatments, and they were also presented with a series of treatments and asked to indicate how often they had received each, the effectiveness of that therapeutic option, and the side effects experienced. This summary combines the findings from both the open-ended responses and the rating scales. Given the small sample and the lack of systematic differences across conditions, responses by condition are not differentiated except where clear differences did occur.

Effectiveness. Overall, it is clear that treatment needs to be individualized to the patient. There is no universal best treatment and newer is not necessarily better. Most patients are using a variety of therapies, but in most cases, they have had to experiment with several therapies or combinations to get something that works. And, often, even when a therapy works, it doesn't work forever. About 45% reported having had (at least one) joint replacement surgery. Nearly 60% reported using topical creams and ointments (e.g. Voltaren) on a regular basis. Nearly half of the patients reported using homeopathic therapies, vitamins, exercise, meditation, and physiotherapy (instead of or in addition to medications. Effectiveness varied from "not at all" to "this has completely eliminated my pain (and swelling) and allowed me to return to regular activities."

About 40% of the respondents reported regular treatment with prescribed medicines (OTC and prescription). Among these, the medications used most frequently on a regular basis were aspirin, corticosteroids, methotrexate (singly or in combination with other drugs), and cyclosporine. Moreover, more than half of those who reported using medications are currently or have in the past used infliximab (Remicade), which is not surprising given that we had specifically advertised for patients who had used infliximab. Other medications used by more than 20% of participants are: adalimumab (Humira), rituximab (RItuxan), abatacept (Orencia), and etancercept (Enbrel). Finally, medications that have been used at least once by some participants (but less than 20%) are: hydorxychloroquine (Plaquenil), lefluomida (Arava), certolizumb (Cimzia), tocilizumab (Actemra), tofacitinib (Xeljanz) and

azathioprine (Imuran, Azasan). Only a small number had been prescribed more than one of the DMARDs drugs.

In terms of effectiveness, there are clearly patients (among all conditions) who are "somewhat" to "very effectively" managed on non-biologic drugs, NSAIDs and DMARDs. Among those who have or are currently using aspirin, about half say it is "somewhat or much" effective and one-fourth reported it being "not at all" effective. About one-third of those who had use corticosteroids said it was "somewhat" effective; one-third who felt it is "much" to "very much" effective, while one-third indicated it was not effective or had become "no longer" effective. The reports on effectiveness of methotrexate ranged from "much" to "very much" for about 40% while responses to lefluomide and hydorxychloroquine were slightly less positive.

The response to the biologic DMARDs also varied considerably among the patients within and across conditions. About three-fourths of the patients using infliximab reported that the treatment was "somewhat" to "very" effective; however about one-fourth said it was either "not at all" effective or had stopped working. In terms of the other drugs that block tumour necrosis factors (TNF) alpha, responses to Humira and Enbrel were similar, with about 20% of respondents reporting the drug as "somewhat" effective and 40% between "much" effective and "very much" effective, and the remainder reporting they were either "not at all" effective or had stopped working. The most positive responses seemed to come from the RA patients and the most negative from patients with psoriatic arthritis or plaque psoriasis; however, the numbers are too small to make meaningful comparisons. There was a less positive rating of rituximab but again there were too few responses to draw meaningful conclusions.
Adverse Effects. Reports of side effects were solicited through open-ended questions and rating scales. Given that this was a patient submission for an SEB (to an existing therapy), we did not seek to identify the specific side effects and their impact since we were not presuming to differentiate at this time. Overall, patients experienced the least side effects to aspirin, with about half expressing no side effects and others from moderate to severe. In terms of the corticosteroids and non-biologic DMARDs, about half of the patients reported no or mild adverse effects, while one-fourth indicated they had one or more experiences of severe adverse effects. In terms of the biologics, users of etancercept and infliximab reported more instances of severe side effects, with the highest rate among users of infliximab. It is not clear whether this is because the survey was directed towards these users who were "over-represented" in the sample relative to users of other therapies or whether the drug did indeed have a higher risk of harms. At the same time, about half of the patients reported being able to switch to another biologic and were using it successfully. It is worth noting that several patients reported that the most effective therapy they had been using was rofexocib (Vioxx) before it was taken off the market; some said they had successfully switch to colcoxib (Celebrex) but some said this alternative did not work or they experienced serious side effects.

2.3 Impact on Caregivers

Slightly more than 10% of the respondents were caregivers, and they echoed the patients' reports of a diagnosis completely changing their lives. For some, the period before getting a definitive diagnosis was the worse, with the patient experiencing symptoms and pain that were not seriously addressed or inappropriately treated. For many, the biggest challenge was the decline in capacity of the person with the condition, especially since many were still in their "working years" and were now sidelined. One caregiver spoke about the tremendous resolve of his wife, diagnosed with ankylosing spondylitis shortly after giving birth to their son, and her determination to provide as much of the care as possible. She was resistant to start medication for fear it would interfere with her ability to be with her son and only

after exhausting all of the non-medication alternatives would she consider infliximab. Her response was not only immediate but also very positive.

Section 3 — Information About the SEB Being Reviewed

Information was collected primarily through the survey, distributed through direct email and social media. Patients were asked their knowledge about and experience with infliximab (Remicade) as well as any exposure to the SEBs (Inflectra and/or Remsima). Because some of the respondents had participated in Advocare workshops on SEBs, we expected there would be some informed respondents.

3.1 What Are Patients' Expectations for the SEB?

None of the respondents had direct experience with either of the infliximab SEBs. However, about two-thirds said they were aware of Inflectra and/or Remsima, with about 50% having a little or some knowledge while about 12% rated themselves as having "much" or "very much" knowledge (no significant difference between the two drugs).

Patients with rheumatoid arthritis and ankylosing spondylitis reported little or no difficulty in accessing infliximab (Remicade), while patients with psoriatic arthritis or plaque psoriasis reported some or much challenge access through the public drug plans. Patients, overall, did not mention "cost" or "co-pay" as a deterrent to getting access to infliximab (or other nonbiologic or biologic DMARDs). That being said, some patients talked about the challenge and sometimes the delay in the application process. In general, however, patients felt that the "case by case" review of a request was appropriate and that on-going monitoring was important, especially because of the high risk of side effects. Few were aware of what was monitored to track effectiveness (whether the drug was working) but felt it was important, especially since they had experience with drug response changing over time.

When asked how they expected the infliximab SEBs to work relative to the originator drug Remicade, most felt it should b about the same. About one-third thought it might be "worse" in terms of managing swelling and stiffness of joints but about 45% said it should be the same, with about one-fifth having no opinion. There were similar responses to expectations for pain management and reduction in fatigue, though a small percentage thought the SEBs might perform better in terms of reducing redness or scaling of the skin and slowing progression of disease. In the comments, those who felt it might be worse said that the SEB companies may not have an exact "copy" of the originator drug and were less experienced with it. Those who said it could be better indicated that they thought the SEB possibly improved on the originator formula.

To gauge perceptions of potential side effects (and therefore reasons not to accept the SEB), respondents were presented with a list of potential side effects and asked to give their opinion as to how the SEB might compare to Remicade. For all side effects, with the exception of lung or respiratory infection, about half of the respondents (42% to 57%) felt that the SEBS should have the same side effects, while a small portion (15% to 29%) said the SEBs could have more or more severe side effects. About one-third said they did not know or had no opinion.
When asked about the cost or affordability of the SEB in comparison to Remicade, most thought it would be priced at about the same or have the same "cost" implications for themselves as patients. About 12% thought the affordability would be worse with the SEBs, while a third did not know. Again,

access based on price was not perceived as an advantage of the SEBs, nor did patients want to be directed to an SEB on the basis of price.

In summary, most respondents (and probably those best informed) indicated that the SEBS would perform similar to Remicade and have somewhat the same risk of side effects, although they are clearly more concerned about the differences in terms of side effects than effectiveness. This is probably not an unreasonable opinion. In the words of one respondent, "I have received Remicade every six weeks for 13 years. Because of the possibility of adverse side effects, I was monitored closely for six years. The monitoring has decreased in intensity but blood work is required every six weeks prior to the Remicade infusion to ensure that the drug does not interfere negatively with my health. I am not willing to substitute Remicade for Remsima."

Importantly, the respondents felt that the SEBs would make little difference in terms of affordability (and hence accessibility). Again, this is probably not an unrealistic expectation.

Section 5 — Additional Information

Respondents were asked how they felt the SEBs should be made available to Canadian patients through an open-ended question and a series of close-ended options. Almost all respondents (92%) said the SEBs should be available through the public drug plans. However, the respondents were almost evenly split in terms of when and how the SEB should be made available to patients. Only half of the respondents said that an infliximab SEB should be used (with physician approval) before the patient has had experience with Remicade; the other half said the SEB should NOT be used without prior Remicade experience. About half said the SEB infliximab should be used to replace Remicade after the patient has been stabilized on Remicade; the other half disagreed. There was a similar split in opinion for reach of the following options: whether a patient who has been on Remicade could be switched to the SEB without physician approval and whether the SEB and Remicade could be interchanged with a single patient without physician consent.

Among the additional comments, several urged for post-market monitoring to ensure that the SEBs were performing safely and effectively. There was a call for patient registries that would differentiate among the infliximab products received. "SEBs are similar, not the same. If there is an adverse reaction, it is important to be able to track which drug a person has received."
Finally, there were several comments about the importance of physicians being the ones to decide, with the patient, whether the persons should receive Remicade or an SEB and that physicians should be notified, if not the one making the decision. "Substitution for people who have responded well to Remicade is best left to the physician and the patient. Government involvement is inappropriate." In all cases, patients should be informed about the drug being prescribed and, when possible, given the right to decide whether to use an SEB or the originator drug. "Maybe, many years down the road, after the SEBs have been in use for as long as Remicade, we could substitute but maybe not even then."

Patient Commando Productions

Information Gathering
The information was gathered through 2 methods:

a) A survey was conducted with patients currently receiving treatment with the original innovator Infliximab (Remicade) therapy. Ninety-four (94) patients in the Greater Toronto Area submitted written responses.

b) Group and individual discussions. Small group discussions (4-6 participants in each group) were conducted in person, while individual discussions were conducted by telephone.

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra / Infliximab
Indication of interest	Rheumatoid Arthritis
Name of the patient group	Patient Commando Productions
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@patientcommando.com
Telephone	647-317-4109
Address	720 Bathurst St., Ste 200, Toronto ON M5S 2R4
Website	http://patientcommando.com/
Permission is granted for CADTH to post this submission	Yes

1.1 Submitting Patient Group

Patient Commando Productions amplifies the patient experience as a guide to improve healthcare practice using multiple platforms:

- the most diverse online collection of patient stories in any medium that enrich our appreciation of the lived illness experience;
- accredited Continuing Medical Education that informs and trains healthcare professionals in narrative competency which evidence supports improved outcomes;
- develops unique collaborations between patients and healthcare professionals focused on improving disease specific therapeutic relationships;
- advocates for patient experience around critical health issues such as the recent program "Canadian Women Changing Healthcare".

Its executive director is also Chair of The Beryl Institute Global Patient and Family Advisory Council, a global community of practice and thought leadership to improve the patient experience, with a worldwide membership exceeding 25,000 which is primarily composed of hospitals and other care institutions.

1.2 Conflict of Interest Declarations

a) We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements: **NONE**

b) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission: **NONE**

Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

Information was gathered through 2 methods:

a) A survey was conducted with patients currently receiving treatment with the originator Infliximab (Remicade) therapy. Ninety-four (94) patients in the Greater Toronto Area submitted written responses.

b) Group and individual discussions. Small group discussions (4-6 participants in each group) were conducted in person, while individual discussions were conducted by telephone.

Patients cite symptoms such as painful, swollen and stiff joints; extreme fatigue, loss of energy; bone loss; immobility and loss of appetite.

People's lives become limited and inhibited in numerous ways. Physical activities are difficult. Many people forego athletic activities and the subsequent socialization that is a part of that.

Social interaction is impacted in other ways affecting parental interaction with their children and care for them in physical ways. This causes imbalanced perspectives from both the parent and the child in comparison to their peers that affect relationships over a long term.

Socializing is inhibited by pain and fatigue. Social isolation and stigma accompany these symptoms with many citing a loss of friends. Family members struggle with changing roles. Some couples experience difficulties maintaining a sexual relationship.

The condition impacts employment depending on the type of work the patient does. Cases have been shared of loss of work due to disability and subsequent development of mental health issues due to unemployment and self-esteem.

2.2 Patients' Experiences with the Current Treatment

All patients who completed the survey or engaged in discussion are currently receiving therapy with the originator Remicade/Infliximab.

Patients are generally satisfied with the impact of the current therapy on their symptoms and quality of life.

Patients express concern about side effects not adequately addressed by their healthcare providers:

- 83.5% felt that the description of their symptoms weren't always accepted as truthful
- Hair loss
- Headaches
- Fatigue

Patients' priority concerns relate to Access to therapy and the Economic Burden of therapy.

- Over 60% cite "High Cost of Medication" as the most likely reason for interruption of treatment with current therapy
- Seniors covered by public plans are worried that government will change regulations and criteria for coverage due to high cost
- 43.8% think that if their employer changes coverage providers then their treatment access will be jeopardized
- 56% feel that treatment could be discontinued if governments announce general cutbacks to healthcare system
- 26% cite a job change as a threat to continued treatment

Patients feel trapped within a system that has limited transparency:

- 89% said that they did not fully understand their treatment plan.
- Many patients were very surprised to find that one pharmacy has a commanding share of the market for the originator drug. Some could not explain why they were having their prescriptions filled by a pharmacy whose name they could not even remember.
- Patients expressed concern that the same foreign corporate entity controls the distribution of the drug, the specialty pharmacy with the bulk of market share, and the majority of the infusion clinics that deliver the treatment. There is a feeling that this market domination exacerbates the economic burden.
- Patients under private coverage were of the unverified impression that their private payer was managing their treatment and that their coverage could be imperilled if they change pharmacy providers .

2.3 Impact on Caregivers

Caregivers share the upheaval of life experienced by patients affecting relationships, roles, management of disease and life's daily demands. For many there is also an economic burden with patients who are unable to continue their work. There are gaps in reimbursement coverage and some have indicated undertaking debt in order to provide coverage for family members.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

Patients' primary therapeutic concern is safety in the use of any subsequent entry biologic.

- 92.4% want physicians to think of safety first when considering any treatment.
- 95.7% believe they should receive treatment that meets the accepted current standards of care and quality.
- Patients expect evidence to support that switching from an innovator therapy to a biosimilar will not impact their treatment outcome.
- If there is no evidence then patients prefer to continue their existing treatment.
- Further to that point, if patients do not have a choice to switch they feel they will continue to be subject to the heavy economic burden of the originator therapy. They feel that this is inherently unfair and feel trapped compared to the freedom of choice that new patients will have.

There is a concern that specialists may have a bias against prescribing a biosimilar even if all the evidence demonstrates equivalent effectiveness.

- 91.4% want equal access to the best treatment without preference.

- This concern is credited to some practitioners having begun offering infusion services in their offices in the last 2 years. While unsubstantiated, the perception is that there may be a relationship between practitioner and manufacturer that may be borderline ethical.
- 69% want to be able to get a second opinion without fear of recrimination.

There is a perspective that the apparent monopolistic control of infusion centres make them exclusive to the originator drug and will limit access to competitive, more cost-effective alternatives thereby artificially maintaining higher costs and limiting patient choice of therapy. There was a 5% price increase when Canadian distribution of the drug came under control of the foreign entity, notwithstanding other price increases over the last few years. There was no advance notice of the price increase and few patients were informed of the reason and there was no recourse to dispute.

Patients' primary expectation of a SEB is that it will lower the cost of treatment and relieve the economic burden on individuals as well as on the system as a whole. Economic and social benefits include:

- reduced fear of an unsustainable healthcare system affecting healthcare policy
- expanded personal employment opportunities by reduced burden on company benefits plans.
- decreased impact on family relationships.
- improved access to treatment for patients not currently undergoing biologic therapy.
- many patients are aware of the SEB price that is 39% less than the originator drug in other countries and feel that Canada should get the same discount.

Section 4 — Key Messages

Patient concerns centre on the major issues of:

- Relief of the economic burden on individuals and the system
- Access to the therapy and treatment providers of their choice
- Equity in the delivery of care and pricing of therapies
- Transparency at all touch points in the delivery of care
- Improving communications between health care professionals and patients on issues of treatment plan and managing side effects.

Section 6 — Comments on Potential Ways SEBs Can be Used

- The SEB will be used instead of the originator (reference/brand name) product with physician approval before patient receives any treatments
  - There are already other treatment options in this class of drug – TNF blockers. Patients will expect physicians to assess the proper therapy for an individual patient that not only includes clinical effectiveness but impact on a patient's social and economic burden.
- 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
  - Patients express high levels of confusion over a switch to another product. They have been told at various times that (a) switching from one biologic that fails to another is no guarantee that the next will be effective; (b) once switched the body develops anti-bodies to the first and treatment cannot be resumed is the second choice fails; (c) there are no problems switching back and forth; and (d) there are newer innovator therapies to choose from.

- The SEB will be used instead of the originator product without physician approval before patient receives any treatments
  - Patient centered care requires collaboration between patients and their healthcare professionals. Decisions made outside of this relationship without direct participation of patients in their treatment plan is completely opposed to the recognition that healthcare practice, in order to be fully effective, needs to follow the principles of patient centered care. It's important to recognize that patients need to continually manage their healthcare. If decision-making is taken out of their hands then self-management suffers. As the population continues to age and develop multiple chronic conditions, the cost to the system and all plans will escalate with reduced engagement in self-management.
- 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
  - Patients are concerned about safety and will demand evidence that supports any change of treatment that is being forced on them by a third party for economic reasons.
- Back and forth replacement between SEB and originator product without physician consent

Since Health Canada states that SEBs are new drugs, patients will expect that any treatment decisions will be make in collaboration with their healthcare professionals.

The Arthritis Society

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra
Indication of interest	Ankylosing spondylitis
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

1.1 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 $185 million in projects that have led to breakthroughs in the diagnosis, treatment and care of people with arthritis. The Arthritis Society is accredited under Imagine Canada's Standards Program. The website www.arthritis.ca provides more detailed information.

1.2 Conflict of Interest Declarations

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Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

Ankylosing spondylitis (AS) is a type of inflammatory arthritis and an autoimmune disease. An autoimmune disease is one where the body's immune system becomes confused and begins to "attack" the body. In AS, the joints in the spine are the target of the immune attack, resulting in pain and stiffness (inflammation) in the back.

The first symptoms of AS typically start in late adolescence or early adulthood (ages 15-30). The inflammation of AS usually starts at the base of the spine, where the spine attaches to the pelvis (sacroiliac [SI] joints). This inflammation can spread upwards to involve other parts of the spine and, in the most severe cases, it can involve the entire spine. As the inflammation continues, new bone forms as the body tries to repair itself. As a result, the bonesof the spine begin to "grow together" or fuse, 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 can also cause pain and stiffness in peripheral joints, such as the hips and shoulders. It can also cause inflammation of the tendons surrounding the joints. This is called enthesitis. Some of the common spots for enthesitis are the back of the heels (Achilles tendonitis), underneath the bottoms of the feet (plantar fasciitis), on the outside of the hips (trochanteric bursitis) and along the breast bone (costochondritis). When the immune system is confused, it can attack other parts of the body other than the joints and tendons. In AS, this attack may also cause inflammation in the eye, a condition called uveitis or iritis. In rare cases, the lungs and heart can also be affected.

AS is a highly variable disease that causes very different symptoms. Some individuals may only experience episodes of mild back pain, while others will have severe chronic pain accompanied by stiffness of the spine affecting their posture and daily activities.

The most universal symptom, however, is chronic low back pain that seems to come (flare) and go for no apparent reason. It is generally worse in the morning when rising from bed and improves with stretching and exercise.

2.2 Patients' Experiences with the Current Treatment

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.

Where they work, current treatments are extremely effective. For others, current treatments are not at all effective, or not effective enough. Through research for this submission we have learned:

- Many patients are not managing their condition as well as they and their physician know is possible.
- Some have had to leave the workforce and others are finding it difficult to self-manage their disease and their overall health using prescribed therapies such as strengthening and cardiovascular exercises and experience muscle weakening thus unstable joints.
- A patient told us "Current treatment is effective, to a point. I will never be able to run across the street or live in a house with stairs, and I'm not yet 40."
- Flares remain unpredictable.

- We heard "My treatment is very effective, for now. I'm scared it will fail me eventually and I will never be able to find another that works."
- A patient told us "I can feel my (biologic) working immediately during the infusion. It has made a huge difference for me."
- Others feel their current therapy is not doing enough and that they are not able to walk for more than about a minute at a time, and "Without my current treatment regimen, I feel sure I would not be able to work."

The July 2014 Patient Empowerment Survey gave us insight into the hardships faced by individuals living with AS. We asked individuals living with AS on a scale from 1-5 to rate how much their AS symptoms limited their day-today activities and impacted their quality of life. 52% reported their ability to work was extremely or somewhat limited because of their ASA, 34% reported their ability to socialize with family and friends was extremely or somewhat limited, 56% reported their ability to exercise and be physically active was extremely or somewhat limited, 51% reported their ability to have an intimate relationship with partner, spouse or significant other was extremely or somewhat limited, and 53% reported their overall quality of life in the past year was extremely or somewhat limited.

Unfortunately, there are many adverse effects that can be present with the pharmaceutical treatment of AS. They include: fever, night sweats, weight loss, tiredness, feeling full after eating only a small amount; 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, clay-colored stools, and jaundice.
There are access issues. The cost of medications requires private insurance for coverage, or some patients and their family members who do not have insurance take on additional work to pay for the pharmaceuticals. The requirements to be approved for medications are onerous on the patient. Many provincial drug plans also require significant paperwork and constant checking in to see of the patient requires the medication.

- Patients have told us: "Medication is very expensive." "I am concerned now that I am retired I will out spend my paid insurance lifetime cap of $75,000 since my medication cost to me monthly after government and insurance is about $2,000. I will then have to go without medication."
- Patients have also reported challenges in finding general practitioners to manage their disease, and that there are lengthy waiting lists to see a rheumatologist in some areas of the country.

For people diagnosed with AS in their 20s and 30s, treatment will be needed over the entire remainder of their lifespan, which could be 50 years or more. As the body may develop a resistance to a medication after several years, it is important that biologics with a variety of targets be made available to people with RA so that their doctors can continue to treat them with the full arsenal of medications available to them.

To help ensure that patients take their medications as prescribed, most manufacturers of biologics offer patient assistance programs that provide reimbursement guidance and disease treatment support. Through information gathering for this submission the Society learned that these built-in support systems can help patients derive the full benefits of their treatment. With respect to accessibility many patient assistance programs help patients navigate both public and private insurance reimbursement and financial assistance; and the clinics associated with the program often offer long business hours for convenient appointments, and access to helplines that are staffed 24 hours a day, seven days a week to answer questions. With respect to effectiveness the patient support programs have many advantages including: pre-infusion health checks to ensure the patient is receiving the medication at the proper time, regular communication between the support program and the patient's physician allowing the

physician to stay informed of treatment results, and a comfortable, safe, non-threatening atmosphere/environment to receive medications which can lead to enhanced compliance and better health outcomes.

The Arthritis Society is supportive of robust patient assistance / support programs and would expect to see quality programs from new SEB entrants to the market.

2.3 Impact on Caregivers

Families, friends, and all caregivers of individuals living with rheumatoid arthritis are hit hard with the demands of caregiving.

Patients have told us: "It's hard on your caregiver when you are vomiting for an entire day because of a medication. They have to plan their life around losing a day (every week) to look after you, or at the very least not be able to count on you to help with family responsibilities."

Caregivers also suffer emotionally when they see the patient suffer knowing that there is little they can do about it because the current treatment regime is not providing the outcomes hoped for, and / or the side effects are harsh.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

The Arthritis Society does not believe that patients currently have expectations for SEBs because the vast majority of patients are completely unaware of SEBs. To address this knowledge gap The Arthritis Society will be releasing education material regarding SEBs targeted to patients in the near future.
The Society believes that SEBs have a role to play in the care and management of those living with inflammatory arthritis, and that SEBs will offer more choice for those living with certain forms of arthritis and has the potential to lower health care costs and increase access.
SEBs like the originator biologic are a class of medicine specially designed to treat inflammatory types of arthritis, such as AS. Biologics are used to suppress inflammation and help prevent damage to joints.

Section 4 — Key Messages

- The Society believes that SEBs have a role to play in the care and management of those living with inflammatory arthritis, and that SEBs will offer more choice for those living with certain forms of arthritis and has the potential to lower health care costs and increase access.
- AS is a highly variable disease that causes very different symptoms. Some individuals may only experience episodes of mild back pain, while others will have severe chronic pain accompanied by stiffness of the spine affecting their posture and daily activities.
- The Society believes 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 identify cost of medication as an access to treatment challenge.
- 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.

Section 6 — Comments on Potential Ways SEBs Can be Used

In June 2014 The Arthritis Society approved a position paper "Access to Medication: Subsequent Entry Biologics (SEBs). Rather than provide comment on the scenerios 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. Since the biologics and SEBs have different chemical structures, potentially adverse outcomes for the patient can occur. With respect to SEBs therapeutic substitution would allow a pharmacist to dispense any biologic medication with a relevant indication rather than the specific medication that was prescribed.

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 are not 'generic' biologics and authorization of an SEB is not a declaration of pharmaceutical or therapeutic equivalence to the reference biologic drug." Health Canada "does not support automatic substitution of a SEB for its reference biologic drug."

The Arthritis Society Position on SEBs:

- The Arthritis Society believes SEBs have a role to play in the care and management of those living with inflammatory arthritis.
- SEBs will offer more choice for those living with certain forms of arthritis and has the potential to lower health care costs and increase access.
- SEBs, while similar to the innovator biologic are not identical and cannot be considered a generic.
- Implement consistent, universal, unique SEB naming practices that will facilitate straightforward traceability.
- Implement a policy that does not allow therapeutic substitution of SEBs and biologics.
- Implement a policy that does not allow automatic interchangeability of innovator biologics and SEBs.
- A process for post-market surveillance must be put in place to track safety and efficacy.

The Arthritis Society

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra
Indication of interest	psoriatic arthritis
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

1.1 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 $185 million in projects that have led to breakthroughs in the diagnosis, treatment and care of people with arthritis. The Arthritis Society is accredited under Imagine Canada's Standards Program. The website www.arthritis.ca provides more detailed information.

1.2 Conflict of Interest Declarations

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Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

Psoriatic arthritis (PsA) is a type of inflammatory arthritis and an autoimmune disease. In PsA, the joints are the target of the immune attack. This causes swelling, pain and warmth (inflammation) in the joints. In most people, psoriatic arthritis starts after the onset of psoriasis. Yet having psoriasis does not mean you will have PsA. In fact, most people with psoriasis will never develop psoriatic arthritis.

PsA usually begins slowly, spreading to other joints over a few weeks to a few months. In rare instances, PsA can develop quickly and be severe. PsA is an unusual type of arthritis because it can look very different from person to person.

Doctors have discovered five general patterns of psoriatic arthritis. In the asymmetric pattern, one of the mildest forms, the psoriatic arthritis affects one to three joints on different sides of the body. In the symmetric pattern, PsA involves many more joints and looks very much like rheumatoid arthritis. In the distal pattern, PsA involves the end joints of the fingers closest to the nails. In the spinal pattern, PsA involves the joints of the spine and the sacroiliac joints linking the spine to the pelvis. Finally, in the destructive pattern, which affects only a few people, PsA is a severe, painful, deforming type of arthritis. This is also known as arthritis mutilans.

PsA can also cause inflammation in tendons around the joints. This is called enthesitis. Some of the common spots for this are the back of the heels, underneath the bottoms of the feet and on the outside of the hips. In other people, PsA can cause the fingers or toes to swell up like sausages. This is referred to as a dactylitis.

2.2 Patients' Experiences with the Current Treatment

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.

Where they work, current treatments are extremely effective. For others, current treatments are not at all effective, or not effective enough. Through research for this submission we have learned:

- Many patients are not managing their condition as well as they and their physician know is possible.
- Some have had to leave the workforce and others are finding it difficult to self-manage their disease and their overall health using prescribed therapies such as strengthening and cardiovascular exercises and experience muscle weakening thus unstable joints.
- A patient told us "Current treatment is effective, to a point. I will never be able to run across the street or live in a house with stairs, and I'm not yet 40."
- Flares remain unpredictable.
- We heard "My treatment is very effective, for now. I'm scared it will fail me eventually and I will never be able to find another that works."
- A patient told us "I can feel my (biologic) working immediately during the infusion. It has made a huge difference for me."
- Others feel their current therapy is not doing enough and that they are not able to walk for more than about a minute at a time, and "Without my current treatment regimen, I feel sure I would not be able to work."

The July 2014 Patient Empowerment Survey gave us insight into the hardships faced by individuals living with PA. We asked individuals living with PA on a scale from 1-5 to rate how much their PA symptoms

limited their day-today activities and impacted their quality of life. 51% reported their ability to work was extremely or somewhat limited because of their PA, 34% reported their ability to socialize with family and friends was extremely or somewhat limited, 62% reported their ability to exercise and be physically active was extremely or somewhat limited, 53% reported their ability to have an intimate relationship with partner, spouse or significant other was extremely or somewhat limited, and 55% reported their overall quality of life in the past year was extremely or somewhat limited.

Unfortunately, there are many adverse effects that can be present with the pharmaceutical treatment of PA. They include: fever, night sweats, weight loss, tiredness, feeling full after eating only a small amount; 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, clay-colored stools, and jaundice.
There are access issues. The cost of medications requires private insurance for coverage, or some patients and their family members who do not have insurance take on additional work to pay for the pharmaceuticals. The requirements to be approved for medications are onerous on the patient. Many provincial drug plans also require significant paperwork and constant checking in to see of the patient requires the medication.

- Patients have told us: "Medication is very expensive." "I am concerned now that I am retired I will out spend my paid insurance lifetime cap of $75,000 since my medication cost to me monthly after government and insurance is about $2,000. I will then have to go without medication."
- Patients have also reported challenges in finding general practitioners to manage their disease, and that there are lengthy waiting lists to see a rheumatologist in some areas of the country.

For people diagnosed with PA in their 20s and 30s, treatment will be needed over the entire remainder of their lifespan, which could be 50 years or more. As the body may develop a resistance to a medication after several years, it is important that biologics with a variety of targets be made available to people with RA so that their doctors can continue to treat them with the full arsenal of medications available to them.

To help ensure that patients take their medications as prescribed, most manufacturers of biologics offer patient assistance programs that provide reimbursement guidance and disease treatment support. Through information gathering for this submission the Society learned that these built-in support systems can help patients derive the full benefits of their treatment. With respect to accessibility many patient assistance programs help patients navigate both public and private insurance reimbursement and financial assistance; and the clinics associated with the program often offer long business hours for convenient appointments, and access to helplines that are staffed 24 hours a day, seven days a week to answer questions. With respect to effectiveness the patient support programs have many advantages including: pre-infusion health checks to ensure the patient is receiving the medication at the proper time, regular communication between the support program and the patient's physician allowing the physician to stay informed of treatment results, and a comfortable, safe, non-threatening atmosphere/environment to receive medications which can lead to enhanced compliance and better health outcomes.

The Arthritis Society is supportive of robust patient assistance / support programs and would expect to see quality programs from new SEB entrants to the market.

2.3 Impact on Caregivers

Families, friends, and all caregivers of individuals living with rheumatoid arthritis are hit hard with the demands of caregiving.

Patients have told us: "It's hard on your caregiver when you are vomiting for an entire day because of a medication. They have to plan their life around losing a day (every week) to look after you, or at the very least not be able to count on you to help with family responsibilities."

Caregivers also suffer emotionally when they see the patient suffer knowing that there is little they can do about it because the current treatment regime is not providing the outcomes hoped for, and / or the side effects are harsh.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

The Arthritis Society does not believe that patients currently have expectations for SEBs because the vast majority of patients are completely unaware of SEBs. To address this knowledge gap The Arthritis Society will be releasing education material regarding SEBs targeted to patients in the near future.
The Society believes that SEBs have a role to play in the care and management of those living with inflammatory arthritis, and that SEBs will offer more choice for those living with certain forms of arthritis and has the potential to lower health care costs and increase access.
SEBs like the originator biologic are a class of medicine specially designed to treat inflammatory types of arthritis, such as PA. Biologics are used to suppress inflammation and help prevent damage to joints.

Section 4 — Key Messages

- The Society believes that SEBs have a role to play in the care and management of those living with inflammatory arthritis, and that SEBs will offer more choice for those living with certain forms of arthritis and has the potential to lower health care costs and increase access.
- The Society believes 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 identify cost of medication as an access to treatment challenge.
- 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.

Section 6 — Comments on Potential Ways SEBs Can be Used

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ISSUES

Therapeutic Substitution

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The Arthritis Society Position on SEBs:

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- Implement a policy that does not allow automatic interchangeability of innovator biologics and SEBs.
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The Arthritis Society

Section 1 — Information About the Submitting Patient Group

Name of the drug	Inflectra
Indication of interest	rheumatoid arthritis
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

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Section 2 — Disease/Condition and Current Treatment Information

2.1 Impact of Condition on Patients

Rheumatoid arthritis (RA) is a type of inflammatory arthritis and an autoimmune disease. An autoimmune disease is one where the body's immune system becomes confused and begins to "attack" the body.

In RA, the target of the immune attack is tissue in the lining of the joints and, sometimes, in other internal organs (such as the eyes, lungs or heart). This causes swelling, pain, inflammation and joint destruction.

RA usually begins slowly, starting in a few joints and then spreading to other joints over a few weeks to a few months. As time goes on, RA involves more and more joints on both sides of the body often in a "symmetrical" pattern. This means if joints in your right hand are swollen, then joints in your left hand will probably be swollen.

The symptoms of RA vary from person to person. Some people have only a few joints involved or mild inflammation, whereas others have many joints involved or severe inflammation. The symptoms of RA also vary from times when the joints feel good to other times (often for no reason at all) when the joints become more stiff, sore and swollen.

2.2 Patients' Experiences with the Current Treatment

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.

Where they work, current treatments are extremely effective. For others, current treatments are not at all effective, or not effective enough. Through research for this submission we have learned:

- Many patients are not managing their condition as well as they and their physician know is possible.
- Some have had to leave the workforce and others are finding it difficult to self-manage their disease and their overall health using prescribed therapies such as strengthening and cardiovascular exercises and experience muscle weakening thus unstable joints.
- A patient told us "Current treatment is effective, to a point. I will never be able to run across the street or live in a house with stairs, and I'm not yet 40."
- Flares remain unpredictable.
- We heard "My treatment is very effective, for now. I'm scared it will fail me eventually and I will never be able to find another that works."
- A patient told us "I can feel my (biologic) working immediately during the infusion. It has made a huge difference for me."
- Others feel their current therapy is not doing enough and that they are not able to walk for more than about a minute at a time, and "Without my current treatment regimen, I feel sure I would not be able to work."

The PES also gave us insight into the hardships faced by individuals living with RA. We asked individuals living with RA on a scale from 1-5 to rate how much their RA symptoms limited their day-today activities and impacted their quality of life. 46% reported their ability to work was extremely or somewhat limited because of their RA, 44% reported their ability to socialize with family and friends was extremely

or somewhat limited, 58% reported their ability to exercise and be physically active was extremely or somewhat limited, 43% reported their ability to have an intimate relationship with partner, spouse or significant other was extremely or somewhat limited, and 48% reported their overall quality of life in the past year was extremely or somewhat limited.

Unfortunately, there are many adverse effects that can be present with the pharmaceutical treatment of RA. They include: fever, night sweats, weight loss, tiredness, feeling full after eating only a small amount; 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, clay-colored stools, and jaundice. Patients have told us:

- "If I try to take a higher dose I have stomach problems."
- "I suffer from nausea and I'm not able to do anything on the day I take methotrexate, so I lose a whole day every week to vomiting."
- "I get huge site reactions from injections."

There are major access issues. The cost of medications requires private insurance for coverage, or some patients and their family members who do not have insurance take on additional work to pay for the pharmaceuticals. The requirements to be approved for medications are onerous on the patient. Many provincial drug plans also require significant paperwork and constant checking in to see of the patient requires the medication.

- Patients have told us: "Medication is very expensive."
- Patients have also reported challenges in finding general practitioners to manage their disease, and that there are lengthy waiting lists to see a rheumatologist in some areas of the country.

For people diagnosed with RA in their 20s and 30s, treatment will be needed over the entire remainder of their lifespan, which could be 50 years or more. As the body may develop a resistance to a medication after several years, it is important that biologics with a variety of targets be made available to people with RA so that their doctors can continue to treat them with the full arsenal of medications available to them.

Patients often need to use a variety of drugs to control their arthritis, some in combinations NSAIDS, DMARDS, biologics, corticosteroids, and natural health products.

To help ensure that patients take their medications as prescribed, most manufacturers of biologics offer patient assistance programs that provide reimbursement guidance and disease treatment support. Through information gathering for this submission the Society learned that these built-in support systems can help patients derive the full benefits of their treatment. With respect to accessibility many patient assistance programs help patients navigate both public and private insurance reimbursement and financial assistance; and the clinics associated with the program often offer long business hours for convenient appointments, and access to helplines that are staffed 24 hours a day, seven days a week to answer questions. With respect to effectiveness the patient support programs have many advantages including: pre-infusion health checks to ensure the patient is receiving the medication at the proper time, regular communication between the support program and the patient's physician allowing the physician to stay informed of treatment results, and a comfortable, safe, non-threatening atmosphere/environment to receive medications which can lead to enhanced compliance and better health outcomes.

The Arthritis Society is supportive of robust patient assistance / support programs and would expect to see quality programs from new SEB entrants to the market.

2.3 Impact on Caregivers

Families, friends, and all caregivers of individuals living with rheumatoid arthritis are hit hard with the demands of caregiving.

Patients have told us: "It's hard on your caregiver when you are vomiting for an entire day because of a medication. They have to plan their life around losing a day (every week) to look after you, or at the very least not be able to count on you to help with family responsibilities."

Caregivers also suffer emotionally when they see the patient suffer knowing that there is little they can do about it because the current treatment regime is not providing the outcomes hoped for, and / or the side effects are harsh.

Section 3 — Information About the SEB Being Reviewed

3.1 What Are Patients' Expectations for the SEB?

The Arthritis Society does not believe that patients currently have expectations for SEBs because the vast majority of patients are completely unaware of SEBs. To address this knowledge gap The Arthritis Society will be releasing education material regarding SEBs targeted to patients in the near future.

The Society believes that SEBs have a role to play in the care and management of those living with inflammatory arthritis, and that SEBs will offer more choice for those living with certain forms of arthritis and has the potential to lower health care costs and increase access.

SEBs like the originator biologic are a class of medicine specially designed to treat inflammatory types of arthritis, such as PA. Biologics are used to suppress inflammation and help prevent damage to joints.

Section 4 — Key Messages

- The Society believes that SEBs have a role to play in the care and management of those living with inflammatory arthritis, and that SEBs will offer more choice for those living with certain forms of arthritis and has the potential to lower health care costs and increase access.
- The Society believes 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.
- The symptoms of RA vary from person to person. Some people have only a few joints involved or mild inflammation, whereas others have many joints involved or severe inflammation. The symptoms of RA also vary from times when the joints feel good to other times (often for no reason at all) when the joints become more stiff, sore and swollen.
- Patients identify cost of medication as an access to treatment challenge.
- 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.

Section 6 — Comments on Potential Ways SEBs Can be Used

In June 2014 The Arthritis Society approved a position paper "Access to Medication: Subsequent Entry Biologics (SEBs). Rather than provide comment on the scenerios 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. Since the biologics and SEBs have different chemical structures, potentially adverse outcomes for the patient can occur. With respect to SEBs therapeutic substitution would allow a pharmacist to dispense any biologic medication with a relevant indication rather than the specific medication that was prescribed.

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 are not 'generic' biologics and authorization of an SEB is not a declaration of pharmaceutical or therapeutic equivalence to the reference biologic drug." Health Canada "does not support automatic substitution of a SEB for its reference biologic drug."

The Arthritis Society Position on SEBs:

- The Arthritis Society believes SEBs have a role to play in the care and management of those living with inflammatory arthritis.
- SEBs will offer more choice for those living with certain forms of arthritis and has the potential to lower health care costs and increase access.
- SEBs, while similar to the innovator biologic are not identical and cannot be considered a generic.
- Implement consistent, universal, unique SEB naming practices that will facilitate straightforward traceability.
- Implement a policy that does not allow therapeutic substitution of SEBs and biologics.
- Implement a policy that does not allow automatic interchangeability of innovator biologics and SEBs.
- A process for post-market surveillance must be put in place to track safety and efficacy.