

CADTH COMMON DRUG REVIEW

Patient Input

IXEKIZUMAB (Taltz)

(Eli Lilly Canada Inc.)

Indication: Ankylosing Spondylitis

CADTH received patient input from:

Arthritis Consumer Experts

Canadian Arthritis Patient Alliance (CAPA) & the Arthritis Society

The Canadian Spondylitis Association

September 23, 2019

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

CADTH 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.

C/O: Canadian Agency for Drugs and Technologies in Health (CADTH)

Re: Patient Input for ixekizumab for ankylosing spondylitis

Date of submission: September 23, 2019

Section 1 — General Information

Name of the drug: ixekizumab

Indication of interest: ankylosing spondylitis

Name of patient group: Arthritis Consumer Experts

Name of the primary contact for this submission:

████████████████████
████████████████████
████████████████

Name of author (if different):

████████████████████
████████████████████

Patient group's contact information:

feedback@jointhealth.org

604-974-1366

Unit 210-1529 West 6th Avenue

Vancouver, BC

V6J 1R1

www.jointhealth.org

Permission is granted to post this submission: Yes

Section 1 – About your Patient Group

Canada's largest, longest running national arthritis patient organization headquartered in Vancouver, BC, Arthritis Consumer Experts (ACE) provides free, science-based information and education programs in both official languages to people with arthritis. ACE serves people living with all forms of arthritis by helping them take control of their disease and improve their quality of life through education and (em)powerment. Founded and led by people with arthritis, ACE also advocates on arthritis health policy issues, through ACE's

JointHealth™ family of programs and the Arthritis Broadcast Network, directly to consumers/patients, media and government. ACE operates as a non-profit in a fully transparent manner and is guided by a strict set of guiding principles, set out by an advisory board comprised of leading scientists, medical professionals and informed arthritis consumers. Ultimately, we are guided by the needs of our members, who are people living with arthritis, and their caregivers.

Link to website: www.jointhehealth.org

Section 2 – Information Gathering

The information was gathered in Canada on the ACE Survey Monkey platform from August to September 2019, without assistance or funding from an outside source. Input was compiled and made grammatically correct by A. Chan and C. Koehn, full time employees of ACE.

Section 3 — Disease Experience

3.1 How does the disease impact the patients' day-to-day life and quality of life?

ACE: Ankylosing spondylitis (AS) has a significant effect on the lives of people living with it and they constantly consider the state of their disease and decide what they can, or more likely, cannot, cope with or achieve, how they can go about their daily lives, and how much help they may need along the way.

- **Patient A:** Living with AS for 30 years and also has Crohns Colitis, psoriatic arthritis, and psoriasis. RA for approximately 30 years. They have limited mobility due to their AS.
- **Patient B:** Living with AS for 23 years. “I am aware that at any time, my back inflammation can flare up and severely limit my activity for a few days. So, I pace myself and pay attention to my posture.”
- **Patient C:** Living with AS for 20 years. “Fatigue, pain, and subsequent deconditioning have lead to other MSK issues (e.g. knee pain). The constant pain has also made me anxious and affects my mood when I am not able to go out to do things I would like to do, or sometimes even my daily activities.”
- **Patient D:** Living with AS for 4 years and experiences unpredictable and disabling pain and fatigue.

3.2 How does the disease impact the caregivers' day-to-day life and quality of life?

ACE: Caregivers of people living with ankylosing spondylitis have indicated that time management is very important to them. When patients are in pain, caregivers have to help with house chores and many other aspects of life at home.

- **Patient A:** “My caregiver has to help me dress, grocery shop, and help me with house chores.”
- **Patient B:** Answered “Not applicable” to this question.
- **Patient C:** “It’s hard for caregivers to understand what it is like when someone has inflammatory arthritis. They often don’t know how best to provide emotional or physical support, and can be frustrating for them. I’m fairly high functioning, but for others who need more care, it would be draining on a caregiver in terms of both time and energy and stress.”

3.3 Are there any aspects of the illness that are more important to control than others?

- **Patient A:** “Movement.”
- **Patient B:** “Back spasms.”
- **Patient C:** “Pain and inflammation primarily – these are the source of the fatigue and low mood and deconditioning from moving/exercising less.”
- **Patient D:** “Fatigue and weight gain.”

Section 4 – Experiences with Currently Available Treatments

How well are patients managing their disease/condition with currently available treatments?

- **Patient A:** Takes Cimzia and methotrexate. In response to “How effective is current therapy in controlling the common aspects of AS?”, the patient answered “average”. They do not experience side effects from the therapy but finds the medication costly.
- **Patient B:** Taking anti-inflammatories and Tylenol as needed. At night, they take an anti-depressant to help with their sleep. They also include exercise in their treatment plan. Their treatment therapy is “good right now” at controlling the common aspects of AS. “My liver and kidney blood tests become “out of range” if I take too many anti-inflammatories or Tylenol.”
- **Patient C:** Taking Humira. “It was previously very effective; however, it’s effectiveness drastically decreased as of 3 months ago. I am still currently in a flare and awaiting to switch to Simponi.” They do not experience side effects and have tolerated the biologic very well.” Their extended medical insurance from work covers the cost of their biologics. They do not have a fear of needles so manage the mode of taking the medication fairly well.
- **Patient D:** Taking Humira and anti-inflammatories. The medication is good at controlling fatigue. Depending on the day, they still feel pain.

ACE: In general, the thousands of AS patients that ACE has interacted with over the past 19 years, have told us that having medication options is important to them, like it is for patients with cancer, HIV and other serious chronic diseases and illnesses. As stated in every patient input we have submitted on our members’ and the public’s behalf, patient input respondents consider the “best treatment” is one that causes the fewest adverse effects and puts patients into remission.

Section 5 – Improved Outcomes

- **Patient A, B, and D:** Did not provide an answer to this section.
- **Patient C:** The following are unmet needs: “Better additional pain control when flaring (even if while on the biologic). NSAIDs have given me an ulcer and I am opioid sensitive so I don’t have many options for pain management.”

Section 6 – Experience with Drug Under Review

None of the patients interviewed have experience with taking ixekizumab for ankylosing spondylitis but two patients provided additional comments for this section:

- **Patient A and D** have no experience with taking ixekizumab for AS and did not provide additional comments for this section.
- **Patient B:** Expects ixekizumab to “eliminate flare ups”. They think that improvement would have to be significant. Side effects such as kidney and liver toxicity are unacceptable.
- **Patient C:** Willing to take ixekizumab but “depends on how serious the side effect is, and the probability of it happening. If life threatening with cases of death, I would be less willing to use it.” For them, 70%+ improvement would be considered adequate response to the medication. “If it allows me to continue working full time, I would consider it adequate too. Like all biologics, ixekizumab should decrease pain and inflammation, improve quality of life, allow better function, improve work productivity and social engagement.”

Section 7 – Companion Diagnostic Test

Not applicable to this submission.

Section 8 – Biosimilar

Not applicable to this submission.

Section 9 – Anything Else?

ACE: Based on a large body of peer-reviewed evidence, ACE recommends a well-rounded treatment plan for AS that includes education (both disease and self-management), appropriate immunosuppressive medication(s), therapeutic and recreational exercise, appropriate amounts of rest during flares, physical therapy, healthy diet and an overall healthy lifestyle. Paramount among these is the timely initiation of the most suitable medication(s), chosen by the patient in consultation with their rheumatologist. Biologics and targeted small molecule medications are proved to effectively address disease signs and symptoms – like swelling, pain and fatigue – but also improve mortality and reduce heart disease and other complications of inflammatory arthritis.

In general, we find patients asking the following questions:

- Is there one or a few advanced therapies that you feel may work the best for me? If yes, why?
- What are the different ways to take the ones you think might work best for me at this point in my disease course?
- What are the most common and the most serious side effects for the advanced therapy you are recommending?
- Do I have to stop what I'm taking now to clear it from my body before starting on the advanced therapy you recommend?
- Can I stop any of the other medications I'm currently taking when I start on the advanced therapy you recommend? If so, when?
- How long do I have to be off one or all my current medications before I can start on the advanced therapy you recommend?
- Can I get pregnant while taking the advance therapy you recommend?
- How quickly do I need to decide?

ACE made minor grammatical corrections to patient input where needed but in no way altered the meaning or intent of the input.

Appendix: Conflict of Interest Declaration

- 1) Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

No. This submission was summarized and written solely by the staff of Arthritis Consumer Experts, free from consultation, advice, influence, or financial support from any outside individual, group or company.

- 2) Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No.

- 3) List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Arthritis Consumer Experts received a grant-in-aid from Eli Lilly in 2018-2019.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Eli Lilly				X

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Cheryl Koehn
 Position: Founder and President
 Patient Group: Arthritis Consumer Experts
 Date: September 23, 2019

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	Ixekizumab for ankylosing spondylitis
Name of the Patient Group	Canadian Arthritis Patient Alliance (CAPA) & the Arthritis Society
Author of the Submission	[REDACTED]
Name of the Primary Contact for This Submission	[REDACTED]
Email	[REDACTED]
Telephone Number	[REDACTED]

1. About Your Patient Group

The Canadian Arthritis Patient Alliance (CAPA) is a grass-roots, patient-driven, independent, national education and advocacy organization with members and supporters across Canada. CAPA creates links between Canadians with arthritis to assist them in becoming advocates and to improve their quality of life. CAPA believes the first expert on arthritis is the person who lives with arthritis, and is an organization for patients run by patients (who are all volunteers). As a virtual organization we have no physical office and communicate with our community primarily through electronic methods, such as our [website](#), quarterly newsletter, e-mail, and social media. CAPA welcomes all Canadians with arthritis, and those who support CAPA's goals, to become members.

The Arthritis Society has been setting lives in motion for over 70 years. Dedicated to a vision of living in a world where people are free from the devastating affects that arthritis has on the lives of Canadians, the Society is Canada's principal health charity providing education, programs and support to 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 \$200 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.

2. Information Gathering

We developed a survey to hear directly from people living with ankylosing spondylitis (AS) about their experiences with AS and any experiences taking ixekizumab. CAPA and the Arthritis Society collaboratively developed the survey and the design was informed by the lived experiences of the CAPA Board Members who all live with various forms of arthritis. The survey was shared via e-mails and social media (CAPA and Arthritis Society Facebook and Twitter accounts) through our respective Canadian networks and communities. The survey was open from August 9 until September 9, 2019.

In addition, a survey was developed by the Canadian Spondylitis Association (CSA), which was distributed through social media channels and the CSA website between August 8, 2019 and September 15, 2019. The results of the survey conducted by CSA were shared with us for the purposes of this submission, and our results were shared with CSA as well.

An Eli Lilly Canada contact provided us with names of the Canadian rheumatologist trialists who had patients enrolled in the AS ixekizumab clinical trial. CAPA, the Arthritis Society and CSA reached out to these rheumatologists via email and asked them to pass along a letter to clinical trial participants that explained CADTH, the Common Drug Review process, and why their input would be of value. The letter provided a link to the CAPA and Arthritis Society survey as well as contact information for Sammy Feilchenfeld, in case they wanted to be in touch via email and/or phone.

For our survey, ten responses were received, of which no individuals had experience taking ixekizumab. The survey collected demographic data, however not all respondents completed this section. Those who completed demographic data (n=4) represented an age range of 31-49. All respondents indicated that their AS was moderate in terms of its severity.

The CSA survey received 62 responses, of which 52 were from Canadian respondents. Unfortunately, no respondents had experience taking ixekizumab. All survey responses used in this submission are from the Arthritis Society/CAPA survey, unless specifically noted as a response from the CSA survey.

3. Disease Experience

Ankylosing spondylitis (AS) is a type of inflammatory arthritis that affects the spine and the sacroiliac joints that attach the pelvis to the base of the spine. With AS inflammation, the immune system attacks the ligaments and tendons attached to bone in the joints of the spine. The bone erodes at these sites and the body tries to repair itself by forming new bone. The bones of the spine begin to fuse, or grow together, causing the spine to become stiff, inflexible and painful. Even though new bone forms, the original bone in the spine can become thin, increasing the risk of spinal fractures. In addition to the spine, AS can cause pain and stiffness in peripheral joints such as the hips and shoulders. As many as 1% of the Canadian adult population lives with AS.

Symptoms that respondents indicated as having the greatest impact on their day-to-day life included joint pain, mobility, fatigue and sleep issues. Symptoms also had an impact on daily activity. Respondents had the following comments on work, life and travelling:

- *“Work can be challenging because I’m a waitress who does lots of walking and lifting, but I tend to manage. Housework and gardening is really hard on my body, so I hired a housekeeper to help me out. I cannot play sports or do vigorous activities.”*
- *“Travelling is very hard. Concentrating at work also is a struggle.”*
- *“Daily mobility issues, lots of appointments that make me miss work”*
- *“I do work but my other activities are limited. I walk for exercise but can’t do that every day.”*

- *“When medication doesn’t work well it’s difficult to go to work and even get dressed and sleep is difficult.”*
- *“SI [sacroiliac] joint pain and costochondritis are my main issues. Severe flare ups have lessened but when they do occur, I get stuck in painful positions that I can't get out of, have been carried to bed because I can't walk, legs give out and it's painful to breathe. Day-to-day I do quite well. With a flare up and a busy job as an ICU RN [Intensive Care Unit Registered Nurse]... it gets really painful. But the more I move the better it is.”*
- *“Fighting to get through every day with some level of normalcy, limited to what I can get achieved, makes work harder. Family life has changed considerably.” – CSA Survey*

AS impacts lives in many ways: completing daily tasks that many well individuals take for granted may become difficult or too exhausting to complete; participating in leisure activities can be difficult; caring for or spending time with family members such as children and loved ones, such as spouses / partners also becomes difficult.

- *“Fatigue is a big issue. It’s difficult to work full time and have a busy household with children.”*
- *“I am not able to clean, cook, do laundry Everything hurts with severe hand and foot pain. I cannot play with kids and work is affected. Cannot sleep well. Very bad fatigue.” – CSA Survey*
- *“In constant pain which affects my mood and physical abilities. Can’t hold a job due to flare ups. Have trouble keeping friends due to difficulty of leaving my home or participating. Basic needs like cleaning and self care are difficult and often aggravate joints to more flare ups.” – CSA Survey*
- *“I am a university student, heading into my senior year. I am unable to do full time classes due to pain and fatigue, so I take a reduced course load. I have not been able to work much over the past 3 years either. Standing in one spot (example in a grocery store line or at a bus stop) is much more difficult for me than walking. I have difficulties with getting things off of low shelves and picking things up from the floor.” – CSA Survey*
- *“Chronic daily pain and fatigue. I fight through it. Can’t clean around my house as I did before. My children have to do this. I can’t garden and take care of the lawn without extreme pain. Basically after any sort of activity, I need a long period of rest. Have to stop and stretch regularly throughout the day to relieve pain and keep muscles from being so tight. Intercourse is difficult and requires a recuperation period after. At the end of my work day I spent an hour in a hot bath with Epsom salts. If I don’t, it’s a rough night. Had to give up playing floor hockey, soccer and skiing. Currently play ice hockey once per week. The gliding seems easier on my body than the impact of running or hitting bumps on a hill. It’s a low-key, women’s pickup league, so no hitting or rough play. I’m tired ALL THE DAMN TIME!!” – CSA Survey*
- *“Well, I lost my career, my home, my family, and my marriage fell apart. At this point, I have no family to impact with my daily routine, and I think it's best to keep it that way? I can barely manage to keep in regular contact with my brothers through Skype.” – CSA Survey*

4. Experiences With Currently Available Treatments

Current medications for AS are designed to control disease, slow its progression and help manage pain, given that there is currently no cure for AS. Many treatments simply help people get through the day. Treatments used to manage AS include non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, sulfasalazine, and various biologic medications (protein-based medicines). The following provides a general description of the treatments used and their side effects:

- NSAIDs [Non-steroidal Anti-Inflammatory Drugs] are used to treat inflammation, which in turn often also affects (i.e. lessens) pain. The NSAIDs may cause many side effects, from stomach upset to changes in kidney function.
- Corticosteroids are commonly used to control/reduce inflammation and while effective, can produce side effects when taken for longer durations and at higher doses. Corticosteroids can cause short-term effects such as weight gain, acne, excess facial hair, mood swings, high blood pressure, high blood sugar, increased infection, stomach ulcers, hyperactivity, and increase in appetite. Long-term effects include osteoporosis, glaucoma and cataracts, osteonecrosis, skin changes, heart disease, and stroke.
- DMARDs such as methotrexate and biologic medications may include other side effects. Methotrexate often causes nausea, hair loss, and may cause liver damage. Its nausea effects are sometimes mitigated by also taking folic acid, splitting doses over the course of a few hours, and/or taking subcutaneously rather than orally. Biologic medications may have side effects such as injection reaction irritation, increase risk of upper respiratory infections, pneumonia, urinary tract infections and skin infections.

Treatment for AS is based on trial and error for each individual. Patients reported that they had tried a number of treatments for AS. Some might work well right away, or take time to improve outcomes. Others may work for some time before the individual needs to change treatment to see changes again.

Often, currently available treatments can be difficult to tolerate and manage. Nearly everyone on the CAPA/Arthritis Society survey noted that they encountered side effects from currently available treatments. However, around two thirds of respondents on the CSA survey stated that they did not have adverse effects from current treatments that are more difficult to tolerate than other treatments that they have tried. Respondents to both surveys shared their experiences with side effects:

- *“NSAID drugs have not made much difference and carry the risk of liver damage. They are not effective. Cosentyx is effective but a monthly dose is not enough to stay pain free. It only lasts 2 to 3 weeks before the pain returns full force. It is also cost prohibitive without a drug plan. Fatigue is improved with this drug, but again the results do not last.”*
- *“I have tried remicade, which was effective but had bad side effects such as increased blood pressure, anxiety... Tried Naproxen, which hurt my GI track. Tried Sulfasalazine, but I'm allergic. Tried percocet, but gave me headaches. Tried Toradol, which seems to work well. I take it only when really needed so as not to irritate my GI track.”*
- *“I have used simponi. It worked well for 8 years then lost effectiveness. Recently switched to humira and seems to be working well. With both treatments I have noticed some skin issues. From being dry to getting small sores that hurt and swell”*

- *“Initially was slated on Indocin. Stopped soon after as it caused extreme weakness, headaches, and did not help my pain. Then prescribed Celebrex. Despite dosage changes, it also did not help my pain. With my most severe flare up after the birth of my daughter, a tapered dose of prednisone worked within hours of starting. Usually I take Advil and Tylenol, use ice and heat, walk and try to exercise when having pain.”*
- *“My doctors tell me my condition is "stabilized". I describe my life as rather miserable. The truth is likely somewhere between the two?” – CSA Survey*

Patients may also pursue non-pharmacological approaches to manage AS symptoms in addition to medication, such as physiotherapy, occupational therapy, massage therapy, counselling, or chiropractic therapy. These approaches can often help to address the symptoms of the disease, such as pain and fatigue. However, there are significant unmet patient needs in terms of accessing non-pharmacological treatments, often because they are not reimbursed through provincial health care systems, the treatment options are simply not offered, or there are lengthy waits.

- *“I have done Chiro [chiropractics], physiotherapy, nerve blocks, lidocaine infusions and taken pain meds such as Atasol 30 and continue on biologic meds”*
- *“Medicinal Marijuana has proven to be quite wonderful. As I tell people, "weed doesn't do much about the pain, but at least I don't mind it quite so much". The psychological effects of living with chronic pain are probably the most debilitating, in my mind. Marijuana definitely helps with that.” – CSA Survey*
- *“Cannabis is by far the most effective acute treatment. Pain killers are 100% ineffective and do not allow areas of my back to relax. Cannabis combined with yoga is very very effective at improving mobility - the cannabis reduces pain and allows areas which tend to tighten up (back and hips) to relax, thereby allowing for effective stretching and strengthening.” – CSA Survey*

5. Improved Outcomes

People living with AS reported that current treatments are difficult to tolerate because of side effects. A variety of side effects are difficult to manage such as those described above. Some of these side effects require treatment with other medications, such as anti-nausea medications. Minimizing these side effects are important outcomes that should be considered when evaluating new therapies. Respondents also noted the impact these treatments had on their daily lives:

- *“NSAIDs have side effects for digestion, daily impact as you can't venture far from a bathroom. Cosentyx has limited side effects such as sensitive skin for 24 hours after injection.”*
- *“The side effects of treatment were the main reason that I do not use daily treatment.”*

Even with currently available treatments for AS, patients' outcomes can vary significantly. Some medications are effective for some people, while not effective for others. Some treatments will effectively manage AS for a short period of time before a person's immune system adapts to a drug's presence (i.e.

becomes non-responsive to it) and they will have to switch to another medication. In some cases, people living with AS may not respond to any of the currently available medications. As a result, patients need a number of medication options to manage their AS throughout their lives. Unfortunately, so little is understood about AS that there is currently no way to predict who will best respond to which medications and/or the best dose of those medications for individuals.

There are outcomes that are important to people living with AS, and these include:

- reduction in pain and fatigue
 - reduction in disease progression
 - reduction in stiffness and swelling
 - increased mobility
 - ability to work and be productive at work
 - ability to carry out activities of daily living
 - decrease in medication side effects.
-
- *“I would like pain-free days and the ability to exercise more, less doctor appointments for nerve blocks”*
 - *“I would hope for a great reduction in pain and stiffness with minimal side effects.”*
 - *“Not willing to experience serious side effects. I would need to be pain-free with a return of physical strength and significantly reduced fatigue to consider it effective. This would allow me to complete normal daily tasks without hinderance.”*
 - *“Honestly, the goal needs to be to stop the disease progression and not decrease my immune system since I work in an ICU as an RN. I cannot have this part of my life impacted to a dangerous level not having an immune system to fight off various illnesses I am subjected to.”*

6. Experience With Drug Under Review

While none of the survey respondents had indicated using ixekizumab for their ankylosing spondylitis, the survey responses addressed in section 5 illustrate the desire for a medication with improved outcomes and potentially less side effects.

7. Companion Diagnostic Test

Not applicable

8. Anything Else?

No further comments at this time.

Appendix: Patient Group Conflict of Interest Declaration

Declaration from CAPA

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

An Eli Lilly Canada contact provided us with names of the Canadian rheumatologists and investigators who had patients enrolled in the ixekizumab clinical trial for ankylosing spondylitis. CAPA, AS and CSA reached out to these researchers and rheumatologists via email and asked them to pass along a letter to clinical trial participants that explained CADTH, the Common Drug Review process, and why their input would be of value. The letter provided a link to the CAPA and AS survey as well as contact information for Sammy Feilchenfeld, in case they wanted to be in touch via email and phone.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

As mentioned earlier, the Arthritis Society and CAPA shared survey results with the Canadian Spondylitis Association (CSA). Some of the patient input for this submission is derived from the CSA survey, where explicitly indicated.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Abbvie			X	
CADTH (travel support for annual symposium)	X			
Janssen			X	
Manulife	X			
Pfizer (including Pfizer Hospira)			X	
Purdue	X			
UCB		X		

4. I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

D. Richards is a self-employed consultant who, in the last 2 years, has received honoraria or speaking

fees from Innomar, Lilly, Manulife, Merck, NovoNordisk.

Name: Dawn Richards
Position: 1st Vice-President
Patient Group: Canadian Arthritis Patient Alliance
Date: September 23, 2019

Declaration from the Arthritis Society

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

See the section above for which CAPA provided details.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

As mentioned earlier, the Arthritis Society and CAPA shared survey results with the Canadian Spondylitis Association (CSA). Some of the patient input for this submission is derived from the CSA survey, where explicitly indicated.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Amgen				X
Abbvie				X
BMS			X	
Celgene				X
Eli Lilly				X
Eupraxia Pharmaceuticals	X			
IMC			X	
Janssen				X
Merck				X
Novartis				X
Pfizer				X
Sanofi			X	
UCB				X

4. I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Helen Anderson

Position: Senior Manager, Education Services

Patient Group: The Arthritis Society

Date: September 23, 2019

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	Ixekizumab (TALTZ) for Ankylosing Spondylitis
Name of the Patient Group	The Canadian Spondylitis Association
Author of the Submission	██████████
Name of the Primary Contact for This Submission	██████████
Email	██
Telephone Number	██████████

1. About Your Patient Group

The Canadian Spondylitis Association is registered with CADTH.

The Canadian Spondylitis Association is a registered not-for-profit organization providing education, programs and support to Canadians living with various forms of Spondyloarthritis, including Ankylosing Spondylitis.

More detailed information can be found on our website @ www.spondylitis.ca

2. Information Gathering

The Canadian Spondylitis Association developed an independent survey to gain insights from individuals with a diagnosis of ankylosing spondylitis (AS) about their journey living with AS and any experiences from individuals who have/are taking ixekizumab. The survey was shared with our community through e-mail and social media channels (website, Facebook and Twitter). The survey was open from August 8 until September 15, 2019.

In collaboration with The Arthritis Society and the Canadian Arthritis Patient Alliance, we contacted an Eli Lilly Canada representative to request, if possible, to be provided with names of Canadian rheumatologist who had patients enrolled in the AS ixekizumab clinical trial. We collectively reached out to the rheumatologists by email requesting them to share a letter with clinical trial participants explaining CADTH, the Common Drug Review process, and invited them to share personal input. The letter provided a link to the CAPA and Arthritis Society survey as well as contact information for Sammy Feilchenfeld at the Arthritis Society, in case they preferred to be in touch email and/or phone.

The CSA survey received 62 responses, of which 52 were from Canadian respondents. Unfortunately, no respondents had experience taking ixekizumab. All information used in this submission is from survey responses provided by Canadian participants completing the CSA survey. Of the 52 responses, 60% were female and 40% male and ranged in ages from over 18 to over 65 years of age with the majority (42%) being between 36-50 years and 30% between 50-65 years. The length of time respondents have been living with a diagnosis of AS ranged from less than 1 year (24%) and between 1 and 5 years (31%) and between 11 and 15 years 11%. When asked how long people lived with symptoms *before* receiving a diagnosis, 30% reported 5-10 years and 21% reported 10-20 years. 16% of respondents lived with symptoms for 20+ years before being diagnosed.

3. Disease Experience

Ankylosing spondylitis (AS) is a chronic, progressive, painful form of inflammatory arthritis, which affects mainly the spine and sacroiliac joints (the joints where the spine attaches to the pelvis). It can also affect cause pain and stiffness in peripheral joints (hips and shoulders), tendons and ligaments.

Ankylosing means stiffening and fusing while spondylitis means inflammation of the spine. Ankylosing spondylitis describes the condition where some of the joints and bones of the spine become fused together because of inflammation. The bones of the spine fusing, or grow together, causes the spine to become stiff, inflexible and painful. As many as 1% of the Canadian population lives with AS.

AS affects both male and females and is diagnosed in children, adolescents and adults. On average, it takes people 7 years to receive a diagnosis. During this time, the disease progresses causing, in many cases, irreversible damage.

The symptoms survey participants indicated as having the greatest impact on their daily life included joint pain (92%), mobility, fatigue (71%) and sleep issues (68%). In addition, 46% and 44% of patients reported experiencing depression and anxiety. Most aspects of day-to-day living is impacted to varying degrees depending on disease progression and symptom management. Many people find it difficult or impossible to do simple things like spending time with family and friends, driving, working, and parenting.

Included below are some additional direct quotes providing insight into how living with Ankylosing Spondylitis impacts people's lives:

Day-to-day impact:

"All aspects of my life are affected. I'm fifty, going on seventy-five. I live like a hermit. Can't work, rarely socialize, don't get out much, went from a gregarious man-a-bout town to a ghost who haunts my previous life. Fortunately, I have a care-worker to comes in once a week to help out with house-cleaning."

“Fighting to get through every day with some level of normalcy, limited to what I can get achieved, makes work harder. Family life has changed considerably.”

“In constant pain which affect my mood and physical abilities. Can’t hold a job due to flare ups. Have trouble keeping friends due to difficulty of leaving my home or participating. Basic needs like cleaning and self-care are difficult and often aggravate joints to more flare ups.”

“Currently I suffer more from chronic fatigue than I do pain. I am unemployed due to chronic fatigue. My range of motion is very limited, so household chores are extremely difficult. My social life has also been impacted, making me feel isolated. I have a lot of psychological problems as a result of my isolation.”

“I am a university student heading into my senior year. I am unable to do full time classes due to pain and fatigue, so I take a reduced course load. I have not been able to work much over the past 3 years either. Standing in one spot (example in a grocery store line or at bus stop) is much more difficult for me than walking. I have difficulties with getting things off of low shelves and picking things up from the floor.”

“I cannot walk! so am largely housebound. Cannot turn over in bed. Big impact on social life. Had to retire early because of it which has impacted on my retirement income.”

“My AS is advanced. I have spine deformation. I have trouble with all day to day tasks. It me look deformed like a hunchback and is very hard to function.”

“I can’t work. Have had to stop activities I loved. Find I am becoming more house bound due to tiredness and pain. Sleep is effected due to pain.”

“I am in pain every day. I’m spending excessive amounts every month on medication as I don’t have a private plan. That alone impacts my life in such serious ways. I hate spending 1/3+ of my monthly salary on medication. I do not take any biologics because I simply can’t afford them. I might be in a better place with pain if I could afford them. My entire day revolves around what I can’t do because I am in pain or I am perpetually exhausted. I’m missing out on so many things in life because I can’t do anything that aggravates the pain more. I’m too tired to do family activities. If I make dinner for the family here, I’m done for days. The fatigue is probably more debilitating than the pain.”

Work / Career Impact:

“Well, I lost my career, my home, my family, and my marriage fell apart. At this point, I have no family to impact with my daily routine, and I think it’s best to keep it that way? I can barely manage to keep in regular contact with my brothers through Skype.”

“Prior to diagnosis/treatment – late for work often and expended most of my sick days each year. Since treatment both have improved the only think which sometimes effect my work is poor sleep.”

“It’s limiting my ability to build and expand and I’m now having to curtail my entrepreneurial activities.”

“I can’t work due to my illness.”

“I have not disclosed and will not. It’s an emotional journey to prepare yourself for work every day no matter how bad the pain is that day. There are some days when I sit I my office on the verge of tears wondering how I will make it to 5pm.”

“I am not reliable. Some days I wake up and I can function. Not much else but just the basics. But some days I am useless. How do you hold down a fulltime job? I have a master’s degree in industrial psychology. I do contact work and some work from home to make ends meet. I would LOVE to work full time. I think its unhealthy being home alone all the time. But I have no idea if I can even sit to drive to work from day to day.”

Impact on caregivers/loved ones:

“My husband has to do cleaning and cooking. I am sad and always fatigued. I cannot care for my kids as I want to due to pain.”

“My kids are 9 and 12 and they know that certain days that are high pain days I just can’t do as much in these days they know I need more help with things around the house. My husband has shed tears watching me go through days, weeks and months of intense pain. There are days I just can’t do what I used too. I feel that I don’t have the stamina or strength that I used to.”

“No family any longer.”

“It has caused tremendous stress on my relationship. I because someone different than who he married. I could no longer ski, skate, hike or bike. I couldn’t entertain the way I once did. My marriage ended and he blamed by health. Maybe he was correct. I don’t really know.”

“My husband and teenage children have had to take over all the household chores. They also have to do all the heavy lifting. The come grocery shopping with me to push the cart and carry the bins.”

“My spouse has struggled emotionally and financially to help support me.”

When asked what aspects of Ankylosing Spondylitis are more important to control, the majority of respondents responded pain, inflammation and fatigue. Some respondent comments include:

“Pain is likely the most obvious. Mobility issues would come a close second. The associated depression would be another. Improved sleep and energy levels would be nice.”

“Controlling flares. Pain that is constant that prevents you from doing everyday things.”

“The lack of awareness. Nighttime pain. Depression. The damage it does to the joints.”

“Fatigue, inflammation, range of motion, depression.”

“Control your inflammation! Managing your inflammation will in turn manage all the issues.”

4. Experiences With Currently Available Treatments

Pharmacologic medications for AS are intended to slow progression of the disease and help manage pain and other symptoms. Treatment options currently available to Canadians vary significantly from one person to another person in how effective they are. Some medications make a significant difference for people and allow them to continue doing all the things they love and for others, some medications simply help them to get through the day. For some, the medication may work well very quickly while for others it may take time. Some patients find sustained symptom relief and can stay on a medication for a long time (several years), while others have shorter bouts of symptom relief, or experience no relief, before needing to move to a different option.

Until there is a cure for AS, people rely on current options available to manage their conditions and hope new treatment options are on the horizon that may improve outcomes.

For many, the treatments currently available can be difficult to tolerate and manage due to the side effects experienced. Because people are unique, some may experience a lot of side effects and some may experience few. Approximately two thirds of respondents who completed our survey indicated that they did not have adverse effects from current treatments that are more difficult to tolerate than other treatments that they have tried. Those who did mention side effects indicated the most common were stomach issues, fatigue following injection and weight gain.

“My doctors tell me my condition is “stabilized”. I describe my life as rather miserable. The truth is likely somewhere between the two?”

“I have been on biological therapy for 9 months and I believe there is a heightened effect on my bowels. My stomach also hurts (sharp stabbing pain) for one week after the injection.”

“Methotrexate caused nausea, dizziness, and fatigue that lasted 3 full days after my injections. I would not work or do school during those days.”

“Weight gain is not desirable.”

“Fatigue day after injections each month.”

In addition to pharmacologic medications, non-pharmacologic treatments play an important role in managing symptoms (stiffness, pain, fatigue and mental health) of AS. Examples of effective non-pharmacologic approaches include physiotherapy, occupational therapy, massage therapy, and chiropractic therapy. Swimming or float therapy are mentioned to be helpful as well. Unfortunately, many people are not able to incorporate many of these treatments into their routine due to lack of access / affordability. These important treatment options are not are not reimbursed through provincial health care systems and for those who have private insurance, the coverage is not adequate for a person living with chronic illness.

“Physiotherapy, yoga, things to stay in motion. Massage helps.”

“I work out regularly and try to swim as much as possible. If I don’t get my exercise in, I know the day will be hard to get through. I also find regular massages are helpful.”

“Cannabis is by far the most effective acute treatment. Pain killers are 100% ineffective and do not allow areas of my back to relax. Cannabis combined with yoga is very very effective at improving mobility – the cannabis reduces pain and allows areas which tend to tighten up (back and hips) to relax, thereby allowing for effective stretching and strengthening.”

“Medicinal Marijuana has proven to be quite wonderful. As I tell people, “weed doesn’t do much about the pain, but at least I don’t mind it quite so much”. The psychological effects of living with chronic pain are probably the most debilitating, in my mind. Marijuana definitely helps with that.”

5. Improved Outcomes

When evaluating new medications, consideration should be given to efficacy, side effects, dosing frequency and ease of administration. Because this condition affects everyone differently and response to medications varies, any molecules that can bring bring improvement to patient outcomes including quality of life and disease management should be available to patients. Medications that can help patients resume living a normal or better life should be an option for Canadians. New options provide hope for people to regain normalcy back into their lives will positively impact patient’s mental health.

Outcomes that are important to people living with AS include:

- reducing pain and fatigue
- reducing progression of the disease
- resolving chronic mental distress (depression & anxiety)
- reducing inflammation
- increasing mobility
- enabling people to work and be productive at work
- ability to carry out activities of daily living including household chores, parent without limits and relationships

“More research is needed, and more treatments are needed. For example, in my case, I can no longer take oral NSAID’s. One biologic has failed and current one not working well. I am worked about what’s going to come next. And I don’t seem to hear much about the development of new medications or treatments.”

6. Experience With Drug Under Review

Although none of the survey respondents who provided input have experience on ixekizumab, many commented positively on knowing there is a new treatment option for Canadians. New therapies provide hope for patients who haven't found a medication that works for them or have few options remaining on their journey forward. It is a relief to know there are more options available.

7. Companion Diagnostic Test

Not applicable.

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

Until there is a cure, new innovative medicines provide options and hope to improve outcomes for patients, their loved ones and the physicians helping to manage their condition.

While AS patients have access to a number of medications in Canada, individual outcomes vary significantly. Treatment for AS is very individual and unique. For some, the medication may work well very quickly while for others it may take time. Some patients find success and can stay on a medication for a long time (several years), while others have shorter bouts of success before needing to move to a different option. As decision makers reviewing medications, it's important to keep in mind that patients need a variety of options to be available. AS is a chronic illness and people will live with it for their entire life.

It is challenging for patient groups to access patients on with lived experience (i.e. participants in clinical trials) through our individual means and therefore providing information at this point in time of experience on product is limited. Although this submission doesn't include input from patients who have participated in ixekizumab trials, it's important for CADTH to review medications based on patient lived experiences and significant impact living with Ankylosing Spondylitis brings to their lives and the lives of loved ones / supports.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

An Eli Lilly Canada contact provided us with names of the Canadian rheumatologists and investigators who had patients enrolled in the ixekizumab clinical trial for ankylosing spondylitis. CAPA, AS and CSA reached out to these researchers and rheumatologists via email and asked them to pass along a letter to clinical trial participants that explained CADTH, the Common Drug Review process, and why their input would be of value. The letter provided a link to the CAPA and AS survey as well as contact information for Sammy Feilchenfeld, in case they wanted to be in touch via email and phone.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

As previously mentioned, the CSA shared survey results with the Arthritis Society and CAPA. The CSA drafted the content included in this submission independently. There is no patient input from their survey included in the CSA patient input submission.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Abbvie			X	
Amgen		X		
Eli Lilly			X	
Merck			X	
Novartis			X	
Pfizer			X	
UCB			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a

real, potential, or perceived conflict of interest situation.

Name: Wendy Gerhart
Position: Executive Director
Patient Group: Canadian Spondylitis Association
Date: September 24, 2019