CADTH

CADTH Reimbursement Review
Patient Input Template

Name of the Drug and Indication	**Anakinra (Kineret)**
Name of the Patient Group	**Canadian Arthritis Patient Alliance / Arthritis Society/ Cassie and Friends**
Author of the Submission	**Laurie Proulx**
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1. About Your Patient Group

CAPA is a grass-roots, patient-driven and managed, 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. Our website is updated regularly and can be viewed at: www.arthritispatient.ca.

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 Arthritis Society is Canada's principal health charity providing education, programs and support to the 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.

Cassie + Friends Society (C+F) is a national patient and parent-led charity dedicated 100% to transforming the lives of kids and families affected by Juvenile Arthritis and other rheumatic diseases through research, education, connection, and support. Working together with youth, parents, healthcare professionals, researchers, and other friends, we help children and families navigate day-to-day life with a chronic condition while never losing sight of our ultimate goal - a pain-free future for all kids living with rheumatic disease. To-date, we have raised over $2.5 million, successfully advocated for better access to treatments and care, and touched the lives of thousands of youth and families. To join our mission and learn more, please visit cassieandfriends.ca.

2. Information Gathering

We developed a survey to hear directly from people living with Systemic Juvenile Idiopathic Arthritis (sJIA) and adult-onset Still's disease (AOSD) about their experiences with the condition and any experiences taking Anakinra. Our organizations 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-mail, and through our respective Canadian networks and communities, including social media and through personal contacts. The author of this submission was diagnosed with Juvenile Idiopathic Arthritis therefore these personal experiences were considered in the development of this submission. More information was obtained through ongoing interactions with patient communities by the participating organizations.

Fourteen survey responses were received and seven people had experience taking Anakinra. Participants were located across Canada ranging from British Columbia to Newfoundland and Labrador. Three participants were located outside of Canada. The survey collected demographic data, however not all participants completed this section. Two-thirds of those who completed the survey were caregivers and the final third of participants live with sJIA/AOSD Still's Disease. Most of the patients were under the age of 20.

3. Disease Experience

Still's disease can take on a pediatric form, known as Systemic Idiopathic Arthritis (sJIA), as well as an adult form, known as AOSD. Still's Disease is an autoinflammatory disease that causes swelling in the joints and causes the immune system to attack healthy cells and tissues. Both conditions are severe and potentially life-threatening. sJIA is a sub-type of JIA affecting between 10% and 15% of all children with JIA which impacts every 1 in 1000 children in Canada. Both conditions result in inflammation of the joints causing them to become red, swollen, painful or hot to the touch as well as widespread inflammation throughout the body resulting in features such as fever and rash. In children, joints can grow around the inflammation, causing abnormal shape and function as the child grows. Joint damage is irreversible and causes significant pain and disability.

Still's disease is a systemic disease that involves other internal organs, such as the heart, liver, spleen, and lymph nodes. People with Still's disease get recurrent fevers (often spiking once to twice per day) as their body tries to deal with the disease which leaves them feeling very tired and unwell. One can expect to live with the disease for the rest of their lives. sJIA can be more challenging to diagnose and treat than other types of JIA, and comes with high financial, family, and societal burdens. Approximately 60% of children will have active disease into adulthood.

Without proper medical control of the disease, the results of Still's disease can be devastating. Major joint surgeries such as joint replacement or fusions can be required at a young age and possibly lead to multiple procedures throughout the lifespan. Because of the extensive damage to their joints, some patients who do not respond to the available treatments might also have to use technical or mobility aids such as bath lifts, canes, or wheelchairs, have their house/car adapted and rely on accessible public transit services to do daily activities.

People living with sJIA and AOSD shared the following perspectives about living with and dealing with their symptoms:

"*The development of itchy, burning, red welt-like rashes that get worse as the day proceeds [are] so embarrassing as [they…] take over the entire body."*

"During flares - extreme fatigue, inability to focus, joint pain, trouble participating in school physical education [and] climbing stairs, eye inflammation requiring 3-4 times daily drops including at school.

"Missing school for appointments, MRIs [magnetic resonance imaging]."

"Macrophage activation syndrome, swollen joints, rash, fever"

"Multiple joints affected. Hands, wrists, knees, ankles, neck. At onset, daily fevers, mild rash, poor blood work. Unable to do sports at level before diagnosis."

The disease impacts patients' and families' lives in many ways. Impacts on mental health and participation in school were noted by 100% of survey respondents. Impacts on participating in physical activity was noted by 60% of survey respondents, followed by self-esteem (60%), family life (30%) and friendships (30%). People living with sJIA and AOSD shared the following perspectives about the impact of the disease on their lives:

"*Steroids create self esteem issues and mental health issues as the weight gain and fat puffy face are hard to tolerate. Although prednisone is effective, the long-term effects are outrageous. Aggressive, unruly type behaviours come with steroids as well. The lack of concentration makes it hard to function effectively at school."*

"Methotrexate injections were the worst to have to give to a 12-year-old on a weekly basis at home. Huge family upheavals in the form of fights, having to force or trick or bribe my child to take the injection."

"Finding job options that can accommodate my needs is very challenging and having to balance all the appointments with school is difficult. Anytime I flare I often require a wheelchair and wrist braces."

"I cannot do everything the other kids do. It is hard to walk sometimes or sit for longer periods. My jaw hurts and it makes me really uncomfortable and hard to chew."

"It has affected schooling. Missed school time due to treatments, pain or being pulled out during times when flu hits the class because my child is immune supressed due to [medication]. Sleepless nights due to pain. Stiffness, swelling and pain. Not being able to participate in

sports or pushing through pain just to participate a little"

People living with the disease are also at risk of co-morbidities, such as uveitis and Crohn's disease. Periods of very active disease are called a 'flare' and for some people, flares can be incapacitating. Flares are not predictable in terms of how bad they will be or how long they will last. They may last for a few hours, days, weeks or even months. People must deal with flares reactively and the unpredictable nature of sJIA and AOSD often makes it feel like a person is not in control of their disease or their lives.

"Since Jane was diagnosed with SJIA in January 2015, at the age of 8, she has never had the opportunity to feel well. She's given up so many of the activities she loves. She spends most of her free time at medical appointments or in bed immobilized by pain."

Parents are generally the primary caregivers of children and youth living with sJIA. They feel additional stress as a result of caring for an ill child and adapting family activities and managing medical care. This includes attending extra medical appointments (e.g., specialists, allied health care professionals), managing medications on a day-to-day basis, dealing with flares in the disease, etc. The parent(s) also need to manage this in addition to the current responsibilities in life, such as work and caring for other children. A survey participant noted the impact on their parents and siblings:

"It required my parents to do the injections and support me during the injections. My brother grew up with me getting these injections and now has a serious needle phobia as an adult."

Caring for a sick child or living with the condition may also impact the relationship between spouses/partners. The parents, patients and spouses/partners are also at risk of depression and marital stress because of living with these additional responsibilities.

There are also financial pressures for people with the condition and their families, including the difficulties in navigating drug reimbursement. The cost of the medication places additional stress on families' finances. Drug access programs, whether private or publicly managed, are difficult to navigate, meaning extra time and effort are required by patients and their families. The following excerpts describe some of the patient and family experiences:

"It has been a financial burden because of lost wages due to treatments. Fortunately, we have medical coverage but that has been very stressful as it is constantly changing the % they are willing to cover or [they] tell you [that you've reached a maximum] for some drugs, or they get to decide if you will be covered for it or not. We have had to apply for patient support to cover the remaining costs as we don't make enough to cover these added costs. On top of this, there is the added stress of the longer damage that may be caused by each drug and being on multiple drugs at one time. It is also very stressful having to jump through hoops with doing specific drugs before being approved for others."

"All medications that help a child are highly overpriced. We have fought hard for expensive medications that sit in the decision of professionals that have no knowledge of this disease. From Anakinra to Canakinumab, these medications should be accessible for a doctor to prescribe as quickly as needed. With death knocking on the door for many people with this disease, we need to make biologics accessible."

"…often it is difficult to access the drugs that are needed such as Kineret. The docs and their staff do their best for patients but often that involves unnecessary bureaucracy with the drug companies and their

distribution systems."

"My Anakinra treatments were significantly delayed as the government initially refused to cover it for me - this resulted in me continuing to flare for much longer than if I had had immediate access to the medication. The significant costs associated with Tocilizumab injections also resulted in me opting to continue to receive the drug by IV infusion in hospital."

4. Experiences With Currently Available Treatments

Medications for sJIA and AOSD aim to control inflammation and minimize disease activity so that no long-term joint or organ damage occurs, as there currently is no cure for the disease. Treatments used include Nonsteroidal anti-inflammatory drugs (NSAIDs), antimalarial medications (hydroxychloroquine and chloroquine), corticosteroids, and immunomodulation drugs, such as methotrexate, cyclophosphamide and canakinumab. The following provides a general description of the treatments used and their side effects:

- NSAIDs are used to treat pain relating to the disease. The NSAIDS may cause many side effects, from stomach upset to changes in kidney function.

- Antimalarial medications such as hydroxychloroquine and chloroquine, the most common unwanted effect of which is some stomach upset. However, if hydroxychloroquine and chloroquine are taken in a high dose and over a long period (more likely in pediatric patients), they may accumulate in the retina and cause a loss of vision and in rare cases, blindness may occur. These effects could be in addition to uveitis caused by sJIA.

- Corticosteroids are commonly used in the treatment of Still's disease and although effective, there are a significant amount of 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.

- Traditional immunomodulation drugs such as methotrexate and leflunomide are also commonly used and have a range of side effects that are difficult to manage. Side effects include nausea, vomiting, hair loss, diarrhea, decrease in white blood count, bone marrow toxicity, liver toxicity, and bladder-related problems. Some biologics are available such as Tocilizumab, Canakinumab, and Etanercept.

Patients shared these experiences regarding their current treatments:

"Every single day or every single week, my daughter has to endure and ingest:

- *Seven injections of anakinra - a biologic that burns like fire under her skin and causes her severe anxiety and emotional breakdowns.*
- *One injection of methotrexate - a form of chemotherapy*
- *Eight tablets of prednisone per day (50mg) - an amount that both you and I know is toxic over the long-term to our child.*

- *Two tablets of cyclosporine per day - the same medication used to prevent organ rejection in people who have received a liver, kidney, or heart transplant. This is because our daughter is now borderline MAS, or Macrophage activation syndrome, a potentially complication of SJIA.*
- *Countless tablets of folic acid to counteract the effects of methotrexate.*
- *Advil to help with the chronic pain of the arthritis that has caused damage to her knee.*

If you add that up, that's eight incredibly painful injections and 80+ pills a week."

Patients reported that they had tried several treatments, which could be difficult to tolerate and manage:

"Steroids have terrible side effects when used for many months. Biologics do not have these side effects and treat sJIA very well."

"*Oral steroids caused every side effect possible and [had] no effectiveness what so ever. The pain of Kineret was so unbearable that it started causing psychological problems as well as becoming a full family ordeal with every injection day and night! Pain and inflammation are still not being fully kept under control. The long lists of side effects of these drugs [are] very scary. Tocilizumab causes lip swelling, so [it's important to] also take Benadryl before hand."*

"Biologics have been the most effective and have prevented further joint damage and/or damage to my organs. The joint injections caused damage to my joints."

"Side effects are loss of hair, poor hair quality, bloating. I do not like getting IV [intravenous] or injections and that is hard. My symptoms are not really improving."

It was also noted that current treatments may lose effectiveness over time, and half of survey participants noted they did not respond to or were intolerant to current treatment options.

"The drugs have all been used separately and in combinations. They have had periods of being effective, periods of less effectiveness and periods of being non-effective. One biologic was ineffective, one was effective and [the other was] mildly effective."

"I reacted poorly to some of them and had to adapt routines for that. Others just didn't work well."

5. Improved Outcomes

People living with sJIA and AOSD reported that current treatments are difficult to tolerate because of side effects. A variety of side effects are difficult to manage such as stomach upset, loss of appetite, hair loss, and difficulties in administering injections. Minimizing these side effects are important outcomes that should be considered when evaluating new therapies. Patients and families shared these perspectives:

"Methotrexate made me very nauseous. Other [treatments] were not effective."

"… Developed nausea after a couple of months and lost her appetite so we were switched to Leflunomide. So very much happier now, thank goodness."

"…and methotrexate made me incredibly nauseous, to the point where I would often miss school."

Overall, there are several outcomes of importance to people living with sJIA and AOSD including:

- a reduction in pain and fatigue
- reduced organ involvement or disease complications, such as uveitis
- increased mobility and participation in physical activities
- ability to participate in school activities and work
- ability to carry out activities of daily living and social roles

The expectations of the drug are to offer another treatment option for patients with sJIA and AOSD. The current risk-benefit profile of Anakinra is like other medications available to treat sJIA and AOSD (e.g., serious infections, allergic reaction). New treatment options have the potential to ease the burden on patients' families, caregivers and the healthcare system.

6. Experience With Drug Under Review

Patients' response to sJIA and AOSD medications vary significantly. Some medications are effective for some people, while not effective for others. Some treatments will only manage the disease for a short period of time before the patient's immune system adapts to a drug presence (i.e., becomes non-responsive to it) and they will have to switch to another medication. In some cases, patients with sJIA and AOSD may not adequately respond to any of the medications currently available. As a result, patients need a number of medication options in order to effectively manage their disease throughout their lives. Access to biologics is usually limited to patients who have not responded to first-line therapies, such as Methotrexate, Leflunomide, and other medications.

There were 7 survey participants who had experience with Anakinra. Many expressed that the medication was effective in controlling their disease symptoms, particularly skin rash, and fevers, and led to a reduction in steroid use. The following perspectives were shared by patients and their families:

"*It controlled the skin rash and fevers well. Much better than steroids alone. I didn't experience many side effects although prednisone had so many. The only side effect that I experienced was site injection rash. The use of a biologic over oral medications is preferred. Also being able to administer the medication at home or on holidays didn't strap me to attend the hospital day units. Biologics have given me my life back and saved me*."

"Symptoms of mas (Macrophage Activation Syndrome) were gone. No need for steroids. Did develop joint inflammation so had to switch to another biologic."

Some patients expressed difficulties in managing the daily injections of the medication, however, some noted that these difficulties were worth the effort:

"It controlled my flares for a number of years (much better than other medications I had been on before becoming ineffective. Injections were very painful but [I learned] to cope with it. Having to do injections everyday made travel challenging. Overall, it definitely improved my quality of life."

"The daily injection sucks but the drug did work to alleviate symptoms and control the disease."

"It worked for a short period. It causes severe pain. The amount of pain is unacceptable, they need to figure out a way for it to not be so painful. The pain caused a lot of tears and psychological problems which is unacceptable."

Some participants noted that taking Anakinra was easier to manage compared to infusions, especially with regard to travelling to hospitals and managing one's schedule or travel from a rural community to a major tertiary care centre:

"…. being able to administer the medication at home or on holidays didn't strap me to attend the hospital day units."

"When we first started spending every 2 weeks in a medical day unit to anakinra, being able to manage at home, to monthly injections on Canakinumab. This has changed how I can manage daily life of school and activities. Having my mom inject me every day was definitely better than attending the hospital. Painful injections were very challenging, but my wellness was the reward."

"…It affects a parent's work schedule and adds the financial cost of parking at hospitals, dispensing fees, etc."

"Kineret was a daily injection which was challenging, but the drug worked so it was worth it. Other biologics tried often required an entire day if [available locally], but if we had to go to <city> for the drug, then it would mean multiple days off work and school."

7. Companion Diagnostic Test

Not applicable

8. Anything Else?

We are pleased to see that Anakinra has been studied in the pediatric population. Unfortunately, the study of medications in the pediatric population is not always undertaken by pharmaceutical companies or researchers and means that medications are often prescribed off-label. For patients and their families, this means that they are making decisions without adequate clinical data demonstrating risks and benefits.

sJIA and AOSD are rare, debilitating disease with **limited treatment options**, making access to those treatments that are proven to be safe and effective even more important to those affected.