Common Drug Review
Patient Group Input Submissions

canakinumab (Ilaris) for the treatment of active systemic juvenile idiopathic arthritis (SJIA) in patients aged two years and older.

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
The Arthritis Society — permission granted to post.
Canadian Arthritis Patient Alliance (CAPA)— permission granted to post.

CADTH received patient group input for this review on or before January 20, 2016

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.

The Arthritis Society

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest		Canakinumab (Ilaris)
Name of the patient group		The Arthritis Society
Name of the primary contact for this submission:		[redacted]
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Permission is granted to post this submission		Yes

1.1 Submitting Organization

The Arthritis Society has been setting lives in motion for over 65 years. Dedicated to a vision of living well while creating a future without arthritis, The Society is Canada's principal health charity providing education, programs and support to the over 4.6 million Canadians living with arthritis. Since its founding in 1948, The Society has been the largest non-government funder of arthritis research in Canada, investing more than $190 million in projects that have led to breakthroughs in the diagnosis, treatment and care of people with arthritis. The Arthritis Society is accredited under Imagine Canada's Standards Program. The website www.arthritis.ca provides more detailed information.

1.2 Conflict of Interest Declarations

The Arthritis Society does not believe that it or those individuals playing a significant role in compiling this submission have a conflict of interest that influences the information provided in this patient group submission. The Arthritis Society accepts funding from many pharmaceutical companies in order to work towards fulfilling its mission of enabling Canadians with arthritis to live well and be effective self managers and to lead and support arthritis research and care. In order to be fully transparent and meet the request to disclose pharmaceutical manufacturers who have provided support to the organization please be aware that over the past 12 months The Arthritis Society has accepted funding from the following members of the pharmaceutical industry: Abbvie, Amgen, Bayer, Bristol Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Purdue, Roche, UCB. The vast majority of The Arthritis Society's funding comes from individual donors as personal charitable giving.

The Society abides by all Canada Revenue Agency and Imagine Canada requirements, and has specific guidelines on advocacy relating to pharmaceuticals that are available upon request.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

Information was obtained from the following sources:

- Contact with three patient families facilitated by physicians involved in the clinical trials.
- One-on-one e-conversations with patient families through The Arthritis Society's engagement on social media and the website.
- The Childhood Arthritis Advisory Council (CAAC) Survey 2013: the Society polled relevant stakeholders, including Canadians families caring for children with childhood arthritis to better understand their needs. The online survey specifically asked about their experience with arthritis and issues relating to treatment.

2.2 Impact of Condition on Patients

What are the disease/condition-related symptoms and problems that impact the patients' day-to-day life and quality of life?

Juvenile idiopathic arthritis (JIA) begins before age 16 and involves swelling in one or more joints lasting at least six weeks.

JIA may include a variety of symptoms that can change from day-to-day and not all symptoms are shared by all children with the disease. The effects of JIA on the child can depend on the severity of her/his symptoms, treatments, and frequency of flare-ups.

One common condition-related symptom that families talk about is their child's pain and how it impacts day to day life:

- One parent said about their 2 ½ years old son "Arthritic pain that was so severe that he could not walk."
- One parent said, "Biggest challenge is pain, and the anxiety that goes with the pain. The inability to be a normal kid, instead forced to grow up too fast and deal with adult issues like pain."
- One parent said, "It is hard dealing with the pain while trying to live as normal a life as possible."
- One father said, "My boy was in pain. He could not get out of bed on his own. We were constantly giving him Advil and he couldn't sleep because he was itching non-stop."

Fevers and skin rashes were symptoms highlighted by families:

- One parent said, "He was hospitalized for a month and had daily spiking fevers."
- One father said, "Then the fevers kicked in. The fevers lasted 22 days until he began treatment at Sick Kids in Toronto. During the fevers, for a period of a few days a rash took over his entire torso which was painful to even look at."

The disease affects the ability of children to participate in physical activities:

- A mother said about her daughter that "her biggest challenge is sports. Playing soccer is too hard on her joints and so every year I have to creatively come up with an excuse as to why she can't play."
- A parent said, "Challenges in school and social life due to limitations on acceptable physical activity when joints are inflamed."
- A parent said "Socially, recreationally, it's difficult because most kids programs have a lot of physical activity so she either sits out or does it, and is in pain."
- A mother said, "She is not able to play with her friends in the playground. The running games etc. And she is too young to let her friends know why she can't keep up to them, so she is excluded. She

doesn't have the words to say that she is hurt and gets disruptive and angry. Mommy knows why she is behaving that way but the teachers and students don't."

- A parent said, "He was registered in soccer at four, but couldn't handle all of the running."
- A parent said, "My daughter is unable to keep up with her friends in the playground."
- A parent indicated, "It can be challenging finding appropriate physical activities that are not overly stressful on affected joints."

The disease has an impact on school participation:

- A parent said "My daughter struggles to fit in at school when she can't do all that the other kids do."
- A mother said, "This is the first time that this school had to deal with a child that has this illness and not sure they quite understand how it affects my daughter. Also, the fact that this illness has delayed my daughter's ability to be up to date with other children make her life a bit harder. Tutors, specialists, teacher aids, speech therapy, etc... Of course, therapists, tutors, etc… is all costly."

Psychological impact:

- One mother said, "Psychologically is the biggest impact. She knows she has something different that none of her friends do and couple that with some of the physical limitations in sports, it makes her sad sometimes."
- "Helping him maintain a positive attitude. Keeping his spirits up when he is having a flare."

Access to effective therapeutic treatment is essential for children living with JIA to participate in the same activities of daily living as their peers.

2.3 Patients' Experiences With Current Therapy

Feedback from parents on current therapy:

- One family provided feedback on the therapy Anakinra. They reported that the medication is effective but the impact on quality of life is a concern. As the father said "We began giving our son an injection of Anakinra everyday at home and his symptoms went away. My wife and I routinely were in tears when giving his injection to the point where my wife refused to give it to him. It is a very painful drug and burns for 1 - 2 min after administering. Tough to give to your 5 year old child every day."
- A mother reported, "Family life has been impacted because our daughter gets moody from Prednisone, and anxious and doesn't cope well when she's in pain so there is a lot of added stress on our family."
- Another family reported, "We have no benefits, so it's a struggle to pay for our daughter's medications."
- A parent reported, "Seeing your child in pain, seeing him take so many medications and hoping it is helping, yet not knowing the full effects when he is so young."

2.4 Impact on Caregivers

There are financial impacts with the cost of medications. Many parents/caregivers reported on the financial stress caused by the treatment of JIA:

- "Drugs are expensive and as a single mother I struggle to make sure I have money for her medication."
- "Medication is very expensive and must receive special approval for payment by the provincial health plan."

- "Very expensive drugs. Necessary to have insurance with work to cover expensive medications."
- "Having a very low income (social assistance) having to purchase all the extras not covered, like needles, syringes, Pediasure, and pills is very stressful!"

Many parents reported taking time off work to go to medical appointments or when their child is sick. There are also costs associated with travelling to their nearest healthcare professional.

- "You need both parents working...having to take time off from work when child is sick or have to travel for medical appointments."
- "We are very early in our journey. So far, the greatest challenge has been missing work to attend appointments."
- "Living so far from the paediatric rheumatology department it is a challenge to work and juggle medical appointments."
- "We had to drive 600km every month to meet with specialist…had to take 3 days off of work."
- "Cost of travelling back and forth to medical appointments in London."
- "We have two boys with JIA so it would be helpful getting appointments and therapies booked together."

Effect of JIA on siblings:

- "At home trying to explain special needs/attention to siblings. Trying to make certain that siblings understand that it *(JIA)* isn't a fun thing"
- "Other siblings feeling neglected."

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Information was obtained from the following sources:

- Contact with three patient families facilitated by physicians involved in the clinical trials.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

We received feedback from three families who took part of the clinical trial. Change in quality of life was highlighted in all feedback. Most frequently mentioned was the positive change from daily injections to an injection monthly or every six weeks. The change has a positive impact on both the child and the parents.

- One father said, "My son is currently taking Canakinumab and it is an amazing drug. Injections are clearly not as painful as Anakinra. And only being 1 injection per month instead of daily, it appears to be just as effective, if not better. He doesn't appear to be getting sick as often. I believe they both slow down his immune system but not as much with Canakinumab…He is playing hockey, not missing any school and back to being the monkey I remember."
- "I am hoping that throughout the trial we help the doctors learn to understand better the cause of SJIA and to better treat it. I believe any adverse effects do not outweigh the symptoms of SJIA. Unless your child does not respond to Canakinumab, I believe it is the best drug to treat SJIA. Over the last 1 ½ years my son has taken more needles than most people do in 10 life times. At this point, the less needles my son has to take and still have a normal childhood is what is important to me."

- One mother said, “Nothing negative, only positive. It gave her the opportunity to not receive a daily injection and live a “normal” quality of life.”
- “Definitely fewer hospital visits, less requirement to take medication.”
- “Without medication she would be hospitalized and unable to walk or do anything with her hands.”
- When asked about hardships from the therapy, the mother responded, “Not really, other than monthly visits to the hospital take away from our vacation benefits at our work.”
- Another mother said, “Without treatment, I am certain that he would not be able to go to school or manage basic daily activities. He now takes Illaris, once every six weeks. With the medication, he is completely symptom free and has just taken up snowboarding. We are fortunate that this medication is covered by our private insurance, so we can be sure that he can continue on as a normal child.”

The families we spoke to who participated in the Canakinumab (Illaris) trial were happy with the therapy. Families whose child is on Canakinumab (Illaris) hope that the drug will work for them in the long-term.

Canadian Arthritis Patient Alliance (CAPA)

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest		Canakinumab (Ilaris) – Systemic Juvenile Idiopathic Arthritis (SJIA)
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]
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	Website	www.arthritispatient.ca
Permission is granted to post this submission		Yes

1.1 Submitting Organization

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, Hoffman-LaRoche, Janssen, Novartis, Ontario Rheumatology Association, Pfizer Canada, Rx&D and UCB Pharma. Additionally, CAPA has also received support in the past from: Canadian Institutes for Health Research, 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:

The author of this submission received honoraria from Sanofi in 2015.

Section 2 — Condition and Current Therapy Information

2.5 Information Gathering

The author of this submission was originally diagnosed with Juvenile Idiopathic Arthritis therefore these personal experiences were considered in the development of this submission. We had one-on-one conversations with another adult who was initially diagnosed with Juvenile Idiopathic Arthritis (JIA) as well as a parent of a child living with Juvenile Idiopathic Arthritis. More information was obtained through personal experiences of the Board of Directors of the Canadian Arthritis Patient Alliance in living with inflammatory arthritis.

2.6 Impact of Condition on Patients

Systemic Juvenile Idiopathic Arthritis (SJIA) is a serious, disabling autoimmune disease that attacks the joint lining, resulting in the destruction of the joint and surrounding bone. The impact of chronic inflammation on a growing joint is significant. Joints can literally grow around the inflammation causing abnormal shape and function as the child grows. Joint damage is irreversible and causes significant pain and disability. SJIA is a systemic disease that can also cause rashes and involve(s) other internal organs, such as the heart, liver, spleen and lymph nodes. Children who have SJIA 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. When diagnosed as a child, one can expect to live with the disease for the rest of their lives.

Without control of the disease, major joint surgeries such as joint replacement or fusions can be required at a young age and possibly lead to multiple procedures throughout the life span. For example, one patient reported having both knees and hips replaced at 13 years of age, a time at which those joints had not completed their growth and is likely to need further surgery as growth continues and the disease is not controlled. 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 has bath lifts, canes or wheelchairs, have their house/car adapted and rely on para-transit to do daily activities.

Unique complications associated with SJIA include growth retardation which can be caused by the disease itself or the use of corticosteroids. Research has shown and it is now common knowledge that newly diagnosed patients should be actively treated early in the disease to avoid irreversible joint damage, control pain and improve overall quality of life for the patient.

When the disease is not controlled, patients endure severe inflammation, pain and fatigue. Patients learn at a young age to live with the unpredictability of the disease and how the disease will change moment to moment, day to day and year to year. It affects every aspect of a patients' day-to-day life including sleep, self-care, walking, participation in school, the ability to concentrate and participate in social activities and the ability to pursue hobbies and interests. The disease can become a serious physical and psychological burden for children and youth when this is the time in their lives when they would normally be focused on fun, school, making friends and discovering who they are as individuals.

2.7 Patients' Experiences With Current Therapy

It is the general consensus that early aggressive treatment of the disease provides the best long-term outcomes for children and youth with SJIA. A number of treatment approaches are used to treat SJIA including Non-steroidal anti-inflammatory drugs (NSAIDS), corticosteroids and disease modifying anti-rheumatic drugs (DMARDS) such as Methotrexate, Anakinra and Tocilizumab.

It is important to note medications that inhibit Interleukin-1 and Interleukin-6 have been shown to be more beneficial to patients living with Systemic JIA. Canakinumab is a medication that specifically targets Interleukin-1 therefore the introduction of this medication provides an additional option for patients living with the disease. Currently, there are only two medications that target the IL-1 or IL-6 pathway thereby limiting patient options. It is also important to note of the two medications which target the IL-1 or IL-6 pathway, only ONE has been fully studied and specifically approved for use in the pediatric population.

Notwithstanding this fact, patients' response to medication can vary significantly. Some are effective for some while not effective for others. Some treatments will only manage the disease for a short period of time before the patients' 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 may not adequately respond to any of the biologics currently available. As a result, patients need a number of medication options in order to effectively manage their disease throughout their lives.

Effective treatments mean that children and youth with JIA do not need to live with the permanent damage, high medical costs (e.g. surgery, mobility aids, accessible housing) and disability. This is particularly important for children and youth living with SJIA who have a lifetime ahead of them. As such, early intervention is an absolute necessity in order to allow them the ability to fully participate in all aspects of life. This includes participation in school, finding a suitable career and employment, becoming a parent (if they desire), etc.

While side effects of existing treatments may vary, they can include: nausea and vomiting, extreme fatigue, decreased immune function (as current medications are immuno-suppressants), injection reactions, and for biologics, auto-immunity is often developed to treatments after prolonged exposure. Canakinumab has similar side effects and mode of administration as currently available treatment options.

2.8 Impact on Caregivers

Parents are the primary caregiver of children and youth living with SJIA. They feel additional stress as a result of caring for an ill child and adapting family and patient activities based on the disability. 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 child with SJIA, the parents, or the child's siblings may sometimes feel guilty about what has happened. Other times, a sibling may resent the extra attention a child with SJIA gets from his or her parents. Caring of a sick child may also impact the relationship with a spouse. The parents are also at risk of depression and marital stress as a result of living with these additional responsibilities.

New treatment options have the potential to ease the burden on patients' families, caregivers and the healthcare system.

Section 3 — Information about the Drug Being Reviewed

3.2 Information Gathering

The author of this submission was originally diagnosed with Juvenile Idiopathic Arthritis therefore these personal experiences were considered in the development of this submission. We had one-on-one conversations with another adult who was initially diagnosed with Juvenile Idiopathic Arthritis (JIA) as well as a parent of a child living with Juvenile Idiopathic Arthritis. More information was obtained through personal experiences of the Board of the Canadian Arthritis Patient Alliance in living with inflammatory arthritis.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

Significant strides in treatment have been made in the last 15-20 years and it is expected that Canakinumab will provide patients with SJIA with another option to manage the disease. Not everyone responds to the biologics currently on the market and if they do, their effectiveness wanes over time. For example, one patient with JIA was able to take Enbrel with effective disease control for five years while another patient was able to take Enbrel (though at higher than approved doses) for 10 years. The process of trial and error then began for these two patients to find an effective medication to control the progression of the disease.

It is important to note medications that inhibit Interleukin-1 and Interleukin-6 have been shown to be more beneficial to patients living with Systemic JIA. Canakinumab is a medication that specifically targets Interleukin-1 therefore the introduction of this medication provides an additional option for patients living with the disease. Currently, there are only two medications that target the IL-1 or IL-6 pathway thereby limiting patient options. It is also important to note of the two medications which target the IL-1 or IL-6 pathway, only ONE has been fully studied and specifically approved for use in the pediatric population.

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

Section 4 — Additional Information

We are pleased to see that Canakinumab has been properly tested in the pediatric population. Unfortunately, the appropriate study of medications in the pediatric population is not always undertaken by pharmaceutical companies and means that medications are often prescribed off-label.