

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	Benlysta (belimumab) for systemic lupus erythematosus (SLE)
Name of the Patient Group	Canadian Arthritis Patient Alliance (CAPA) & The Arthritis Society
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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 that are more effective 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. We are a virtual organization with no physical location 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 (TAS) 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 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 SLE about their experiences with the condition and any experiences taking Benlysta (belimumab). The survey also included a question relating to a recent [Health Canada warning](#) that Benlysta (belimumab) could cause depression, suicidal behavior and self-injury. This question asked whether they would still consider taking Benlysta (belimumab) with these known risks. CAPA and TAS 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 through our respective Canadian networks and communities,

such as Lupus Canada, regional SLE support groups and rheumatologists who operate Lupus clinics in Canada. A link to the survey was also sent out through the CAPA and TAS Facebook and Twitter accounts. The survey was open from May 22, 2019 to June 12, 2019.

Fourteen survey responses were received and six people had experience taking Benlysta (belimumab). A CAPA Board Member who lives with inflammatory arthritis reviewed the survey results. The survey collected demographic data, however only half of respondents completed this section. Those who completed demographic data all identified as female, and represented a range of ages from 25-34 years to over 65 years. An equal number of respondents have lived with SLE for shorter durations (less than 5 years) and longer durations (more than 20 years).

3. Disease Experience

Systemic lupus erythematosus (SLE) affects about one in every 2,000 Canadians. Men, women and children can all be diagnosed with SLE but it is far more common in women (90% of persons with SLE are women). SLE is a chronic autoimmune disease in which the body's immune system attacks and causes inflammation in its own tissues. Inflammation results in swelling, pain, cognitive impairment and other symptoms. As a result of SLE, the skin, joints, kidneys, heart, lungs, blood vessels, the nervous system and almost any other organ can be affected. SLE can vary in severity from mild to very severe. A person may experience active periods (commonly known as flares or flare-ups) and times where there is decreased activity or even inactivity (remission). There is currently no cure for SLE

People living with SLE who completed the survey made the following comments about the day-to-day effects of their symptoms:

“Joint pain, skin rash, mouth sores, fatigue and edema. I get tired very easily and my feet get sore if I try to do too much. Makes it difficult to keep up with daily life and socially.”

“I have joint and muscle pain, and difficulty walking very far. Staying in bed for more than four hours is difficult. I have shortness of breath, likely from having heart failure the last year and a half. I had a mild heart attack caused by lupus, as myocarditis. I also have recently been told I have asthma.”

“Complete exhaustion, facial rash, body rash, sore swollen joints, sore muscles, problems with eyesight because of medications, lung problems, I could go on forever.”

“During flare I have hair loss, arthritis and nephritis but mostly I am dealing with skin lesions, butterfly rash and fatigue.”

The disease impacts patients' lives in a variety of ways, such as completing daily household chores, like grocery shopping, doing laundry, cooking meals, and self-care. Participating in leisure activities can also be difficult as well as caring for children and loved ones, such as spouses / partners:

“There are so many things that I have had to give up over the years, driving, gardening, most of my crafting, needlework, vacuuming, yard work. When my husband came down with Alzheimer's I had to have a lot of help come in to help take care of him. I somehow managed for 10 years but had to put him in a home for the last 5 yrs. before he passed”

“Shopping for groceries is difficult, as are food prep and cooking a meal. Any task requiring bending or kneeling is hard, I need to use a stool or chair to do things. Lifting wet laundry is hard to do, making the bed. “

People also reported difficulties in contributing and participating at work due to the fatigue, pain, and other symptoms of the disease:

“Daily, I am affected by fatigue and joint pain. For me I need to control the exhaustion the most as it makes it difficult to do my job, teacher. I do work a full time job however there are days, especially towards the end of the week where I am extremely tired and find it difficult to work.”

“...Been off work numerous times. Impacts entire life when in a flare.”

“Extreme fatigue, nauseous, joint pain, brain fog and lack of concentration- all of this because I find it extremely hard to complete my work, on some days I find it difficult to write a sentence.”

“The fatigue and need for 10ish hours of sleep to function makes working full time a challenge.”

The impacts of the disease also extend to caregivers such as spouses / partners and children. Often, these people take on additional household chores such as cooking, cleaning, shopping, etc. to support the person living with SLE. Caregivers also take on additional activities, such as supporting their spouses / partners in getting to and from medical appointments.

“My husband often has to come (home) after a 14 hour shift and cook dinner for us because I am too exhausted to move or stand for a long enough period of time to cook something on the stove.”

“My husband and son are amazing and have taken on more of the responsibilities at home...cooking, cleaning, gardening, etc.”

“My husband does most of the shopping and a lot of the housework. He drives to appointments as I have been sick for six months, and don't feel I can take it on again.”

In some cases, paid caregivers assist people living with SLE to carry out activities of daily living particularly in situations where they do not have family to support them:

“I try to do it all myself but I do have a cleaning lady who comes once a week and she also does my laundry which helps tremendously!”

“I have no family here to help but because I am over 65 I get some help...2 hours per month of housework, yard work, and someone comes once a week to take me out for a drive. It's not much but it's better than nothing. I know I should have more help...”

People living with the disease are also at risk of co-morbidities, such as depression and mental health issues. 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 SLE often makes it feel like a person is not in control of their disease.

4. Experiences With Currently Available Treatments

Medications for SLE aim to control inflammation and minimize disease activity so that no long-term organ damage occurs, as there currently is no cure for SLE. Treatments used to manage SLE include Non-steroidal anti-inflammatory drugs (NSAIDs), antimalarial medications (hydroxychloroquine and chloroquine), corticosteroids, and immunomodulation drugs, such as methotrexate, azathioprine, mycophenolate mofetil and cyclophosphamide. 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. Several of these side effects can cause trouble as they may imitate lupus problems or complicate lupus problems that already exist.
- Antimalarial medications such as hydroxychloroquine and chloroquine are very useful in treating sun sensitive skin rashes or other types of lupus rashes. It is also used to treat lupus fatigue, arthritis and other milder symptoms of SLE. The most common unwanted effect is some stomach upset. However, if hydroxychloroquine and chloroquine are taken in a high dose and over a long period, they may accumulate in the background of the eye (retina) and cause a loss of vision and in rare cases, blindness may occur.
- Corticosteroids are commonly used in the treatment of SLE 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.
- Immunomodulation drugs are also commonly used in the treatment of SLE and also 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.
- Anticoagulant drugs are used to treat some people with SLE with antiphospholipid antibodies which interfere with the normal functioning of cells, and can cause blood clots to form (often in the lower legs) or blood vessels to become blocked (causing strokes). Anticoagulant drugs prescribed include low-dose Aspirin, Warfarin, and Heparin. The most common side effect of anticoagulants is bruising or bleeding and there are risks to overprescribing the medication such as prolonged bleeding, black stools and excessive bruising.

Patients reported that they had tried a number of treatments used for SLE. The disease symptoms may flare or be triggered by sunlight, infections, or medication which then require changes in the treatment approach. Often, currently available treatments can be difficult to tolerate and manage:

“I used prednisone to begin with...side effects... mood swings, moon face, unable to sleep, agitated at times. Plaquenil... upset stomach sometimes. Methotrexate injection weekly... nausea, weight loss and had to take other medications to control the nausea. Extremely difficult to tolerate...was unable to go out the day I took it.”

“High doses of prednisone (had) terrible side effects. Methotrexate had allergic reaction. (I) tolerate plaquenil and imuran.”

“Have taken plaquenil since the beginning but it wasn't enough on its own after about 2 years. Imuran was not effective at controlling my lupus nephritis and I was switched to MMF/cellcept and that has been working well to control my symptoms until my most recent flare.”

“In recent years I’ve been on Methotrexate, both oral and injectable, Arava, Imuran, Cyclosporine and recently, Cyclophosphamide. Most of these have been hard to tolerate, with nausea, headache, tremors, anxiety. Irritable bowel and urinary tract infection. None of these have helped much with my joint pain.”

“When first diagnosed I was put on Plaquinel and it worked wonders for many years but I then unfortunately developed neuropathy from this medication. Prednisone has worked well but I am now having issues with bone density.”

Patients may also pursue non-pharmacological approaches to treatment of SLE, such as physiotherapy, occupational therapy, massage therapy, counselling, acupuncture and medical cannabis. 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 wait lists delaying access to care.

5. Improved Outcomes

People living with SLE 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, mood swings, and osteoporosis. Some of these side effects require treatment with other medications, such as bisphosphonates (osteoporosis), and anti-nausea medications. Minimizing these side effects are important outcomes that should be considered when evaluating new therapies.

Even with currently available treatments for SLE, patients’ responses can vary significantly. Some medications are effective for some people while not effective for others. Some treatments will manage the disease for a short period of time before the patients’ 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 SLE may not adequately respond to any of the currently available medications. As a result, patients need a number of medication options to manage their disease throughout their lives.

Overall, there are several outcomes of importance to people living with SLE including:

- a reduction in pain and fatigue
- reduced organ involvement
- treatment of lupus nephritis
- reduction in disease complications, such as blood clots
- increased mobility
- ability to work and be productive at work
- ability to carry out activities of daily living and social roles
- ability to effectively carry out caregiving and parenting tasks.

6. Experience With Drug Under Review

Benlysta (belimumab) was approved for use in Canada in 2011 and there are some experiences with the medication for people living with SLE who have private insurance or pay out of pocket for the medication. It is the first medication in years to come onto the Canadian market specifically for the treatment of SLE. **It**

is the only monoclonal antibody used to treat SLE and therefore represents a treatment advance and new option for people living with SLE. Effective treatments mean that people with SLE do not need to live with the permanent damage, high medical costs (e.g. caregiver support, mobility aids, accessible housing), inability to work and disability.

There were six people who completed the survey who had experiences taking Benlysta (belimumab) for the treatment of SLE. All reported that side effects were reduced significantly. They also reported an overall decrease in their disease symptoms including pain and fatigue, and increased ability to participate in activities of daily living, such as work.

"Up to benlysta, the only drug that would work that I could tolerate was prednisone. Long term effects were a concern. I live in the Toronto area, so access to treatment is not a major concern. Although the prednisone helped to control the disease, the long-term effects of high doses over the 46 years I have had SLE was/is a concern."

"Currently on benlysta and seems to be keeping my skin conditions under control and allowing me to keep mycophenolate mofetil at a lower dose therefore increasing my white cell count."

"Benlysta has been a lifesaver... the side effects are minimal...headache and tiredness. With benlysta I am rarely tired at the end of a work week. My joint pain is almost nonexistent. ALL my hair has grown back no more ulcers in my mouth. I expect that continued use of benlysta will only improve my health further."

"I'm still in the very early stages of my treatment with Benlysta but so far no side effects"

"No side effects and symptoms seem well managed except for lesions on my fingers of unknown cause."

"... Prednisone use has been greatly reduced. Blood counts totally into the normal range. Still mild joint pain, likely due to osteoarthritis. Continuing with small doses of prednisone. No side effects that I can tell. I attend the infusion clinic for treatments with no significant disruption to my regular routine. Benlysta is the best thing that has happened for me with my SLE. Best overall health I've had in years!"

The survey had questions concerning a recent [Health Canada warning](#) that belimumab could cause depression, suicidal behavior and self-injury. People were asked whether they would still consider taking belimumab with these known risks. Five people answered this question and all five noted that they would still take Benlysta even knowing these side effects were a possibility. Some even noted that SLE already affected their mental health (co-morbidity) or that other medications such as Prednisone had similar side effects.

"I have not experienced any of the potential side effects listed above. Prior to being diagnosed I was miserable... I was in so much pain that I was unable to sleep, live my life like I had up until I got sick. I would often cry as many doctors refused to believe I had lupus. I never want to go back to where I was...I have come a long way since (date of diagnosis)."

"I would (keep taking the medication) until I notice any of these symptoms. I've tried everything else to control my SLE so I'm running out of options."

"Because it is an important option for treatment as there are so few for lupus. I think perhaps if this is the case that patients are closely monitored. Honestly I was way more depressed on prednisone and had way more side effects and would take benlysta over that any day."

"If anything, I've experienced mild depression. But, already on treatment for that prior to Benlysta."

Concerns were expressed about the mode of administration of the drug including the lengthy time for drug infusions (3 hours) and the difficulty in taking time off work. Travel is made difficult by the use of a self-injector.

“Benlysta has been good but working full time is impossible because no job lets you take a half day every month for the infusion and the self-injector needs to be refrigerated which doesn't work well for travel. I think a lot more could be done for these issue.”

“The infusion makes working full time difficult since no one lets you take the time off and it honestly takes about 3 to 4 hours by the time the drug dissolves. Also the self-injector has to be refrigerated which is a limiting factor for me since I travel a lot for work and personal.”

6. Companion Diagnostic Test

Not applicable

7. Anything Else?

No further comments at this time.

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