CADTH

CADTH COMMON DRUG REVIEW

Patient Input

Dupilumab (Dupixent)

(Sanofi Genzyme, a division of sanofi-aventis Canada Inc.)

Indication: atopic dermatitis

CADTH received patient input from:
Canadian Skin Patient Alliance
Eczema Society of Canada

November 12, 2019

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Dupixent (Moderate to severe atopic dermatitis)**
Name of the Patient Group	**Canadian Skin Patient Alliance**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	**1-877-505-2772**

1. About Your Patient Group

The Canadian Skin Patient Alliance (CSPA) is a national non-profit organization dedicated to advocating, educating and supporting Canadians living with diseases, conditions and traumas that affect skin, hair and nails. The CSPA is registered with CADTH.

Our mission is to promote skin health and improve the quality of life of Canadians living with skin conditions, diseases and traumas. We advocate for best treatment options for all skin patients; we educate on issues affecting these patients; and we support the members of our affiliate organizations who serve specific patient communities such as eczema, melanoma and psoriasis.

2. Information Gathering

The CSPA developed the Atopic Dermatitis Patient Experience (ADPE) Survey using Survey Monkey, which was reviewed for clarity and comprehensiveness by a Canadian dermatologist and members of the public. The ADPE survey was disseminated between November 3-24, 2017 using social media strategies designed to target those in Canada living with atopic dermatitis (AD) and their caregivers. In total, 194 eligible responses were received; 92% (120) of patients and 87% (54) of caregivers were Canadian residents. The small sample of responses from US and international patients were included as many experiences and needs are universal. Of the 132 patient respondents living with AD, 55% had moderate to severe AD, 78% were female and the average age was 42 years old although respondents' ages ranged from 18 to 92 years. The remaining 62 responses were from caregivers, of which 68% said they cared for someone living with moderate to severe AD.

To better understand patient experiences with Dupixent, the CSPA published a separate survey using Survey Monkey that was circulated to our patient community using social media strategies from September 8 to November 18, 2019. We received 12 responses to that survey, of which seven identified

that they were Canadian. CADTH also shared three detailed submissions by Canadian individuals (one patient and two caregivers) with CSPA, which have been incorporated into this submission.

3. Disease Experience

Atopic dermatitis (AD) is a chronic, inflammatory skin condition that affects up to 17% of individuals in Canada. The impact of AD varies considerably depending on severity. AD is classified into mild (45% of patients), moderate (45%) and severe (10%) forms, which are defined by frequency of itching, amount of skin affected, and presence of skin thickening and cracking. While mild AD is characterized by dry, red and itchy skin, moderate to severe AD patients experience these symptoms as well as thickened skin and lesions that ooze and bleed during flare-ups.

"Having chronic moderate to severe AD is like having chicken pox 24 hours a day, 7 days a week."[1]

"Prior to being on Dupixent, ***I always had an urge to itch. This led to cuts on large portions of my body.*** *I was always bleeding from somewhere.* ***The thought of itching consumed my life****; I was always thinking about the itching or the pain or the impact of living with AD. Contact between the cloth and my skin made me itchy.* ***People would never understand how it feels to want to itch so much that you rip your skin open, over and over and over again.*** *I have experienced waking up in the middle of the night to my legs and arms scratched open and blood and skin covering the sheets.* ***This has caused significant negative impacts to my quality of life.*** *There is no stopping the itch. It was there when I was awake and when I slept. It was so exhausting. I still fear having to deal with those issues again.*

My skin was consistently flaking; it was so dry that it would crack and weep by itself. *People would see the sores and the scars and make comments about my appearance. Seeing piles of skin on the floor and on chairs was a constant reminder of how AD controlled my life.*

The pain of being covered in AD on the majority of the surface of my body was terrible. *I itched and rubbed my skin so much the hair on my eyebrows started falling out. I remember my neck being so bad and so itchy that it was always bleeding on my shirt collars.* ***Showers were so painful; the feeling of water hitting the sores stung so much.***

I would unconsciously itch when I was stressed or nervous. ***If I had a particularly rough night, any time I moved my body the following day would result in intense pain.*** *If I moved my head, my neck be on fire and I would feel the wounds open. If I stood up, my legs and torso would cause me so much pain. Every time I walked I would feel exactly where I scraped the skin off the night before;* ***I would typically find blood on my pants at the end of the day****. I had eczema on my mouth, my lips and my eyelids. If I opened my mouth too wide, it would cause the skin to crack and bleed. My skin was so delicate, but I would rip through it because the feeling of itching was so addicting I could not stop."*[2]

"People often underestimate this disease but it is all consuming and so hard to manage. Sometimes I can't even think straight because I'm so itchy. ***I have to work, be a mom, and function all while feeling so irritable due to lack of sleep and itchy skin."***[1]

"When my flare-ups are bad, my skin oozes and blisters, ***preventing me from working****."*[1]

"When my son's flares are bad, ***we can't fully live our lives or relax without worrying*** *about what he's touching, eating, etc. that could make it worse."*[3]

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[1] ADPE patient respondent
[2] Patient with severe AD who later tried Dupixent
[3] ADPE caregiver respondent

Flareups are an ever-present and unpredictable aspect of living with AD, especially those with moderate to severe forms of the disease. Four in five patients with moderate to severe AD responded that they are concerned about their next flare. Half (51.5%) of those with moderate to severe AD experience flares at least monthly. Three in five ADPE caregiver respondents (61%) identified intermittent flareups; of these caregivers, one in five (21%) identified flareups on a weekly or monthly basis.

Complications and comorbidities of moderate to severe AD include oozing, crusted lesions from *Staphylococcus aureus* infections (34% of ADPE patient respondents; 19% of caregiver respondents) and blisters from herpes virus infections (12% of patients; 6% of caregivers). AD patients are also at increased risk of developing asthma and allergies.

"My son caught hand, foot and mouth disease. The area that he has his eczema (elbows) got covered in blisters / rash with his other areas unaffected. I did not realize that ***the area affected by the eczema would make it easier for other skin disorders to appear****."*[4]

"I have had posterior capsular ***cataracts*** *and anterior capsular cataracts in both my right and left eyes. I have also had a* ***retinal detachment*** *in my right eye following cataract surgery in my right eye."*[5]

ADPE patient respondents with moderate to severe AD reported an average of 2.3 nights of **interrupted sleep** each month. While three in four patients (74%) reported losing at least one night of sleep each month, one in five (20%) lost at least 10 nights of sleep each month. One in four caregivers (27%) reported that the person that they care for loses 7 or more nights of sleep a month due to their condition. This is consistent with international studies that have documented the association between the persistent itch of AD and sleep disturbance. The short and long-term effects of interrupted sleep are challenging for everyone, but are particularly detrimental for children whose resulting fatigue has the potential to affect growth, emotional well-being and ability to learn.

*"****I worry about my child's development*** *due to constant, interrupted sleep."*[4]

"Sleeping less than 5 hours a night was a regular occurrence for me. Waking up to uncontrolled itching was normal. ***I hated sleeping; the idea of itching myself until I bleed every single night was absolutely haunting, but the lack of sleep was also exhausting.*** *I had to take Hydroxyzine or Doxepin to sedate myself. I know I almost fell asleep while driving many times; nodding off at stop lights because I only got a few hours of sleep during the week.* ***The lack of sleep was the biggest impact; I remember falling asleep everywhere and feeling half-awake for my entire university career. I could not focus on school.*** *I am disappointed when I see how much of a disadvantage I had compared to other students.*

*The lack of sleep made my daily life stressful and challenging; I remember the feeling of being perfectly okay if my life ended; it would mean the itching would stop****. I wondered what it was like to have a full night's rest. The only time I truly felt like I could sleep properly was if I died.****"*[5]

"I remember lying awake at night, unable to sleep, after hearing his screaming in the shower when the water would touch his raw skin. ***He would find himself crying and depressed but not understand why.*** *He would hide in the shadows of the darkness and adopt a nocturnal routine so he would not have to see his reflection in the mirror.* ***We went through the motions of living but not really living at all.****"*[6]

Impacts of moderate to severe AD permeate patients' lives: nearly half (46%) of ADPE patient respondents reported a poor effect on their work or school life and two in three (68%) reported a negative

[4] ADPE caregiver respondent
[5] Patient with severe AD who later used Dupixent
[6] Parent whose child participated in Dupixent clinical trial

impact on their personal life. Anxiety (45%) and depression (37%) significantly impact patients with moderate to severe AD.

"I was covered in eczema. I was bright red and it made me uncomfortable to be around people. I was embarrassed from my skin, the constant flaking. I hated looking in the mirror. I remember fighting with myself to try and stop scratching because it caused so much pain. ***I could not concentrate on anything.***

I struggled to pay attention *to school, friends and my own family. I was always sad or upset because of the chronic pain and itching. I know I was a burden to my parents and family.* ***It made me angry, sad, upset, depressed. It is hard to put into words what being trapped in your own body feels like****. "*[7]

"Having this condition has had a tremendous impact on my life. I don't sleep and ***I have trouble completing my daily activities*** *without feeling debilitated by the itch and burning of my skin."*[8]

*"****Damage and scarring*** *to skin have caused me* ***high anxiety****."*[8]

Caregivers report that one in five (22%) of the people for whom they care **miss at least one day of school or work monthly**, while the ability of one in four (28%) of the people for whom they care to be in school or at work is negatively impacted. Moreover, two-thirds of caregivers (68%) indicated that this condition **negatively affects their own lives**. The financial and emotional implications of absenteeism can be very detrimental on the well-being of those with this condition.

"My son was ***unable to attend school or sit through class*** *because of the unbearable discomfort from his skin. When my son did attend school, he would leave class frequently for the relief of the cool breeze outside, sometimes abandoning school altogether.* ***My son used to miss weeks and weeks of school.***

During the worst times, ***he would refuse to get up, lying immobile in bed all day****; he would cover his head with a blanket because of the* ***debilitating pain*** *he felt from the raw exposed skin on his face, scalp and body.* ***He would refuse to sleep*** *because once asleep, the skin on his face would be destroyed by his unconscious and uncontrollable scratching. His skin would often be raw, bloody, and susceptible to infection. We tried gloves on his hands and even* ***spent many sleepless nights holding his hands*** *to no avail."*[9]

"The years after my son's AD worsened were a ***constant struggle*** *and* ***cycle of unending doctor appointments and treatments, none of which had any lasting effectiveness****. Doctor appointments included frequent visits to the medical clinic, bi-weekly appointments to the pediatric dermatology clinic at [our children's hospital] and various other specialist appointments, including a child psychologist as we were very concerned with how the disease was affecting our son's mental well-being, and a number of unscheduled* ***visits to the emergency departments on the days we were desperate for help****.*

It was also hard on my wife and me. My wife would stay home to look after our son. I would often have to take time off work to take him to his various medical appointments. ***Our lives revolved around trying to relieve our son's suffering."***[9]

4. Experiences With Currently Available Treatments

Both patients and caregivers reported that currently available treatments have limited effect. Caregivers in particular often opt for non-prescription options, possibly due to fear of using potentially harsh medications on their children; they may also be instructed by their healthcare providers to be cautious of using such treatment in younger patients. Of prescribed treatments, topical corticosteroids seem to offer the most improvement, though they are not always a long-term solution without side effects. Several

[7] Patient with severe AD who later used Dupixent
[8] ADPE patient respondent
[9] Parent whose child participated in Dupixent clinical trial

patients described their experiences with **steroid withdrawal** after years of use. This corroborates a 2006 survey of Canadian patients which found that 71% were concerned about the safety profile of topical corticosteroids.[10] While patients and caregivers are clearly willing to try effective medications to treat this condition, safe, effective and long-term options are limited.

Four in five ADPE survey respondents (78% of patients; 82% of caregivers) **tried multiple treatments** before finding relief. Of those with moderate to severe AD, a significant number reported trying 5 or more treatments (44% patients, 34% caregivers); some even reported having to try 10 or more treatments (23% of patients; 11% of caregivers).

"We tried any and all treatments suggested [for our son], including the full gamut of topical steroids, Elidel and other non-steroidal creams, oral steroids (several treatments lasting weeks at a time), light therapy and naturopathic and herbal remedies involving removing most foods from his diet. ***None of these had any lasting benefits, and in many cases the rebound effect made our son's eczema and suffering much worse."***[11]

"My creams are just a band-aid solution."[12]

"The steroid creams that the doctors prescribed my son only ***provided temporary relief*** *and ultimately made the eczema* ***return more fiercely each time****; soon the steroid creams stopped working altogether."*[11]

In terms of **oral medications**, more than half of ADPE respondents have tried antihistamines but only 7.4% of patients and 7.1% of caregivers reported receiving significant relief from them. Nearly all ADPE patient respondents (97%) and caregiver respondents (89%) with moderate to severe AD have used **topical corticosteroids** although their patterns of use differed: they may use them continuously for the long term (35% of patients; 18% of caregivers), at regular intervals for fixed periods (45% of patients; 36% of caregivers), or infrequently (17% of patients; 35% of caregivers).

"I'm less than thrilled about having to use a corticosteroid and am ***very concerned about it becoming less and less effective over time****."* [12]

"Constant application, localized treatment and inability to completely treat many issues with AD are a few drawbacks [of corticosteroids]. Also, there are complications when using these treatment options: thinning skin, ocular impacts, etc. ***Cost is low but this is not an adequate treatment option for severe AD*** *sufferers."*[13]

"Alternative drugs to Dupilumab had ***worse side-effects*** *and* ***could not be used long term****."* [11]

Immunosuppressive medications have been used by four in 10 (39%) of those with moderate to severe AD, despite their use being off-label only and with the potential to cause significant side effects. Among ADPE respondents, 1% of patients and 4% of caregivers reported continuous long term use of immunosuppressive medications (cyclosporine A, azathioprine, methotrexate and oral corticosteroids), while 14% of patients and 4% of caregivers used such medications during regular intervals for fixed periods, and 24% of patients and of caregivers used them infrequently. However, six in 10 (61%) patient respondents and seven in 10 (68%) caregiver respondents reported never having used immunosuppressive medications.

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[10] Barbeau M. & Lalonde H. Burden of atopic dermatitis in Canada. *Int J Dermatol* 2006; 45:31-36.
[11] Parent whose child participated in Dupixent clinical trial
[12] ADPE patient respondent
[13] Patient with severe AD who later tried Dupixent

*"Methotrexate and other immune-suppressors are treatment options but have **severe complications and require constant monitoring** from a doctor. These options do not actually target the disease specifically and cannot control severe AD. **Itching still remains and eczema can still be found on the entire body.** This is not an adequate treatment option when compared to Dupixent."*[14]

Other methods of **controlling and preventing symptoms** used by patients with moderate to severe AD include UVA or UVB phototherapy, skin care maintenance such as specific bathing routines (e.g., oatmeal baths, bleach baths), moisturizers, natural and herbal remedies, and acupuncture. Those with AD also report that they avoid certain foods and clothing, refrain from hot baths and wear long sleeves to prevent symptoms or reduce exacerbations.

AD patients often experience **treatment fatigue**, where one treatment that has proven effective for them gradually becomes less effective, leaving them faced with the trial and error process of determining which other treatment may provide them with some benefit. In addition to providing a treatment for patients with uncontrolled moderate to severe AD, a new treatment option can provide relief for some patients whose moderate to severe AD is currently well-controlled but may not be in the near future.

"I haven't found a cure or perfect routine. One thing works for months and then suddenly it doesn't anymore and you have to start over."[15]

"The costs associated with the trial and error nature of treatment regimens is very frustrating." [15]

While more than half of patient and of caregiver respondents noted they were not experiencing any **side effects from treatment**, more than one in four (27%) patients with moderate to severe AD struggle to manage the side effects of treatments. These impact the willingness to adhere to treatments of 24% of ADPE patient respondents with moderate to severe AD. Adverse effects experienced by ADPE patient respondents with moderate to severe AD include spider veins (47%), thinning of the skin (30.3%), headache (25.8%), fatigue (24.2%), premature aging (22.7%) and blistering (19.7%). Caregiver respondents identified thinning of the skin, headache and fatigue as the three most concerning side effects of currently available treatments: *"I've yet to find a treatment that works and is worth the side effects."* [15]

The **costs of currently available treatments** are a burden for many and a complete barrier for some patients. For ADPE patient respondents with moderate to severe AD, the cost of treatments precluded 17% from starting a course of treatment and resulted in 16% stopping a course of treatment. Caregivers reported slightly less of an impact: cost precluded 11% of caregivers from starting a new course of treatment and the resulted in the same number stopping a course of treatment.

Frequently trying to keep ahead of a disease for which available treatments at best manage symptoms can itself be very costly. ADPE patient respondents with moderate to severe AD reported spending $107-$315 monthly **out-of-pocket** on oral medications, up to $100 monthly on topical treatments and up to $700 treating AD symptoms with skin care maintenance, skin washing with antiseptic remedies, natural and herbal remedies and alternative medicines such as acupuncture. Caregiver respondents ranged between $100-180 in out-of-pocket spending for oral medications, up to $400 for topical treatments and up to $660 for other tools to manage symptoms.

5. Improved Outcomes

[14] Patient with severe AD who later used Dupixent
[15] ADPE patient respondent

Patients living with moderate to severe AD describe the excruciating, “disfiguring” and debilitating nature of their symptoms. As described above, AD causes **itching, burning and pain**, each of which can decrease patients’ ability to **sleep, work, attend school, parent, and complete activities** of daily living.

Poor sleep is challenging for patients of all ages and has a particularly detrimental impact on younger patients (including teenagers), as it can compromise health child and youth development. When these symptoms are adequately addressed, patients are better **able to sleep properly**. Patients in school are better equipped to **learn** and those who work are able to be **more productive**. Caregivers who also experience disrupted sleep can be healthier, more productive, and have a higher quality of life. Patients who parent are better able to meet their families’ needs when they have slept properly, without disruptions due to AD symptoms.

Where moderate to severe AD is not adequately controlled, skin may crack, ooze and bleed. **Breaks in the skin’s surface** allow bacteria and other causes of **infection** to enter the body, putting patients with AD at elevated risk of acquiring an infection. Improvement in these outcomes would reduce the risk of infection and the burden associated with moderate to severe AD. Living in skin that is constantly cracking, oozing and bleeding also has a significant impact on people’s daily lives as they have to carry a change of clothes with them so they can continue to function in a work or school environment.

The **mental and emotional impact** of living with moderate to severe AD must not be understated. Those who live with skin diseases are regularly confronted by stigma. AD patients often describe hurtful reactions of other people to the appearance of their skin, which is particularly acute during a flareup. There is a misconception that AD is contagious, resulting in frequent instances where people are actively rejected by colleagues, fellow students, and members of the public. AD patients often experience isolation, low self-esteem, and poor school performance by children and youth. Where the symptoms of AD are adequately controlled, patients will be better able to participate in social occasions without the fear of **stigmatization**, improving their mental and emotional health.

*“The eczema on my eyelids is **disfiguring**, and prevents me from wearing make-up or contact lenses. I am embarrassed to be seen during flareups which happen almost weekly.”* [16]

*“**It makes me hesitate to join people at gatherings and outings** because I’m embarrassed to be seen with nasty rashes and flakes.”* [16]

6. Experience With Drug Under Review

We heard from eight patients who had used Dupixent (dupilumab) to treat their moderate to severe AD. Five of the respondents to the CSPA Dupixent survey commented on their experiences using the drug to treat their AD, four of whom had a positive experience and one of whom *“disliked it altogether”* and experienced *“terrible side effects”*.[16] As noted above, one patient and two caregivers who provided patient input directly to CADTH consented to have their experiences with Dupixent shared as part of this submission.

*“This drug is **much easier to use** than other therapies; one injection bi-weekly is **easy to plan** and **getting a supply** for the month is not difficult. Refrigeration is required. I have experienced dry eyes that I fully control with eye drops when I feel dryness. **This drug seems to completely control severe AD** for patients. No other drug has been able to do that (for me and many others).*

*With Dupixent, **I have been able to sleep without issues**; **I am not constantly itchy**. I can concentrate at work and have the ability to live my life without having to worry about my AD. I am able to exercise and socialize without much difficulty and **it is life changing**. I currently do long course triathlons because I*

[16] ADPE patient respondent

can finally focus on things without having this disease control my life. ***There is no way I could do what I do today if I couldn't control my severe AD*** *with Dupixent.*

There are no alternatives to Dupixent for severe AD patients. The cost of this drug is high so without coverage, severe AD sufferers are forced to use inadequate treatment options that can result in complications. Now that I am on Dupixent, ***I can live a normal life****. Without Dupixent, I am forced to choose an inadequate treatment option due to the cost of the drug. Without Dupixent, I will suffer again."*[17]

"My skin has responded positively to Dupixent which has ***cleared my skin and eliminated the redness and intense itching****. I have had no side effects."* [18]

*"****My skin is less scaly, no longer itchy and smoother to the touch****. I can now sleep better and have a better quality of life. I can now wear short sleeves and I feel so much better overall. No negative impacts."* [18]

"I started Dupixent after initial success and then gradual failure of methotrexate use over five years to manage my severe eczema (main involvement is eyes and both hands). I was back to the point where there was significant pain in both hands, which significantly impeded my ability to work (on the computer, doing meeting facilitation) and activities of daily living due to pain and bleeding associated with my skin cracking and sores, etc. Within two weeks of starting Dupixent I noticed a significant decrease in itching and pain, ***by four weeks I had significant clearance of eczema patches around eyes and on hands, and complete clearance of patches by eight weeks****. I have not had any side effects associated with Dupixent."*[18]

"I have been using Dupixent for several years. I am so happy with the results. I have no more itchy skin, red patches or flaky skin. ***I have my life back****."* [18]

"Being part of the study on the drug, Dupilumab, has saved our son's life and ours. After four years of a worsening condition, ***my son started playing music on the piano again****. He started to smile and enjoy time with his family again. It is still a struggle to mend the 4 years of his short life that went missing during his adolescence but we are slowly working there."* [19]

"Within a month of his first injection of dupilumab we began to see signs of improvement. There was steady improvement over the next few months and our son's symptoms improved sufficiently for him to be ***able to regularly attend classes*** *and for us to start the process of trying to re-engage him in social and physical activities. In July 2019, the terms of the clinical trial required my son's dupilumab injections to stop as his skin was in relatively good condition.* ***He continued without severe symptoms*** *until only recently, and he restarted dupilumab injections."* [19]

7. Anything Else?

Skin diseases, conditions and traumas are often dismissed as "just a rash". For patients, they are far more than that. Skin diseases and conditions often reflect imbalances in inflammatory and other systems, and can be caused by a virus, cancer, bacteria, fungi, genetics, wounds, hormones, allergens, and other disorders, which can cause devastating impacts. Skin patients deserve to be treated with respect and dignity by the health system, which includes its embrace of new treatment options.

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[17] Patient who later used Dupixent
[18] CSPA Dupixent survey respondent
[19] Parent whose child participated in Dupixent clinical trial

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.

This submission was prepared by the CSPA without help from outside the organization.

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.

The data used to support this submission was collected and analyzed by the CSPA. We also drew on the data collected and analyzed in The Skin I'm In: A National Report of the Patient and Caregiver Experience with Atopic Dermatitis (February 2018), support for which the CSPA contracted JRL Research.

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
Sanofi Canada	X			
Pfizer Canada			X	
Abbvie Canada				X
Merck Canada		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: Rachael Manion
Position: Executive Director
Patient Group: Canadian Skin Patient Alliance
Date: November 18, 2019

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Patient Input Template for CADTH CDR

Name of the Drug and Indication	Dupilumab / Dupixent for moderate-to-severe atopic dermatitis patients aged 12 and older
Name of the Patient Group	Eczema Society of Canada
Author of the Submission	Eczema Society of Canada
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	1-855-329-3621

1. About Your Patient Group

The Eczema Society of Canada (ESC) is a registered Canadian charity dedicated to improving the lives of Canadians living with eczema. With the help of dedicated expert physicians and contributors, ESC delivers evidence-based, up-to-date disease and treatment information to Canadians living with eczema, including patients and caregivers, as well as healthcare providers. For more information, please visit www.eczemahelp.ca.

2. Information Gathering

Information for this submission was gathered via written questionnaires, interviews, and by patients and caregivers providing statements and testimonials about their experience with uncontrolled moderate-to-severe atopic dermatitis (AD) and their experience with dupilumab and other systemic medications. AD is the most common form of eczema, and ranges from mild to severe. Patients who have shared their experiences using dupilumab obtained access to the drug through the clinical trial, compassionate care programs, or private insurance plans. All responses and testimonials are anonymous.

This input submission also contains patient and caregiver survey data. In 2016 ESC conducted online quality of life surveys with 1035 respondents from across Canada, including both adults and caregivers of children living with AD. The data in this submission pertains to respondents who reported on moderate or severe AD, and also contains content specifically related to adolescents with AD. In 2019 ESC conducted an online survey of 299 respondents from across Canada pertaining specifically to systemic treatments for AD. Data in this submission pertains to both adult and pediatric populations as reported from the systemic treatments survey.

3. Disease Experience

This inflammatory skin disease causes dry, itchy skin, which develops red, raw, rashes that can bleed and ooze. The symptoms of moderate-to-severe AD can be debilitating and life altering for sufferers as well as caregivers and family members. For patients with a more severe form of

AD, the itchiness can be intense and occur all day and night, interrupting all aspects of life, including work, school, social relationships, and sleep.

Living with the chronic itch and pain (due to skin changes, lesions, and open sores) can take a significant toll on quality of life. Sleep is significantly impacted due to the itch and pain caused by the disease; 79% of survey respondents suffer from interrupted sleep, with 29% having poor sleep more than 14 nights per month. Some patients report reliance on sleeping pills as they are otherwise awake all night due to itch. Others report sometimes falling asleep during the day and experiencing daytime exhaustion, changes in mood, and impatience due to fatigue.

Patients have also reported missing work and school, with adolescents reporting bullying due to their condition. Patients also report being bed ridden during severe flares when their skin is covered in open wounds, sores, and rash, while the intense itch drives them to scratch and further damage those open wounds. Patients also share stories of bleeding through their clothing, and needing to frequently change clothing.

AD also impacts mental health, with 64% of surveyed patients reporting feelings of anxiety and 44% reporting depression related to their AD. In addition, sufferers also report poor self-esteem, loss of energy, increased stress, and even suicidal thoughts. A recent Canadian study revealed that patients with AD were 20% more likely to die from suicide than the general population.[1]

Itch is consistently rated as the most bothersome symptom of the disease by patients. Three out of four adolescents with moderate-to-severe AD report their day-to-day life is negatively impacted by their condition, and more than half have missed school due to their AD.

The top three quality of life challenges of the disease, as reported by adolescents, are:

(1) Avoidance of social activities
(2) Inability to participate in sports and physical activities, and
(3) Interrupted sleep

For adolescents suffering with AD, living with an uncontrolled chronic disease can compound stressors already associated with the teen years. The negative impact of AD on mood, sleep, social interactions, self-esteem, and school performance can be especially difficult to manage for patients in this age group.

Patient testimonials:

"It's all-consuming and all over my body. Everything is on pause [during a flare] until it gets a little better. In order to work, I have to wrap my hands in a splint to keep the worst cuts shut. This doesn't even cover the constant embarrassment. People stare at me. People get disgusted. And people just don't understand."

"*When our child went into high school, the bullying started. The name-calling, isolation, and nasty rumors about him being "contagious" all took an immense toll. It broke our hearts. It got so bad, we decided to keep him home while we desperately searched for something to save him, to give him hope."*

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[1] Drucker AM, Thiruchelvam D, Redelmeier DA Eczema and subsequent suicide: a matched case–control study BMJ Open 2018;8:e023776. doi: 10.1136/bmjopen-2018-023776 https://bmjopen.bmj.com/content/8/11/e023776.full

"Sometimes the itch is so intense, I tear myself up in my sleep. My doctor prescribed me a sleeping pill, but I'm a single parent and need to be responsive, so taking it is not an option for me. I'm left with no other choice but to just suffer through the pain and exhaustion."

"I often shy away from social encounters due to the embarrassment of my skin, constant shedding, and sores all over my body."

"Our son is now in his teen years and he has lived like a prisoner in his own body. He's never had healthy skin since he was an infant. We use the medicated creams exactly as our doctor tells us to, and while he may get initial relief, the disease inevitably flares up again, and we are back at square one. We have one of the best dermatologists in the country and we still cannot get this relentless disease under control."

4. Experiences With Currently Available Treatments

Typical management of AD includes frequent bathing and moisturizing, trigger avoidance, and topical medications. This is currently the mainstay of therapy. For some patients, despite their best efforts for trigger avoidance, flare prevention, and adherence to topical therapy, their AD is still not well managed and current therapies are inadequate. For this group of patients there is a significant gap in effective therapies.

It is consistently reported that itch is the most bothersome symptom of AD, and topical treatments do not improve the itch. In fact, upon initial use, many patients reported that topical treatments can make the itch and pain worse, and it is common to cycle from one topical medication to another. Among patients with moderate-to-severe AD who have tried topical treatments to manage their condition, 41% have tried four to nine different topical treatments, and 29% have tried 15 or more different topical treatments.

There is a significant gap in care for patients who are not well managed on currently available therapies. For patients with recalcitrant AD that does not respond adequately to topical therapy, systemic therapy is the next step. Before dupilumab was approved, systemic therapy included phototherapy/light therapy, oral corticosteroids, and off-label systemic immunosuppressants.

Phototherapy/light therapy may be helpful for some patients, however our recent survey on systemic medications indicated phototherapy was not helpful for controlling the disease for most respondents. Access to phototherapy is also a barrier, as it is only available in city centres across Canada and travelling for treatment can be very challenging. In addition, the long-term safety of phototherapy (such as increased risk of skin cancer) is a concern for patients, as are immediate side effects such as burning of the skin and pigmentation changes.

Oral corticosteroids may work well for some patients in the short term, but many reported terrible rebound flares when they came off the drug. Further, the side effect profile of this class of medication makes it unsuitable for long-term use for a chronic condition such as AD.

Off-label immunosuppressive medications are sometimes used to provide temporary relief to patients who are desperate, as these medications cannot be used long term. These off-label therapies often come with serious side effects both in the short term (e.g. nausea) and long term (e.g. organ damage).

ESC's 2019 survey on systemic therapies revealed the following percentages of patients surveyed who had to stop the following treatments due to lack of efficacy, management difficulty, and/or side effects:

- Cyclosporine: 100%
- Systemic corticosteroids: 91%
- Methotrexate: 76%
- Phototherapy: 73%
- Dupilumab: 12%

This data highlights the unmet need for effective, long term, and safe therapies for chronic AD.

Patient testimonials:

"I was trying every cream I was prescribed, and my skin got a little better and then would flare again. I've tried the diets, I've tried light therapy, and neither worked. I felt completely hopeless."

"I tried an [off-label] oral pill with mixed results, and it caused severe immunosuppression, such that I developed infections and was forced to take months off work. The infections were very severe, often with very high fevers and many sores all over my body."

"I stopped taking methotrexate because it stopped working. I don't want to be on a drug with so many potential side effects, especially if it's not doing its job. I'm worried about how it will affect my kidneys and my liver."

"I've used topical medications my whole life and now sections of my skin are permanently damaged, and the worst part is that I still live with the eczema."

"We found out that my teen was only allowed to be on prednisone for a short time. I almost wish we never tried it; yes, it was this magic pill that helped us for a few days, but we knew it was only a matter of time until the eczema was going to come back. It gave a snippet of what life without eczema was like, only to have it taken away."

5. Improved Outcomes

Patients are seeking a treatment that will reduce or ideally eliminate the incessant itch, break the cycle of flares, and allow their skin to heal. Of patients who were interviewed, many have tried some other systemic therapy (after many years of attempting to manage with topical

therapies and lifestyle modifications) before starting dupilumab. These patients most often are lifelong sufferers who have never had good control of their AD for long periods of time.

Our recent survey of the patient experience with systemic therapies revealed that the patient desired outcomes from a therapy are improvements to:

(1) Itch
(2) Rash
(3) Open sores

Surveys and interviews conducted by ESC point to the same recurring challenge – patients are most bothered by the persistent and intense itch associated with AD.

Patient testimonials:

"What improvements would I want in a medication for eczema? I want to start my day without having to scrub crusted skin off my eyes so I can open them fully. I want to go swimming without thinking of the consequences. I want to not be stared at. I want what so many people take for granted every day. For that, I now take an injection biweekly [dupilumab] even though I'm terrified of needles. I'll even take the side effects if it means I can feel like I have some control over my day-to-day life."

"I'm black and have darker skin, and my topical treatments cause patches of discoloration which makes me self-conscious and in some ways bothers me more [than the rash]."

"The bar is set so low as to what I would want from a treatment.
I really want a treatment that actually works and eliminates my symptoms – stopping the inflammation inside me – instead of just masking the symptoms over and over again."

6. Experience with Drug Under Review

Patients interviewed who are currently taking dupilumab reported significant improvements in their disease symptoms and quality of life. This finding was confirmed by our 2019 survey data. Patients reported being able to sleep, return to work, increase their productivity and concentration at work and school, resume intimate and social relationships, and exercise. Caregivers of adolescents reported their child's mood significantly improved after taking dupilumab.

One patient interviewed by ESC indicated that while his neck and face were not fully clear of AD after taking dupilumab, the complete clearing he experienced on his limbs, hands, feet, back, and trunk – which were once covered in crusted rash – allowed him to regain his quality of life. He no longer itched incessantly or bled through his clothing, and he could get back to work and rebuild his confidence. For this patient, dealing with minor rash on his neck and face – a rash that finally did not itch – was life changing, even though the drug did not clear him completely

from his AD. This helps to illustrate that AD is a complex disease, and treatment of the disease is also complex.

Of the systemic survey respondents who have taken dupilumab, 80% agreed it has contributed to the optimal management of their AD. 75% of respondents also agreed that the benefits outweigh potential side effects.

Some patients interviewed experienced conjunctivitis, a side effect of taking dupilumab, however none of these individuals stopped therapy due to this side effect. Some found the conjunctivitis very minor. One patient reported a bout of conjunctivitis that lasted almost two months, but he indicated the tradeoff was worth it for him. For this patient, irritated eyes were manageable when compared to an entire body that was irritated and itchy.

Percentage of respondents who reported improvements in the following areas while using various systemic therapies:		
ITCH: Dupilumab 93% Systemic Corticosteroids 89% Methotrexate 82% Cyclosporine 79% Light therapy 61%	**SLEEP:** Dupilumab 85% Cyclosporine 73% Light therapy 65% Methotrexate 61% Systemic Corticosteroids 59%	**PRODUCTIVITY AT SCHOOL AND/OR WORK:** Dupilumab 77% Cyclosporine 63% Light therapy 45% Systemic Corticosteroids 45% Methotrexate 33%
**Source: Eczema Society of Canada 2019 patient survey on the use of systemic medications for atopic dermatitis.*		

Patient testimonials:

"[Dupilumab] has been the most effective form of treatment for me. The itch is non-existent neck down and I'm not used to living like that."

"This treatment did the impossible – it took the itch away. I never knew it was possible and my quality of life has changed drastically because of it. I no longer rip my skin apart and my outbreaks are gone."

***"**This treatment opened my world. I was able to find success at work and in my personal life by way of intimate relationships; things I never thought to be possible for me due to my eczema."*

7. Companion Diagnostic Test

N/A

8. Anything Else?

AD patients, including adolescents, with recalcitrant moderate-to-severe AD suffer with significant discomfort, pain, diminished quality of life with. These patients are desperate for safe and effective treatments. Dupilumab is a new treatment that has been shown to be effective in reducing signs and symptoms of AD, and most notably, improving or eliminating itch, the most bothersome symptom of AD. Based on ESC's interviews and survey feedback, dupilumab is reported as a life-altering medication.

Uncontrolled moderate-to-severe AD can be a devastating condition and there is a clinically significant unmet need for new therapies in this patient population. Equitable access to medications is critically important to us as a patient organization and to our patient community. ESC wants to ensure the true burden of this disease is understood and appreciated, and we want to demonstrate the essential need for access to new therapies for AD here in Canada.

Patient testimonials:

"I can't describe the level of hopelessness you feel when there's something out there that could help you, but the system in place won't give you access."

"If someone you loved was suffering with this disease, and there was a medication out there that could help them but it costs too much, it is inhumane to not give them access."

"I'm all for the government watching our money, but if you have chronic, recalcitrant eczema that doesn't respond to other treatments, you need to be able to try Dupixent. Yes, eczema is not technically a "deadly" disease, but I've learned there are a lot of teenagers that don't make it through. The government needs to understand that it's not just an itch, it's your whole mental health."

Appendix: Patient Group 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.

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.**

   ESC receives funding from 28 sources, including donations, funding organizations, and corporations, which include pharmaceutical companies.

   Sanofi Canada has provided funding to Eczema Society of Canada in the past two years and has in 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
Sanofi Canada				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: Amanda Creswell-Melville
Position: Executive Director
Patient Group: Eczema Society of Canada
Date: November 7th 2019