

CADTH COMMON DRUG REVIEW

Patient Input

DUPIBUMAB (DUPIXENT)

Sanofi-Genzyme

Indication: For the treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT™ can be used with or without topical corticosteroids.

CADTH received patient input for this review from:

Eczema Society of Canada

October 4, 2017

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Patient Group	Eczema Society of Canada
Name of the drug CADTH is reviewing and indication(s)	Dupilumab / Dupixent
Name of the patient group	Eczema Society of Canada
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1. Submitting Organization

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 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 health care providers.

2. Conflict of Interest Declarations

We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:

- a) Eczema Society of Canada (ESC) receives funding from private citizen donations, funds and foundations (including Canada Helps, Fed Ex Cares Employee Community Fund, Fondation Pierre Fabre, United Way) and corporate sponsors including Actelion Pharmaceuticals Ltd, Astellas Pharma Canada, Beiersdorf Canada, Blistex Inc, Galderma Canada, Glaxo SmithKline Canada, Johnson & Johnson Inc, L'Oreal Canada Inc, Paladin Labs Inc, PEDIAPHARM Inc, Pierre Fabre Dermo-Cosmétique Canada Inc, Sanofi Canada, Sanofi Genzyme Canada, Shoppers Drug Mart Inc, Skinfix Inc, Unilever Inc, Valeant Canada, Wellspring Pharmaceuticals.
- b) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission: No conflicts to declare.

3. Condition and Current Therapy Information

The information provided in this submission was collected through an online survey. In total, 377 Canadian adults with atopic dermatitis (AD) and their caregivers responded to the online survey. As well, a number of one-on-one interviews took place with individuals across Canada. Of our total respondents, 88% suffer with moderate or severe AD. The focus of the survey and interview questions was moderate and severe AD, the AD severity for which Dupilumab is indicated.

For the purpose of the survey and discussion herein, AD severity was defined as:

- **Moderate AD:** areas of dry skin, frequent itching, redness, with or without broken or localised skin thickening.
- **Severe AD:** widespread areas of dry skin, incessant itching, redness with or without broken skin, extensive skin thickening, bleeding, oozing, and cracking.

Impact of Condition on Patients

Atopic dermatitis (AD), commonly known as eczema, is an inflammatory skin condition characterized by intense itching which manifests with a red, raised rash that can ooze, crust and bleed. Patients may experience mild eczema, with fewer lesions, and the spectrum continues to severe, recalcitrant AD where patients could have entire body involvement. Patients report that this intense itch can persist all day, and often worsens at night, affecting sleep. Living with chronic itch, pain and chronic cycles of flares (acute worsening of the disease) takes a significant toll on quality of life.

Of those who responded to the survey, 87% stated that AD negatively affects their day-to-day life. Among these individuals:

- 79% suffer from interrupted and/or loss of sleep due to their AD, and of those individuals, 50% reported that sleep is impacted 8 or more nights per month, and 29% reported that 14 or more nights per month were impacted.
- 64% live with anxiety related to their AD.
- 44% experience depression related to their AD.
- 48% avoid social activities.
- 40% avoid intimacy.
- 47% avoid exercise and physical activity.
- 32% miss work and/or important life events.
- 30% had to change their career or give up certain activities.
- Most respondents reported additional negative impacts of AD on their quality of life including poor self-esteem, loss of energy, increased stress, and suicidal thoughts.

“The worst part of eczema is itch and then sleep. I itch all day long and night long and can’t sleep. I wake up in the night due to scratching. It’s a terrible cycle of itching, scratching, and eczema flare ups.”

– Adult living with severe AD

“Atopic eczema [atopic dermatitis] is completely physically and emotionally draining. The itch is always there and is sometimes so intense that you just can’t live with it anymore.”

– Adult living with severe AD

My AD [atopic dermatitis] has been a never ending battle all my life. Sometimes I feel it is a losing battle”

– Adult living with severe AD

Every aspect of my life is limited due to my eczema. I itch all day, I’m always tired, I can’t exercise, and I can’t do many activities because of the way my skin feels AND looks.”

– Adult living with severe AD

“Sometimes I wake in the night because the itch and pain is so intense.”

– Adult living with severe AD

“My eczema impacts my mental health too – I experience depression and terrible anxiety because of the flare ups. The flares are so unpredictable and I have anxiety about waking up in the morning with my face covered in eczema, or leeding skin because I ripped it apart scratching in the night”

– Adult living with severe AD

Patients’ Experiences with Current Therapy

91% of respondents report that their atopic dermatitis (AD) is not well-controlled. 41% of respondents report that they have treatment needs not being met by existing therapies, and 25% of respondents report that they have lived 10 years or more without adequate treatment.

“I have lived with atopic dermatitis since childhood and I’ve tried every treatment you can imagine. Nothing works my eczema, including Prednisone. My doctor said it will destroy my health if I keep using it, but nothing else works.”

– Adult living with severe AD

“The creams and ointments all help in the short term, but the eczema comes right back. When I apply the medicines, the stinging and burning from the medicine, and the itch the creams cause, are almost worse than the eczema itself.”

– Adult living with severe AD

98% of respondents have used topical corticosteroids, and 51% of respondents have used topical calcineurin inhibitors to treat their AD. Among those with AD who have tried topical treatments, 41% have tried four to nine different topical treatments, and 29% have tried 15 or more topical treatments to manage their AD.

Overall, the moderate to severe patients who responded said they have tried the following AD treatments, when given the option to choose all that apply:

Treatment Type	% Tried
Topical corticosteroids (e.g. hydrocortisone, betamethasone, clobetasol)	98%
Topical calcineurin inhibitors (e.g. tacrolimus/Protopic, pimecrolimus/Elidel)	51%
Bathing and moisturizing techniques	89%
Oral antihistamines (e.g. Benadryl, Atarax)	69%
Light therapy (Phototherapy)	30%

When discussing how their AD is managed by these medications, patients indicated the following:

- Of those who have used topical corticosteroids, 39% said that these medications either offered inadequate control or poor control.
- 36% of those who have tried topical corticosteroids reported experiencing adverse effects.
- Of those who have used topical calcineurin inhibitors, 46% said that these medications either offered inadequate control or poor control.
- 14% of those who have tried topical calcineurin inhibitors reported experiencing adverse effects.

When asked to choose all that apply when thinking about their overall experience with eczema treatments, respondents noted:

Overall Experience with treatments Feedback:	% Chosen
It's uncomfortable	49%
It's difficult to dress after applying treatments	52%
It's physically painful to apply the treatments	32%
It's difficult to find time during the day to apply the medications	44%
It's difficult to adhere to topical treatment plan	38%
Topical medications interfere with my work and/or day-to-day life	38%
It is an effective way to manage my eczema	37%

63% of respondents who have tried off-label systemic therapies report that they did not work well to manage their atopic dermatitis.

For patients with recalcitrant AD, off-label systemic therapies are sometimes used. AD is a chronic condition requiring lifelong therapy. However, these systemic therapies are not suitable for long-term use.

- Most patients (69%) who responded to the survey had not tried phototherapy (light therapy) as phototherapy is not widely available across Canada. Even patients in major centres such as Vancouver and Toronto have limited access. The long-term safety of phototherapy, including cancer risks, has not been established.
- Among respondents who had tried phototherapy, 90% reported that phototherapy did not work well to manage their atopic dermatitis.
- 94% of respondents who tried phototherapy reported experiencing adverse effects.
- When asked about systemic agents, 73% had not tried them, and 11% said that systemic agents were not recommended to them.
- Of those who have tried systemic agents, 63% said that these medications offered inadequate or poor control of their AD.
- Systemic corticosteroids, such as Prednisone, cannot be used long term, and therefore are not suitable for the long-term management of a chronic condition.
- Off-label systemic agents are not studied in the treatment of AD and carry significant risk of side effects.
- Among those who have tried systemic agents, 50% reported experiencing adverse effects.

When asked to think about their *overall treatment* program for AD, 32% of respondents noted that they have had difficulty obtaining the treatments they have used to manage their AD. In particular, several respondents noted that phototherapy was not available in their community, while some said they cannot travel to access phototherapy. Some respondents noted that their personal and/or employer benefits plans did not reimburse topical corticosteroids, topical calcineurin inhibitors, phototherapy or systemic agents, while others indicated their provincial public drug plan did not reimburse for some of the medicines they need.

41% of patients with AD said they have treatment needs that are not being met by current therapies.

“I’ve had eczema since I was a child – so for more than four decades I’ve tried creams, and lotions and anything to make my skin feel better. The eczema always comes back – no matter what medicated cream I use – and it seems to come back more red and angrier each time.”

– Adult living with moderate AD

"I'm throwing my money away with all these medications that don't work."

– Adult living with severe AD

"My skin feels so thick and so dry that I don't think the medicines work anymore. There is no cream that can help this skin."

– Adult living with severe AD

Impact on Caregivers

In interviews, caregivers reported feelings of helplessness and frustration while the patient is suffering with a condition that cannot be controlled and continues to flare. Caregivers surveyed were asked about the impact AD treatments have on their daily routine or lifestyle, and the survey indicated they also experience sleep loss, along with anxiety and depression.

4. Information about the Drug Being Reviewed

The information provided in this section was obtained through one-on-one interviews and written questionnaires.

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

Atopic dermatitis patients in Canada expect to have access to innovative medicines that address gaps in the current treatment options, namely medications that will address moderate-to-severe atopic dermatitis and the associated symptoms of itch and rash. While currently therapies are able to treat inflammation and rash with varying success, patients are seeking a treatment that will break the cycle of flares and manage the itch.

"The flare-ups cause my skin to crack and split, which causes terrible pain. I would like a drug that would address the itching and the rashes of the eczema. I think if we could get rid of the itch the eczema would not flare."

– Adult living with severe AD

"What would I want from new treatments? I would want it to work! It would need to actually take away or reduce the itch and allow my skin to heal."

– Adult living with severe AD

"I have suffered my entire life with eczema. I bleed through my clothes and find blood on my bed sheets after a night of itching. I would love any treatment that can improve my eczema and actually reduce the flares. It's a constant battle of putting out first."

– Adult living with severe AD

Patients also ranked the top quality of life improvements they hope new therapies will bring them; these are presented in order of importance:

1. Fewer interruptions of sleep/episodes of loss of sleep.
2. Reduction in anxiety/fewer episodes of anxiety.
3. Improved ability and/or willingness to participate in social events.
4. Improved ability to maintain career/participate in certain activities.
5. Reduction in depression/fewer depressive episodes.
6. Improved ability/willingness to exercise and participate in physical activities.
7. Improved attendance at work/important life events.
8. Improved ability/willingness to be intimate with someone.

Based on patients' experiences with the new drug as part of a clinical trial ESC has learned that Dupilumab is a life-altering medication and the first medication to dramatically reduce or eliminate flare-ups, and most significantly, reduce or eliminate itch, which is the hallmark of this disease.

"Dupilumab has had a tremendously positive impact on my condition and my life, but the most significant change has been to my sleep. I get 7 to 8 hours of sleep every night. Before starting Dupilumab, I never had a good night's sleep for as long as I can remember – maybe never."

- Participant in the Canadian Dupilumab trial

"The most significant change from this drug to the other treatments I have tried, is that it worked, but also it seems like a cure – the eczema is gone. The itch is gone."

- Participant in the Canadian Dupilumab trial

"It [Dupixent] has been the only medicine that I've used that works to control my AD with currently no side effects. I would say that my mood and ability to handle life generally improved by several orders of magnitude. I wasn't itching every day, and worried about itching and flaking skin on my face, neck and body."

- Participant in the Canadian Dupilumab trial

In terms of the drug's effectiveness in symptom management, participants in the Canadian Dupilumab trial reported:

"Skin outbreaks are gone and the itching is significantly reduced. This drug is the first treatment to actually manage the disease, and it actually feels like this drug prevents the flares from occurring. I no longer rip apart my skin from itching and inflammation."

"I want to reiterate that there has been no real therapy or drug that manages severe AD presently available. This is the first drug in my entire life that I have used that actually manages and makes the AD almost a non-issue..."

"Over the last 3 to 4 years on the Dupilumab drug trial, my severe eczema was under control for the first time in my life; I was able to work productively, focus on building my business, and enjoy the outdoors with my family and friends."

When asked what this drug does less effectively than current therapies available, a Dupilumab trial participant responded:

"NOTHING! It 1000% manages my eczema better than anything else!"

When asked about adverse effects reported, Dupilumab trial participants reported:

"It was my understanding that the drug has minimal side effects and I've not experienced any."

"I have experienced no adverse effects and I've been on the drug for almost three years."

When asked if the drug was easier to use than other treatments, Dupilumab trial participants reported:

"The once-weekly injection of Dupilumab is much less frequent than other treatments for eczema, and this is much more convenient as I don't need to be constantly applying topical creams and ointments. It's just a small needle. It impacts my quality of life positively in that I no longer need to be constantly laundering clothes and bed sheets from the transfer of creams and ointments."

Feedback was positive on how the drug is expected to change patients' long-term health and well-being:

"My life now has a higher potential for enjoyment and happiness now that my condition is under control. There was a period of time where I didn't want to have kids because I was worried I would pass this condition on to my child. Now I feel better that there is hope that even if my child did have eczema, they could get treatment."

“The drug is life-changing. I used to have an invisible ceiling hanging over my life that is no longer there. I don’t want other people to have to suffer the way I have suffered.”

5. Additional Information

Patients who were part of the Dupilumab trial have indicated that they drug is the first treatment in their lives to actually manage the disease and take away the itch, however these patients are now struggling as the trial is over and their AD is returning. Patients tell us:

“The trials are now finished and I have had no access to Dupilumab since then. I am very worried about what will happen to my condition when I can longer get this drug.”

- Participant in the Canadian Dupilumab trial

“Now [that the trial is over], I am experiencing a severe eczema outbreak because I no longer have access to Dupilumab. Currently, I am suffering from a severe eczema outbreak over the majority of my body. It is painful and uncomfortable due to extreme itch and oozing, and it's mentally draining. I have spent the last 3 weeks confined to my bed and apartment. It is difficult to maintain a positive mental attitude, and am trying to understand how to move forward with life and work due to a lack of effective treatments for severe eczema.”

- Participant in the Canadian Dupilumab trial

Dupilumab is the only targeted therapy available to patients with moderate-to-severe AD. These patients interviewed have been suffering with this chronic condition and constant relapses and flares – the treatment for which is as tiring, painful, and frustrating as the disease itself. AD patients have been waiting for an effective treatment for a long time, with much discomfort, and significantly diminished quality of life. Based on patients’ experiences involved in the clinical trial, we have learned that Dupilumab is a life-altering medication. It should be publicly available for Canadian patients for whom it is indicated. Once available, it will significantly improve the quality of life for the patients living with recalcitrant moderate-to- severe AD.