CADTH

CADTH COMMON DRUG REVIEW

Patient Input

CRISABOROLE (Eucrisa)

(Pfizer Canada Inc.)
Indication: atopic dermatitis

CADTH received patient input from:

Canadian Skin Patient Alliance

Eczema Society of Canada

June 15, 2018

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**TBC (crisaborole) for 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	[redacted]

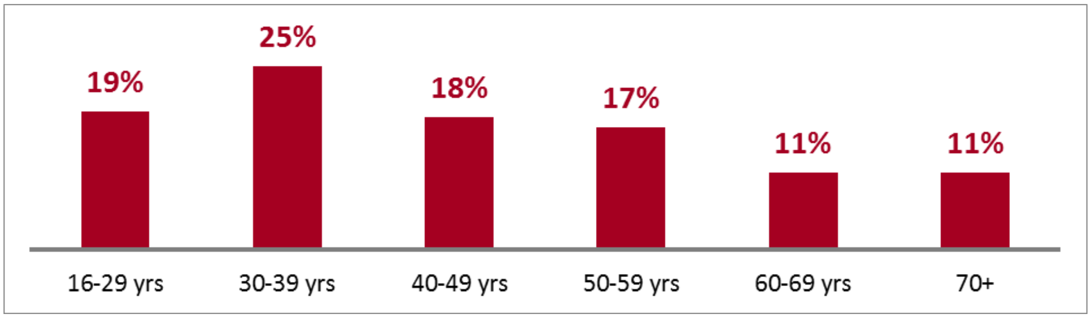
1. About Your Patient Group

The Canadian Skin Patient Alliance is a registered patient group with CADTH: http://www.canadianskin.ca/en/.

2. Information Gathering

The data gathered for this particular patient submission was from two separate surveys:

-The CSPA led the first survey which took place in November 2017 and was completed by 194 individuals living in Canada – 132 patients living with atopic dermatitis and 62 from caregivers of children living with atopic dermatitis. Of the 132 eligible respondents, 78% were female, and the average age was 42 years with a range of 18 to 92 years.



The purpose of this survey was to better understand how individuals with atopic dermatitis and those who act as their caregivers are affected by this condition. To read the full survey report "The Skin I'm In: A National Report on the Patient and Caregiver Experience with Atopic Dermatitis" see: www.canadianskin.ca/adreport.

-The second survey took place from Monday April 30th to Sunday May 13th and was distributed through the National Eczema Association (NEA) in the U.S. The purpose of this second survey was targeted to better understand the patient experience with crisaborole. And given that there were no clinical trials for this treatment in Canada, we reached out to partner with the NEA. This was very successful with 28 individuals completing the survey; 9 of the 28 respondents reporting that they took part in a clinical trial for crisaborole, known as Eucrisa in the US. And in total, 25 of the 28 had experience with Eucrisa since it was approved for use in the U.S. (includes those who were on the clinical trial), two of whom identified themselves as caregivers of children with atopic dermatitis.

3. Disease Experience

"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."

This quotation from a patient living with atopic dermatitis is very telling. Atopic dermatitis (AD) is a chronic, inflammatory skin condition, affecting up to 20% of adults and 9% of children in Canada. Mild AD is characterized by itchy skin while those with moderate to severe AD experience thickened skin, and lesions that ooze and bleed during flare-ups.

The impact of AD varies considerably depending on severity. According to the CSPA survey results, those with mild AD reported minor impact overall, and 28% are not currently using medicated treatment. However, those with moderate/severe AD reported an average of 2.3 nights of interrupted sleep monthly; 48% reported a poor effect on their work/school life; and 68% reported a negative impact on their personal life. Caregivers are also impacted; 68% indicated that AD negatively affects their lives.

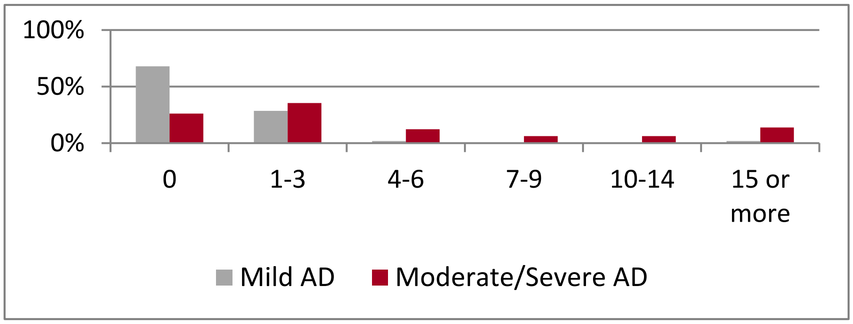
AD appears to be closely associated with other comorbidities with over half of respondents suffering from seasonal allergies, and one-third from food allergies. This condition also renders respondents more susceptible to certain complications: 38% reported a past episode of oozing lesions due to a Staphylococcus aureus infection.

Sleep is noted as a significant impact of living with AD. From the CSPA study:

- 32% of those with mild AD lose one or more days of sleep every month
- 74% of those with moderate/severe AD lose at least one night of sleep monthly due to symptoms, while 20% lose 10 or more days a month.

"It's just awful. It goes into remission for weeks and then comes back with a full of vengeance. I wake up at about 2 and 3 every morning have to shower because my skin is literally on fire and itches so badly."

#of Nights of Sleep Affected per Month



"I am always within a week of a new outbreak. Sometimes the itching is so intense that I experience sleep deprivation for weeks on end."

AD also impacts various aspects of a person’s life, manifesting in ways that can be detrimental to daily living. Of those with mild AD, the most common effects are anxiety (20%), negative effect on ability to be intimate with a partner (16%), and depression and fatigue (14% each). For those with moderate/severe AD, sleep deprivation is the most prevalent effect (46%), followed by anxiety (45%) and depression (37%) (from CSPA survey data.)

“I've had this since puberty, it's primarily on my hands. I love to create artwork and it inhibits me from doing this for months at a time. It can get depressing.”

“I am very sensitive to artificial fragrances (perfumes, candles, air fresheners) and can only use products with no scents. I had to leave high school because of my sensitivity and attend school online.”

This is what we heard from other individual patients about their experiences and impact of living with atopic dermatitis:

“Makes it hard for everyday life and getting jobs that won’t bother my hands. I get dry itchy skin, little blisters that oozes, pilling, redness.”

“Sometimes daily tasks are hard to complete from pain.”

“I have had continuous flare ups over the course of 7 years. From head to toe. Red, weeping, sores, burning, lots of pain. It has contributed to my depression heavily and made working and living very hard.”

“I am the caregiver for the children with AD and their care has a regular impact on our family life and often feels overwhelming.”

All patients stated that the most important aspects of the illness that are more important to control is the itch, pain, dryness and redness of atopic dermatitis.

“My son just wants to have normal skin!”

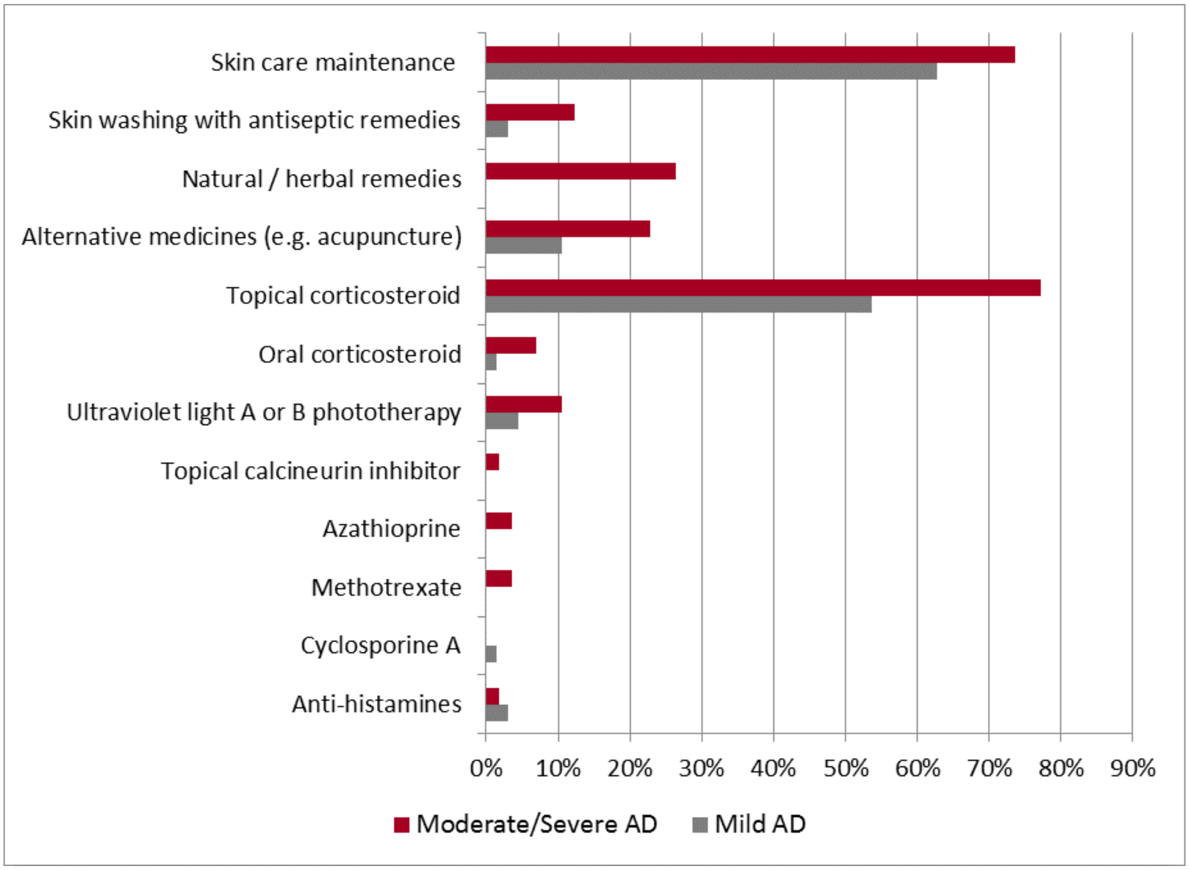
4. Experiences With Currently Available Treatments

The majority of respondents (78%) in the CSPA survey reported trying multiple treatments before finding some relief.

- For those with mild AD, the most common number of treatments tried was 2
- 23% of those with moderate/severe AD have tried more than 10 treatments
- 44% of those with moderate/severe AD have tried 5 or more treatments

Respondents are currently using various non-medicated methods of controlling and preventing symptoms including skin care maintenance such as specific bathing routines and moisturizer application, natural and herbal remedies and acupuncture. For medicated treatments, topical corticosteroids are most commonly used by both those with mild and moderate/severe AD.

Chart of Current Medication Use (CSPA Study):



In terms of effectiveness, topical corticosteroids offered the greatest effectiveness with more than 40% of respondents reporting significant improvement in symptoms. But it is not a cure and flares do return.

"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."

In terms of side effects, for those with mild AD, more than half of the CSPA survey respondents experienced skin thinning from a medication, while spider veins and blistering were the next most common effects. For those with moderate/severe AD, spider veins was most common (47%), followed by thinning of the skin and headaches.

In this same survey, we asked respondents about their monthly out-of-pocket costs per AD treatments and therapies. There was a large variation in expenses including medications, other symptom treatments, preventative measures. Some patients reported that the substantial cost of a medication precluded them from being able to begin a course of treatment whereas others reported that they have previously stopped using a treatment due to cost.

5. Improved Outcomes

AD patients are looking for the same outcomes in new therapies. They want to live without the pain and itch of the disease, so that they can resume living a "normal" life that is not complicated by this disease.

And given the concerns (as stated above) of the effects of corticosteroids on their skin, they are looking for steroid-free options that will clear their skin. This is what we heard directly from patients:

“I expect my treatments to keep flare ups from getting out of control and to allow me to live a normal life.”

“I just want something to give me relief from the chronic itch and burn.”

“A medication that will completely clear the flares allowing full use of hands.”

“I hope that one day, we can have a solution so people with atopic dermatitis don't have to live in constant pain.”

From a caregiver and family perspective, there are many impacts on daily live and the quality of life for everyone close to an AD patient.

“I am the caregiver for the children with AD and their care has a regular impact on our family life and often feels overwhelming.”

“My daughter’s sleep is greatly affected due to constant itching. When she does not sleep, none of us sleep.”

There are also impacts on the social/personal life for these patients, particular young ones:

“My young son was diagnosed 1.5 years ago. Severe eczema. Started on back of his leg then spread over time. Required hospitalization at one point for infection.”

“Two of my sons have severe atopic dermatitis. For one of them it has delayed his fine and gross motor skills, interferes with their sleep, prevents them from participating in certain activities.”

“My child suffers embarrassment and self-consciousness due to her eczema. She wants to shave her legs as her hair is very dark, but shaving irritates and flares her eczema, so she wears pants to cover her legs.”

If new treatments helped to manage the disease, these issues would not be as significant and their quality of life would be improved.

6. Experience With Drug Under Review

As mentioned in the section two, nine of the 28 respondents accessed the medication via a clinical trial, whereas the other 16 were given samples at a health care facility or prescribed the medication by their physician in the U.S. All respondents stated that this drug was the same to use as other treatments they had tried. Given that it is a topical treatment, the ease of use is on par with other topical treatments.

For side effects, the most significant was a burning sensation on application. 83% of the respondents who had experience with crisaborole experienced pain, burning or stinging where the medication was applied.

“Eucrisa hurts and stings the worst. It is my least favorite medication despite the benefits of being to use it anywhere.”

“Didn’t help at all and only caused burning pain when applied.”

Yet many patients stated that they were willing to put up with the discomfort, given how well it worked for those individuals:

“Eucrisa has made a positive difference for me personally.”

“Recently our allergist gave us samples of Eucrisa. I was surprised at how quickly the cream started to clear the eczema. I believe it went away in about half the time as it will typically take a prescription corticosteroid cream.”

“My daughter has been using eucrisa for a few months and it’s keeping her symptoms manageable. It’s not making it go away but it’s the best her skin has looked in a long time.”

Others felt that it made no difference to their AD:

“It worked for a short time, and then did nothing. It didn’t ever reduce the itch.”

The downside to this drug is the cost of it in the U.S. It will be interesting to see if this is an issue once introduced in Canada.

“Eucrisa has been a godsend…but completely unaffordable.”

“I was given eucrisa to try from a coworker on a bad flare up and I couldn’t believe how fast it worked and helped !! I went to my dermatologist the following week and got A script for myself I love it! My only complaint is how expensive!”

7. Companion Diagnostic Test

Not applicable to this submission

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

1. Eczema is so misunderstood. Doctors and pharmaceuticals don't understand how to treat which is very frustrating for patients.

2. Adherence to topical treatments is a challenge, particularly for children. In patient focus groups held with Leo Pharma in 2016, we heard that patients most typically use topical treatments for management of flares, rather than for a predetermined length of time. The reasons given were costs, damage to clothing as well as the time it takes:

   “I should pay more attention to it when it’s not flaring up. But for me it’s more when it’s flaring up that I think about it and put the cream on. When it’s not there I don’t need to think about it too much.”

3. New treatments are needed for patients who are suffering and for whom current therapies are inadequate. It has been years since there has been any new options for patients living with AD so we are pleased to see new options for these patients.

4. It is not “just a rash.” Skin diseases are the most misunderstood. We get calls from patients saying “I wish it was a cancer diagnosis as people who take it more seriously.” In our Patient Charter of rights, we state that skin patients have the right to be acknowledged of living with a serious illness as a result of their diagnosis which can be just as significant to them as other diseases are to other patients.

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.

   Other than the help from the National Eczema Association in the US to distribute the survey (as detailed in second two, we did not receive any outside help to complete this submission.

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.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Pfizer			X	
Novartis			X	
Janssen		X		
Galderma		X		
Abbvie			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: Kathryn Andrews-Clay
Position: Executive Director
Patient Group: Canadian Skin Patient Alliance
Date: June 8, 2018

Patient Group Input Template for CADTH CDR

Name of the Drug and Indication	**Crisaborole – Mild to Moderate Atopic Dermatitis**
Name of the Patient Group	**Eczema Society of Canada**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted] [redacted]
Email	[redacted]
Telephone Number	[redacted]

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 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. For more information, please visit www.eczemahelp.ca.

2. Information Gathering

Recently ESC set out to better understand the burden of disease of Canadians living with atopic dermatitis (AD), and the existing barriers to better care.

ESC conducted online surveys of Canadians living with AD and had a total of 1,035 respondents from all provinces across Canada. Of those respondents, 377 were adults living with AD and their caregivers, and 658 were children living with AD and their caregivers. Mild or moderate AD is often thought of dismissively as simply dry, itchy skin; however, even mild disease can have significant impact on sufferers. The adult survey gathered data from 137 adults who live with moderate AD, and the children's survey gathered data on 384 children who live with mild or moderate AD.

3. Disease Experience

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. Eczema Society of Canada defines mild eczema as areas of dry skin, infrequent itching, with or without small areas of redness, and defines moderate eczema as areas of dry skin, frequent itching, and redness, with or without broken skin or localised skin thickening.

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 the adults living with moderate AD who responded to the survey, 82 per cent reported that their day-to-day life is negatively impacted by their AD. Among those individuals:

- 73% suffer from interrupted and/or loss of sleep due to their AD, and of those individuals, 38% reported that sleep is impacted 8 or more nights per month.
- 61% live with anxiety related to their AD
- 32% experience depression related to their AD
- 40% avoid social activities
- 33% avoid exercise and physical activity
- 26% avoid intimacy
- 26% miss work and/or important life events
- 23% have had to change their career or give up certain activities

Of the responses pertaining to children who live with mild or moderate AD, one in four experience sleep loss 8 night per month due to their AD. In addition:

- 24% miss school ten (10) days or more each year due to their AD
- 21% of children report anxiety related to their condition
- 16% experience difficulty participating in sports or physical activities
- 7% are bullied and/or picked on by peers
- 4% experience depression due to their AD

It was also reported that 44% of parents/caregivers report sleep loss due to their child's AD, and 27% experience anxiety specifically related to their child's disease.

4. Experiences With Currently Available Treatments

87% of adult respondents living with moderate AD report their disease is not well-controlled. Additionally, nearly three quarters (74%) of respondents have been suffering for more than a year without adequate treatment, and a third (33%) report that they have lived six years or longer without adequate treatment. Sadly, nearly one in four (24%) report having lived a decade or longer without adequate treatment.

AD sufferers also cycle through many different medications. Four out of five (80%) report having used four or more different treatments to manage their AD, 31% having used 10 or more, and 22% having used 15 or more different treatments to manage their condition.

Overall, the moderate adult 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)	44%
Bathing and moisturizing techniques	86%
Oral antihistamines (e.g. Benadryl, Atarax)	57%
Light therapy (Phototherapy)	24%

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	48%
It's difficult to dress after applying treatments	47%
It's physically painful to apply the treatments	22%

Current therapies are also inadequate for many children living with mild or moderate AD, with 65% of respondents reporting their child has tried four or more different therapies to manage the condition, and only 29% report that their child's AD is well controlled.

Adherence to therapy is also a challenge with 67% of caregivers reporting that they experience difficulty following or adhering to their child's AD treatment plan. Medication safety is also a primary concern for caregivers of children with AD.

5. Improved Outcomes

The primary desired outcome is better control of the disease, as patients report that with current therapies, while they may achieve some temporary relief, there is still a constant cycling on and off of medications as their disease flares. In addition to better disease control, patients are also seeking relief from itch and would like therapies that are simple to adopt into their lifestyle and care routines.

6. Experience With Drug Under Review

The drug under review was not part of Canadian clinical trials so ESC does not have any input from Canadian patients who have had access to this drug.

7. Companion Diagnostic Test

N/A

8. Biosimilar

N/A

9. Anything Else?

AD patients in Canada have been suffering with significant discomfort, and diminished quality of life, even for patients with mild disease. AD is a chronic condition that is marked by recurrent flares – the available treatments for which can be inadequate for some patients. AD patients in Canada expect to have access to innovative medicines that address gaps in the current treatment options.

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Company	Check Appropriate Dollar Range			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In Excess of $50,000
FUNDING ORGANIZATIONS/GRANT PROGRAMS				
Private Citizen Donations		x		
Canada Helps	x			
Fed Ex Cares Employee Community Fund	x			
IBM Canada	x			
CORPORATE SPONSORS				
Actelion Pharmaceuticals Ltd				x
Beiersdorf Canada			x	
Bioderma Canada		x		
Blistex Inc			x	
Familiprix Canada			x	
Galderma Canada			x	
Glaxo SmithKline Canada				x
Johnson & Johnson Inc				x
Leo Pharma Canada			x	

L'Oreal Canada Inc			x	
Paladin Labs Inc				x
Pierre Fabre Dermo-Cosmétique Canada Inc				x
Pfizer Global		x		
Pfizer Canada				x
Sanofi Consumer Canada			x	
Sanofi Genzyme Canada				x
Unilever Inc				x
Valeant Canada			x	
Wellspring Pharmaceuticals			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: June 6th 2018