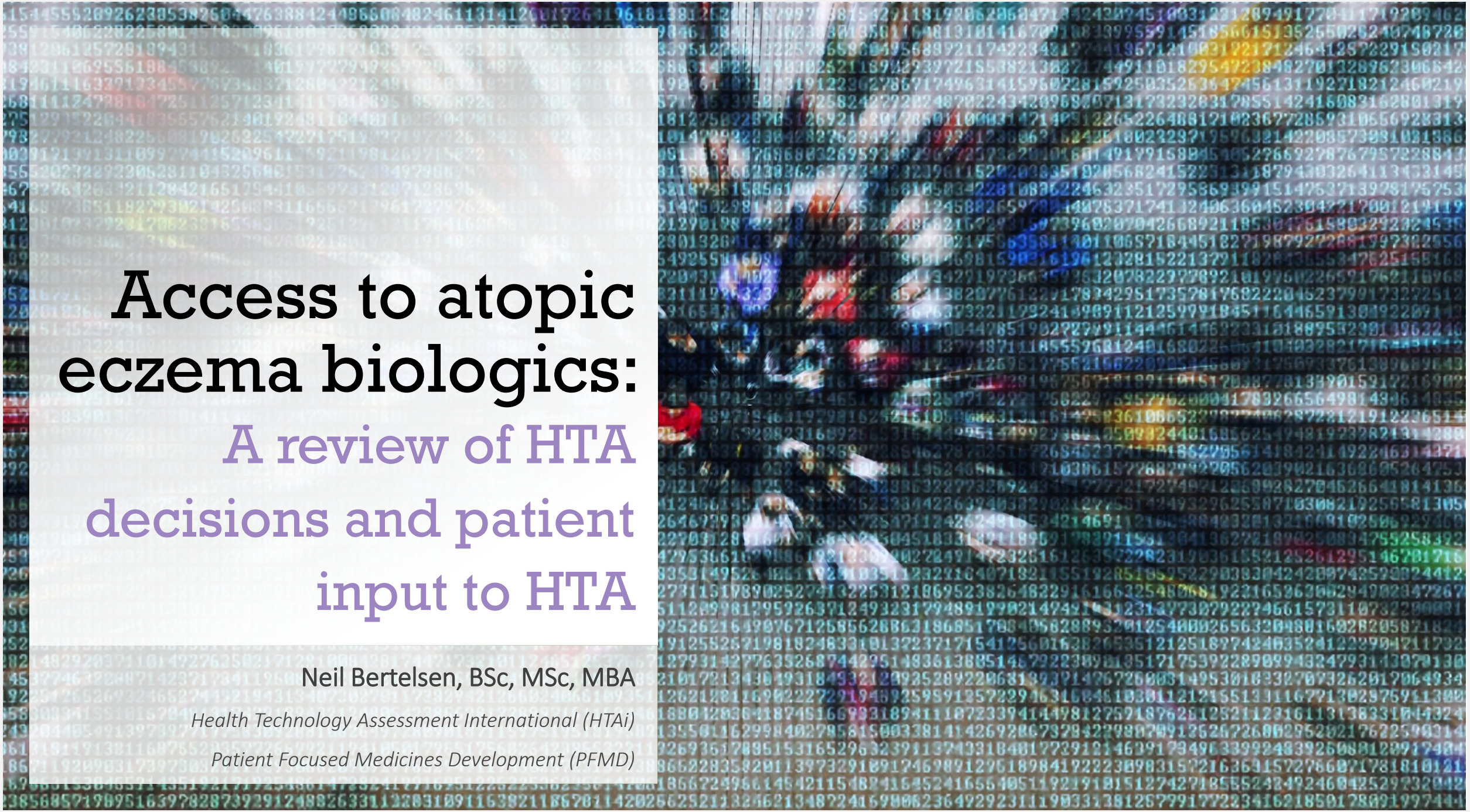


# Access to atopic eczema biologics:

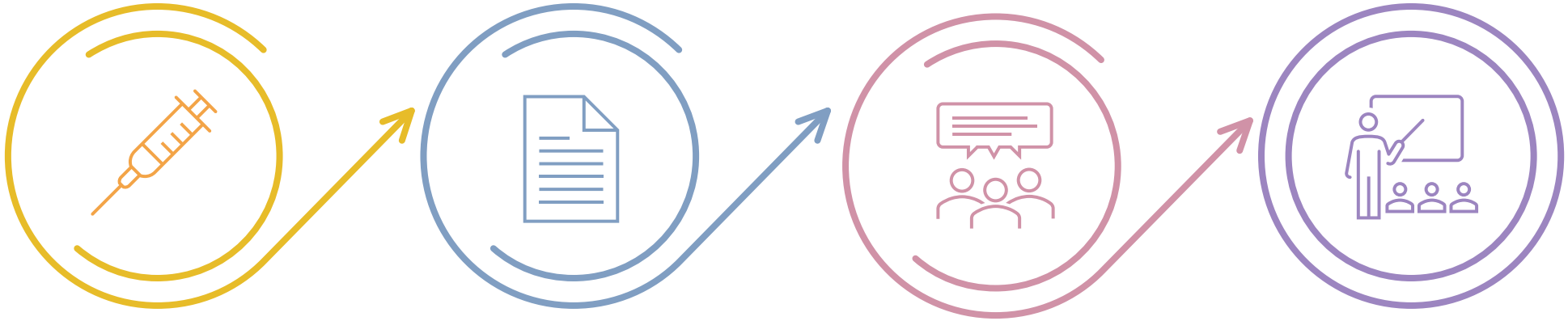
## A review of HTA decisions and patient input to HTA

Neil Bertelsen, BSc, MSc, MBA

*Health Technology Assessment International (HTAi)*

*Patient Focused Medicines Development (PFMD)*

# Methodology



Focus on one biologic and indication for a consistent analysis

Identify HTA reports in the public domain to analyse

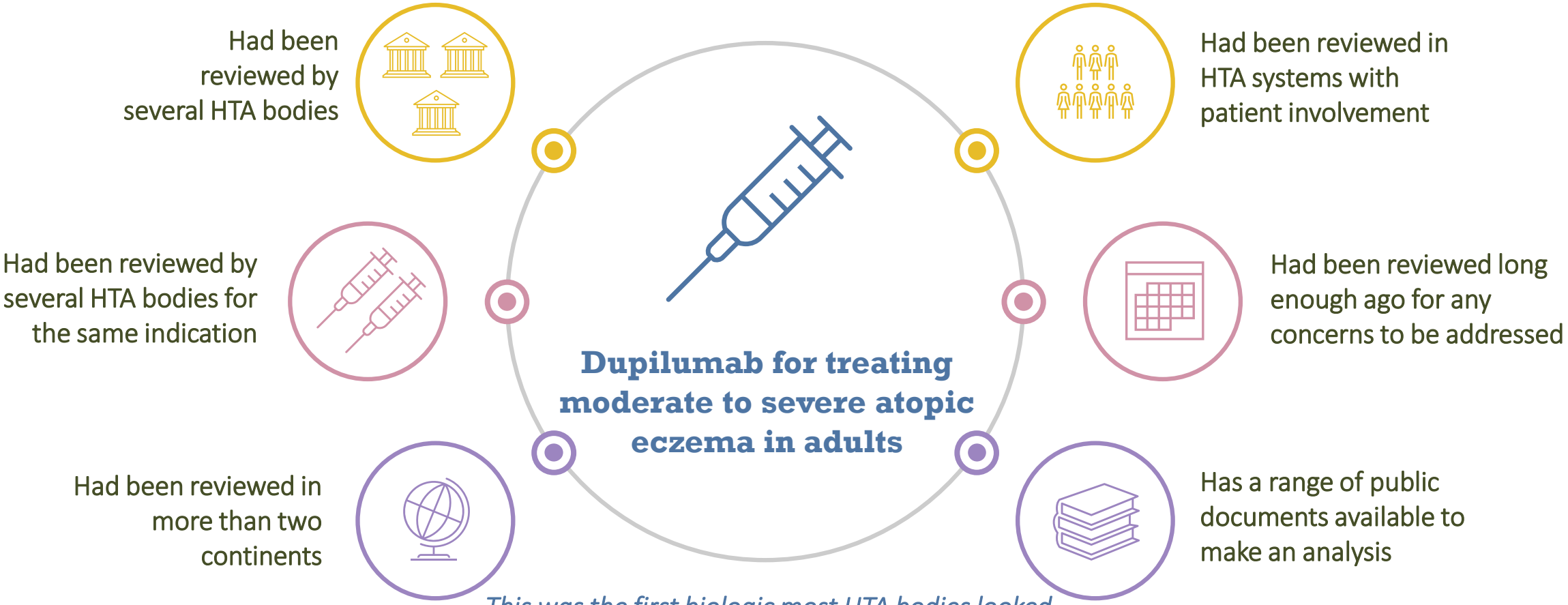
Review concerns from HTA bodies and patient input to address concerns

Identify key learnings for the patient advocate community in future HTA processes

# The biologic and indication

Selection process of potential biologics to focus this review process

# To review HTA reports, a biologic was selected that had the following attributes




*This was the first biologic most HTA bodies looked at and has the most public documentation*

# HTA Reports

Which HTA bodies' reports were used in this analysis?

# HTA reports from initial submissions in 2017/18 (1)

| | | Why was this chosen? |
|---|---|---|
| NICE (England) | Aug 2018: Dupilumab recommended with restrictions for adults with moderate to severe atopic eczema[1] | • Initial rejection which was later overturned<br>• Lots of input from the patient advocate community<br>• The innovation of biologics recognized |
| CADTH (Canada) | July 2018: Dupilumab was not recommended for reimbursement[2] (note in 2020 this was overturned[3]) | • Not recommended for reimbursement<br>• This was despite patient input<br>• A later review reversed this decision |
| PBAC (Australia) | July 2018: Dupilumab was rejected (and again in 2019), but was finally approved for reimbursement in 2020[4] | • Original submission and resubmission were both rejected for reimbursement<br>• A refocused submission with restrictions approved |



1: https://www.nice.org.uk/guidance/ta534/documents/committee-papers-2
2: https://www.cadth.ca/sites/default/files/cdr/complete/SR0533_cdr_complete_Dupixent_July_9_2018.pdf
3: https://www.cadth.ca/sites/default/files/cdr/complete/SR0636%20Dupixent%20-%20CDEC%20Final%20%20Recommendation%20April%2024%2C%202020%20for%20posting.pdf
4: https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2020-03/files/dupilimumab-psd-march-2020.docx

# Summary of key lessons (1)

*See detailed summaries of each HTA after this section*


**Patient population** for reimbursement is a critical driver

In all six HTA assessments analyzed, a key driver of the decision was the definition of the patient population and therefore the potential numbers to be treated. This led to the therapy being available but for a restricted group of patients

**Patient impacts** were clearly defined by patient group input

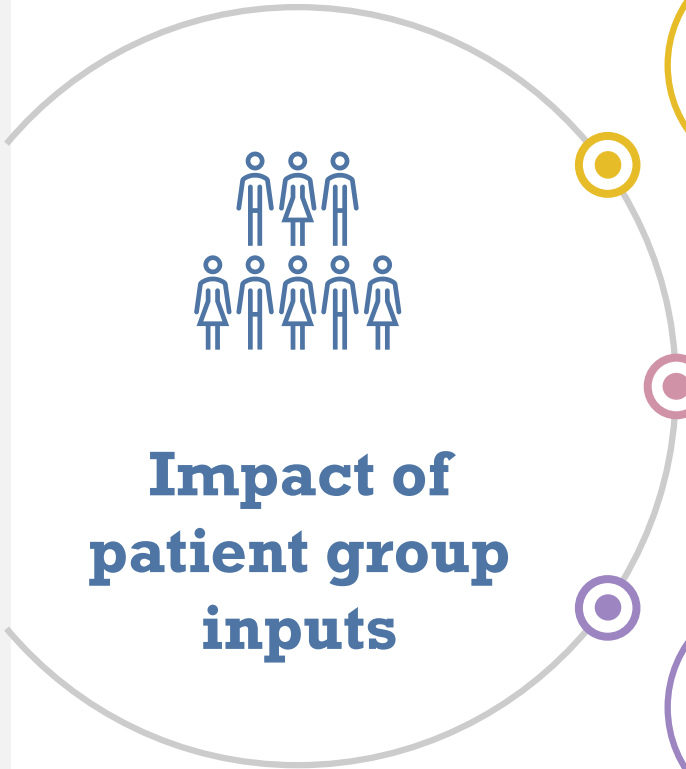
In all submissions analyzed, the patient group submissions were recognized as providing important context on the impacts of atopic eczema. These negative and severe impacts were called out in the final reports (even when the decision was negative)

**Evidence challenges** were cited as the reason for some rejections

Either the choice of comparator used in the clinical trials or the assumptions in the economic models were challenged. This often led to a rejection followed by a positive recommendation when new data or revised models were submitted

# Summary of key lessons (2)

*See detailed summaries of each HTA after this section*




**Adding context**
particularly around unmet needs of patients

Patient group inputs were very focused and clear on the impact of the condition and on the failures of current treatment options to manage atopic eczema for many people. These insights were not questioned or challenged by the committees.

**Other factors**
drove the negative decisions, outside of patient group control

All cases had an initial negative decision before new data was provided or models were adjusted. In some cases, new patient access schemes or risk share agreements were negotiated. These actions fall outside the scope of patient group input.

**Setting a precedent**
for atopic eczema treatment access

By clearly articulating the severe burden and unmet need facing people with atopic eczema, and the need for access to innovative medicines, the eventual positive recommendations set a precedent for access to reimbursed biologics. However it must be noted that this is for a restricted patient population only

# NICE (England)

# Timeline of the NICE dupilumab HTA

**Initial assessment** → **Consultation** → **Final recommendation**

| Scoping phase OCT 2017 | Initial Evidence Submission JAN/FEB 2018 | Committee Meeting 1 MAR 2018 | Consultation APR 2018 | Committee meeting 2 JUN 2018 | Final Appraisal Decision / Recommendation AUG 2018 |
|---|---|---|---|---|---|
| To determine the areas of focus for the appraisal | To collect evidence from affected stakeholders | To make a draft recommendation | To allow input on the draft recommendation | To discuss the comments | The final recommendation |
|  |  |  |  |  | |
| **Patient input** | **Patient input** | **Patient input** | **Patient input** | **Patient input** | |
| No patient input found. Input from the industry, medical societies and pharmacist associations only | Submission from the National Eczema Society | Patient expert from Allergy UK | Comments from Allergy UK and the National Eczema Society | Unclear in documentation if patients and patient groups were invited back | |

https://www.nice.org.uk/guidance/ta534/history

# Patient input into the initial evidence submission

**Initial Evidence Submission JAN/FEB 2018**

To collect evidence from affected stakeholders

**Patient input**

Submission from the National Eczema Society

## Key points raised:

- Living with eczema can be significantly life challenging
- The incessant itch of eczema can be intolerable - difficult to carry out day-to-day tasks
- Simply getting dressed (and finding skin friendly clothing) can be very difficult
- More severe eczema can be painful with damaged skin cracks and bleeds
- Holding a pencil, typing, or holding your baby will be extraordinarily painful if hands are affected
- A visible condition still often perceived as infectious or a result of poor personal hygiene
- For those whose eczema is unresponsive to topical treatments topical steroids and topical calcineurin inhibitors) the options are quite limited
- Worries about the potential adverse effects of topical steroids and frightened at the prospect of using any of the currently available systemic options
- Systemic treatments are quite limited and all suppress the immune system

# Initial (draft) recommendation (MAR 2018)

Committee Meeting 1 MAR 2018

To make a draft recommendation

## Patient input

Patient expert from Allergy UK

## Draft recommendation:

- Dupilumab is not recommended, within its marketing authorisation, for treating moderate to severe atopic dermatitis in adults when systemic therapy is suitable.

## Main reasons driving this decision:

- **The cost-effectiveness estimates were more expensive than usually paid for**
- Although there was acceptance of the impact of severe atopic eczema, there were questions about how good the current assessment scores are in capturing the impact of the condition. In particular, the Eczema Area and Severity Index (EASI) was flagged at being poor at capturing itch and some types of eczema lesions and can underestimate the severity in people with darker skin – need to combine several scores to capture the impact- EASI + Patient Oriented Eczema Measure (POEM) + Dermatology Life Quality Index (DLQI)
- Questions on the changes to these scores that reflect meaningful practical changes for patients
- Some assumptions in the economic model were questioned (particularly, whether all people on 'best supportive care' would not maintain any benefit after three years)
- The cost of delivering 'best supportive care' was thought to be over-estimated in the economic model
- *However, the committee agreed that dupilumab is innovative and step-change in managing atopic dermatitis*

# Consultation on the draft recommendation by patient groups

AllergyUK 1991 - 2021

**Consultation APR 2018**

To allow input on the draft recommendation

## Patient input

Comments from Allergy UK and the National Eczema Society

**Key points raised:**

### Supplied a Patient Survey:

- 305 people were surveyed
- 58% said it impacts on their personal relationships
- 10% spent over 30 days a year managing their eczema e.g. by applying creams
- 86% said that the management of the condition impacts their day to day activities
- 7 in 10 said their sleep was affected
- 1 in 10 consume more alcohol when their eczema is at it's worst
- Over 70% reported feeling depressed
- Nearly 1/4 missed more than 6 days of work per year due to their condition, whilst approx. 15% missed 16 or more days

# Consultation on the draft recommendation by patient groups

Consultation
APR 2018

To allow input on the draft recommendation

## Patient input

Comments from Allergy UK and the National Eczema Society

AllergyUK
1991 - 2021

**Key points raised:**

### High unmet need:

- Lack of knowledge at primary care level leads to inadequate management of eczema
- Toxic and unacceptable side effects of long term use of immunosuppressants and steroids
- Need a more targeted therapy with minimal side effects for severe disease and better long term management

# Consultation on the draft recommendation by patient groups

Consultation
APR 2018

To allow input on the draft recommendation

## Patient input

Comments from Allergy UK and the National Eczema Society

**Key points raised:**

### Concern that NICE have not understood impact of atopic eczema on patients

- NICE has not considered fully the physical health, psychological and social impacts on quality of life of people with moderate to severe atopic eczema
- Adults tell us their life is a torment. There is no let-up in symptoms and no hope despite trying current treatments - there is no end to the daily suffering. Suicidal thoughts

### Concern that NICE have not considered side-effects of systemic treatments

- Systemic treatments of uncertain efficacy with the potential for significant long-term harm through severe adverse side effects
- Only one systemic treatment, ciclosporin, is licenced with a maximum duration of 8 weeks
- The new treatment offers the potential of safer therapy and the opportunity for significantly reduced topical steroid treatment

# Consultation on the draft recommendation by patient groups

NATIONAL ECZEMA SOCIETY

**Consultation APR 2018**

To allow input on the draft recommendation

**Patient input**

Comments from Allergy UK and the National Eczema Society

## Key points raised:

### Concern that NICE is treating atopic eczema unfairly

- NICE is not demonstrating parity with other severe chronic conditions like psoriasis, urticaria, asthma and arthritis - all of which have had life-changing biologic treatments approved by NICE
- Especially harsh to withhold funding from the first game-changing new drug treatment for severe eczema in many years

### Concern about the assumptions made by NICE on the use of current treatments

- NICE has not considered fully the variable availability of systemic treatments and local clinical preferences in prescribing
- There is no NICE quality standard or clinical guideline for the treatment of atopic eczema
- Phototherapy, for example, is not universally available and patients often find it extremely difficult to travel for frequent therapy sessions

# How the consultation changed the recommendation

**Final Appraisal Decision / Recommendation AUG 2018**

The final recommendation

## Revised evidence submitted

Company submitted a new economic model to address NICE concerns and added new data from the Open Label Extension study. The company also revised its patient access scheme which altered the cost-effectiveness calculations to bring them within the range that NICE normally considers acceptable

## How NICE responded to the patient input during the consultation

### Concern that NICE is treating atopic eczema unfairly

The final appraisal document recognises the clinical effectiveness and innovation of dupilumab

### Concern about the assumptions made by NICE on the use of current treatments

The final appraisal document recognises the limited treatment options available to people with atopic dermatitis

### Concern that NICE have not understood impact of atopic eczema on patients

The committee recognised the financial implications of having atopic dermatitis. The impact of the disease has also been considered in the patient and professional group submissions. The committee recognised the social and psychological impact of having atopic dermatitis.

# The final recommendation (1)

**Final Appraisal Decision / Recommendation AUG 2018**

The final recommendation

**Dupilumab is recommended as an option for treating moderate to severe atopic dermatitis in adults, only if:**

- The disease has not responded to at least 1 other systemic therapy, such as ciclosporin, methotrexate, azathioprine and mycophenolate mofetil, or these are contraindicated or not tolerated
- The company provides dupilumab according to the commercial arrangement

**Stop dupilumab at 16 weeks if the atopic dermatitis has not responded adequately. An adequate response is:**

- At least a 50% reduction in the Eczema Area and Severity Index score (EASI 50) from when treatment started and
- at least a 4-point reduction in the Dermatology Life Quality Index (DLQI) from when treatment started.

# The final recommendation (2)

Final Appraisal Decision / Recommendation AUG 2018

The final recommendation

**When using the EASI, healthcare professionals should take into account skin colour and how this could affect the EASI score, and make the clinical adjustments they consider appropriate.**

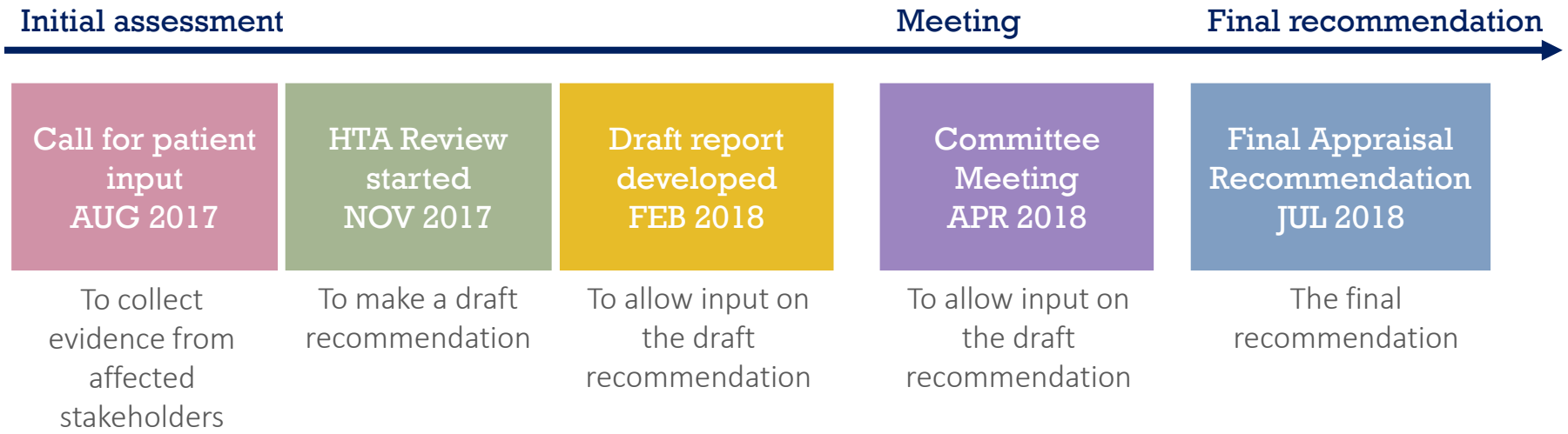
**When using the DLQI, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DLQI, and make any adjustments they consider appropriate.**



https://www.nice.org.uk/guidance/ta534/documents/committee-papers-2

# CADTH (Canada)

# Timeline of the CADTH dupilumab HTA in 2017/18




**Patient input**

Submission from Eczema Society of Canada

*Note that from the public available documents it is unclear if patient groups were further consulted beyond the initial call for patient input*

https://www.cadth.ca/sites/default/files/cdr/complete/SR0533_cdr_complete_Dupixent_July_9_2018.pdf

# Patient input into the initial evidence submission

Call for patient input
AUG 2017

To collect evidence from affected stakeholders

**Patient input**

Submission from Eczema Society of Canada

## Eczema Society of Canada

**Key points raised (using a patient survey):**

IMPACT OF ATOPIC ECZEMA

- 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.

https://www.cadth.ca/sites/default/files/cdr/relatedinfo/SR0533_Duxipent_Patient_Submsissions.pdf

# Patient input into the initial evidence submission

Call for patient input AUG 2017

To collect evidence from affected stakeholders

**Patient input**

Submission from Eczema Society of Canada

## Eczema Society of Canada

**Key points raised (using a patient survey):**

**PATIENT EXPERIENCE WITH CURRENT THERAPIES**

- 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
- 25% of respondents report that they have lived 10 years or more without adequate treatment.
- 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.
- 63% of respondents who have tried off-label systemic therapies report that they did not work well to manage their atopic dermatitis



https://www.cadth.ca/sites/default/files/cdr/relatedinfo/SR0533_Duxipent_Patient_Submsissions.pdf

# Patient input into the initial evidence submission

Call for patient input
AUG 2017

To collect evidence from affected stakeholders

**Patient input**

Submission from Eczema Society of Canada

## Eczema Society of Canada

**Key points raised (using patient interviews):**

PATIENT EXPERIENCE OF THE NEW THERAPY

- The patient group included quotes from patients who have tried dupilumab in clinical studies and reported significant improvements in their health and wellbeing
- Many quotes expressed the fact that this is the first time that they have had their atopic eczema under control
- Several expressed the impact on their sleep and daily functioning as well as symptom control such as itch
- Several also expressed concern about controlling their eczema now that the trial had ended and a decision on reimbursed access was still to be made



https://www.cadth.ca/sites/default/files/cdr/relatedinfo/SR0533_Duxipent_Patient_Submsissions.pdf

# Concerns raised by CADTH in the final assessment

**Final Appraisal Recommendation JUL 2018**

The final recommendation

## The patient population being considered for reimbursement

- The assessment was for reimbursement for patients whose disease is not adequately controlled by topical prescription therapies (or when those therapies are not advisable)
- *Note: This is a much wider patient population than the previous example at NICE (England)*

## Main concerns raised:

### Lack of evidence against drugs commonly used to treat atopic eczema

- The four phase III, placebo-controlled, randomized controlled trials reviewed were not designed to compare dupilumab with other drugs commonly used in the treatment of atopic dermatitis.
- Although these trials demonstrated that a statistically significantly greater percentage of patients had improvements in AD severity, symptoms, and quality of life with dupilumab treatment compared with placebo, the magnitude of clinical benefit with dupilumab compared with existing alternative treatments is unknown.

### Lack of evidence on long-term safety

- There are several notable gaps in the clinical evidence regarding dupilumab, including data to assess the long-term safety of dupilumab, concerns with the generalizability of the trial results to patients who would be expected to use dupilumab in clinical practice, and an absence of efficacy and safety data for the use of dupilumab in patients where topical prescription therapies are not advisable.



https://www.cadth.ca/sites/default/files/cdr/complete/SR0533_cdr_complete_Dupixent_July_9_2018.pdf

# The final recommendation (2018)

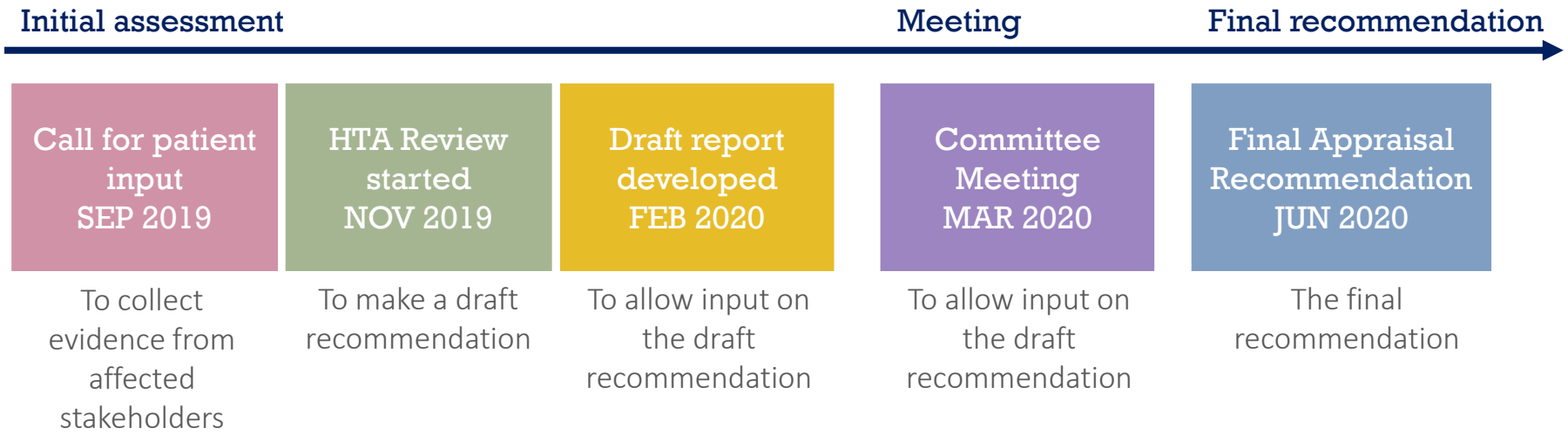
Final Appraisal Recommendation JUL 2018

The final recommendation

**The CADTH Canadian Drug Expert Committee (CDEC) recommends that dupilumab not be reimbursed for the treatment of adult patients with moderate-to-severe atopic dermatitis (AD) whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.**

https://www.cadth.ca/sites/default/files/cdr/complete/SR0533_cdr_complete_Dupixent_July_9_2018.pdf

# But that was not the end of the story. Reviewed again in 2020




## Patient input

Submission from:
Eczema Society of Canada
Canadian Skin Patient Alliance

*Note that from the public available documents it is unclear if patient groups were further consulted beyond the initial call for patient input*

https://www.cadth.ca/dupilumab-0

# Patient input into the evidence submission (1)

Call for patient input
SEP 2019

To collect evidence from affected stakeholders

**Patient input**

Submission from:
Eczema Society of Canada
Canadian Skin Patient Alliance

## Eczema Society of Canada

**Key points raised (same survey data as first submission was shared, plus:):**

IMPACT OF ATOPIC ECZEMA

- Symptoms of moderate-to-severe AD can be debilitating and life altering
- For those with more severe form of AD, the itchiness can be intense and occur all day & night, interrupting all aspects of life, including work, school, social relationships and sleep
- Some patients report reliance on sleeping pills. Others report sometimes falling asleep during the day and experiencing daytime exhaustion, changes in mood, and impatience due to fatigue
- Patients also reported missing work/school. Adolescents report bullying due to their condition
- Patients report being bed-ridden during severe flares, with skin covered in open wounds
- Patients also report bleeding through their clothing, and needing to frequently change clothing
- Sufferers also report poor self-esteem, loss of energy, stress, and even suicidal thoughts
- Itch is consistently rated as the most bothersome symptom of the disease by patients.

# Patient input into the evidence submission (2)

Call for patient input
SEP 2019

To collect evidence from affected stakeholders

**Patient input**

Submission from:
Eczema Society of Canada
Canadian Skin Patient Alliance

## Eczema Society of Canada

**Key points raised:**

### EXPERIENCE WITH CURRENT TREATMENTS

- For some patients, 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
- For patients with AD that does not respond adequately to topical therapy, systemic therapy is the next step (phototherapy, oral corticosteroids, and off-label systemic immunosuppressants)
- Recent survey on systemic medications indicated phototherapy was not helpful for controlling the disease for most respondents. Access to phototherapy is also a barrier (only in city centres)
- Oral corticosteroids may work well for some patients in the short term, but many reported terrible rebound flares when they came off the drug and 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. These often come with serious side effects (e.g. nausea and organ damage).



https://www.cadth.ca/sites/default/files/cdr/relatedinfo/SR0636%20Dupixent%20-%20Patient%20Input%20Summary%20December%202019.pdf

# Patient input into the evidence submission (3)

Call for patient input
SEP 2019

To collect evidence from affected stakeholders

**Patient input**

Submission from:
Eczema Society of Canada
Canadian Skin Patient Alliance

## Eczema Society of Canada

**Key points raised:**

### EXPERIENCE WITH CURRENT TREATMENTS

- Eczema Society of Canada also shared the results of a 2019 survey looking at the percentage of patients surveyed who had to stop the following treatments due t lack of efficacy, management difficulty, and/or side-effects:
  - Cyclosporine: 100%
  - Systemic corticosteroids: 91%
  - Methotrexate: 76%
  - Phototherapy: 73%
  - Dupilumab: 12%

https://www.cadth.ca/sites/default/files/cdr/relatedinfo/SR0636%20Dupixent%20-%20Patient%20Input%20Summary%20December%202019.pdf

# Patient input into the evidence submission (4)

## Canadian Skin Patient Alliance

Call for patient input
SEP 2019

To collect evidence from affected stakeholders

**Patient input**

Submission from:
Eczema Society of Canada
Canadian Skin Patient Alliance

**Key points raised:**

### IMPACT OF ATOPIC ECZEMA

- Affects up to 17% of individuals in Canada
- Canadian Skin Patient Alliance used quotes from patients to express the impact, e.g.:
- **The impact of itching**
  - *The thought of itching consumed my life*
  - *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 to work, be a mom, and function all while feeling so irritable due to lack of sleep and itchy skin*
- In a survey, half (51.5%) of those with moderate to severe AD experience flares at least monthly
- Complications and comorbidities (such as infections) further impact patients
- One in five with moderate to severe AD reported losing at least 10 nights of sleep a month

https://www.cadth.ca/sites/default/files/cdr/relatedinfo/SR0636%20Dupixent%20-%20Patient%20Input%20Summary%20December%202019.pdf

# Patient input into the evidence submission (5)

Call for patient input
SEP 2019

To collect evidence from affected stakeholders

## Patient input

Submission from:
Eczema Society of Canada
Canadian Skin Patient Alliance

## Canadian Skin Patient Alliance

**Key points raised:**

### IMPACT OF ATOPIC ECZEMA

- Affects up to 17% of individuals in Canada
- Canadian Skin Patient Alliance used quotes from patients to express the impact, e.g.:
- The impact of itching: *"The thought of itching consumed my life" / "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 to work, be a mom, and function all while feeling so irritable due to lack of sleep and itchy skin"*
- The group also used an Atopic Dermatitis Patient Experience survey with 194 eligible responses:
  - Half (51.5%) of those with moderate to severe AD experience flares at least monthly
  - One in five with moderate to severe AD reported losing at least 10 nights of sleep a month
  - Nearly half (46%) of ADPE patient respondents reported a poor effect on their work or school life
  - Two in three (68%) reported a negative impact on their personal life
  - Anxiety (45%) and depression (37%) significantly impact patients with moderate to severe AD.



https://www.cadth.ca/sites/default/files/cdr/relatedinfo/SR0636%20Dupixent%20-%20Patient%20Input%20Summary%20December%202019.pdf

# Patient input into the evidence submission (6)

## Canadian Skin Patient Alliance

Call for patient input
SEP 2019

To collect evidence from affected stakeholders

### Patient input

Submission from:
Eczema Society of Canada
Canadian Skin Patient Alliance

**Key points raised:**

### EXPERIENCE WITH CURRENT TREATMENTS

- Both patients and caregivers reported that currently available treatments have limited effect
- Four in five survey respondents (78% of patients; 82% of caregivers) tried multiple treatments before finding relief
- Immunosuppressive medications have been used by four in 10 (39%) of survey respondents with moderate to severe AD, despite their use being off-label only
- Among survey respondents, 1% of patients and 4% of caregivers reported continuous long term use of immunosuppressive medications
- The survey also showed that 14% of patients and 4% of caregivers used such medications during regular intervals for fixed periods
- The costs of currently available treatments are a burden for many and a complete barrier for some patients

# Patient input into the evidence submission (7)

## Canadian Skin Patient Alliance

Call for patient input
SEP 2019

To collect evidence from affected stakeholders

**Patient input**

Submission from:
Eczema Society of Canada
Canadian Skin Patient Alliance

**Key points raised:**

### EXPERIENCE WITH DRUG UNDER REVIEW

- The group had received feedback from 8 patients who had used the drug and presented the feedback as quotes:
  - *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.*
  - *With Dupixent, I have been able to sleep without issues; I am not constantly itchy.*
  - *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.*
  - *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.*
  - *Being part of the study on the drug, Dupilumab, has saved our son's life and ours.*

https://www.cadth.ca/sites/default/files/cdr/relatedinfo/SR0636%20Dupixent%20-%20Patient%20Input%20Summary%20December%202019.pdf

# Comments noted by CADTH in the 2020 assessment

**Final Appraisal Recommendation JUN 2020**

The final recommendation

## Differences between the 2018 and 2020 assessments

- New data meant that adolescents 12yo and over were included in this assessment

## Main comments noted:

### Evidence of superiority over placebo

- Dupilumab demonstrated superiority in improving signs and symptoms of AD compared to placebo

### Patients in the studies had few alternative options

- There are few treatment options after topical therapies and immunosuppressants have failed
- The patients studied were those with an inadequate response to topical therapies or topical therapies were not advisable, and where cyclosporine treatment was inadequate, associated with toxicities or not recommended due to contraindications
- There is only limited access to phototherapy across Canada

### Intense symptoms impact quality of life

- Patient and clinician input that AD is associated with intense symptoms that can lead to sleep disruption, anxiety, depression, social isolation and impaired quality of life

# The final recommendation (2020)

Final Appraisal Recommendation JUN 2020

The final recommendation

**The CADTH Canadian Drug Expert Committee recommends that dupilumab should be reimbursed for the treatment of atopic dermatitis only if the following conditions are met:**

## Initiation criteria

- Patients aged 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable
- Patients must have had an adequate trial or be ineligible for each of the following therapies: phototherapy (where available), methotrexate, and cyclosporine
- Patients who have had an adequate trial phototherapy, methotrexate, and/or cyclosporine must have documented refractory disease or intolerance
- The physician must provide the Eczema Area and Severity Index (EASI) score and Physician Global Assessment score at the time of initial request for reimbursement
- The maximum duration of initial authorization is six months

## Renewal criteria

- The physician must provide proof of beneficial clinical effect when requesting continuation of reimbursement, defined as a 75% or greater improvement from baseline in the EASI score (EASI-75) six months after treatment initiation
- The physician must provide proof of maintenance of the EASI-75 response from baseline every six months for subsequent authorizations

## Prescribing conditions

- The patient must be under the care of a dermatologist
- Dupilumab is not to be used in combination with phototherapy or immunosuppressant drugs, such as methotrexate or cyclosporine

## Pricing conditions

- Reduction in price

# PBAC (Australia)

# Timeline of the PBAC dupilumab HTA 2018, 2019 and 2020

## Overview of the three HTA recommendations

| ORIGINAL SUBMISSION<br>July 2018 | FIRST RESUBMISSION<br>July 2019 | SECOND RESUBMISSION<br>March 2020 |
|---|---|---|
| *Reimbursement sought for adults with severe AD (IGA score 4) who have had inadequate response or intolerance to cyclosporin A (CsA), or for whom CsA is contra-indicated* | *Reimbursement sought for moderate to severe atopic dermatitis AD (PGA score of 3 or 4) who have had an inadequate response to topical therapy (topical corticosteroids [TCS]/topical calcineurin inhibitor [TCI])* | *Reimbursement sought for adults with severe AD (defined as a PGA of 4 AND an Eczema Area and Severity Index [EASI] of ≥20 ) who have had an inadequate response to topical therapies (TCS/TCI)* |
| *Not recommended for reimbursement* | *Not recommended for reimbursement* | *Recommended for reimbursement* |

***Patient group submission to PBAC processes is provided via a consultation process on a website where individual patients and physicians as well as patient groups can submit comments and evidence***

https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2020-03/files/dupilimumab-psd-march-2020.pdf

# Key concerns raised in the 2019 submission

## And how they were addressed in the 2020 resubmission

| FIRST RESUBMISSION<br>July 2019<br><br>CONCERNS RAISED | SECOND RESUBMISSION<br>March 2020 |
|---|---|
| **Eligibility Criteria**<br>• Initial assessment of disease severity should be based on both PGA and EASI scores | **Eligibility Criteria**<br>• Amended to be based on both PGA and EASI scores |
| **Response Criteria**<br>• Both DLQI and EASI-75 were important measures of response and should be included in the response criteria | **Response Criteria**<br>• Partially addressed: Response criteria is defined as EASI-50 (not EASI-75) and 4 point improvement in DLQI |
| **Economic Model**<br>• Frequency of hospitalizations questioned<br>• 10 year time horizon of model not justified | **Economic model**<br>• Physician survey provides evidence on hospitalizations<br>• Model time horizon reduced to 5 years |
| **Financial Estimates**<br>• Financial costs was very high and remained uncertain<br>• A risk share agreement would be necessary to manage uncertainties in patient estrimates | **Financial Estimates**<br>• A narrower population (severe patients only)<br>• Sponsor willing to negotiate a risk share agreement |

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# Patient input into the evidence submission

## Note that public documents only contain a summary of the patient group input

- The PBAC noted the advice from Allergy & Anaphylaxis Australia (A&AA) that their stance on the need for dupilumab remains unchanged from previous advice.
- A&AA noted that dupilumab "has given people with severe AD hope and for some, a will to go on"
- A&AA considered that PBS listing of dupilumab will be life-changing for patients with severe AD and urged that listing of dupilumab be given urgent and serious consideration.

- The PBAC noted the advice from The Eczema Association of Australasia Inc that the use of dupilumab may provide a much needed treatment option in an area that has few treatments available and no new treatments approved for a long time.
- The Association stated that dupilumab can be used long-term, unlike other treatments which can only be used for short periods because of side effects that require close monitoring.

- The PBAC noted the advice from Eczema Support Australia that patients with severe AD can experience "social isolation, sleep deprivation, co-morbidities, pain, infection and intense itch", which "can result in depression, anxiety and suicidal thoughts in conjunction with the negative impact on schooling, loss of work or career choice and relationship breakdown"
- A recent systematic review and meta- analysis was noted that found patients with AD are 44% more likely to exhibit suicidal ideation and 36% more likely to attempt suicide compared to patients without AD. The advice also noted the financial burden associated with AD treatment and the hope that access to dupilumab offers to patients with debilitating AD.



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# The PBAC Outcome

## Recommendation and rationale

**SECOND RESUBMISSION**
**March 2020**

**The PBAC recommended the listing of dupilumab for the treatment of patients aged 12 years and older with severe atopic dermatitis (AD) who are inadequately controlled on topical therapies.**

*The PBAC acknowledged there is significant disease burden from AD and a high clinical need for effective treatments for severe AD. The PBAC noted the considerable number of consumer comments from professionals and individuals which reflected the substantial impact AD has on patients' physical and emotional wellbeing and the financial impact of AD and existing treatments for patients and their families. The PBAC also noted the support for the PBS listing of dupilumab from several professional organisations and patient representative organisations which reflected the same considerations as provided in the consumer comments.*

PBAC acknowledged the significant reduction in the extent of disease and improved patient quality of life with dupilumab over standard of care in a therapeutic area of high clinical need.

The PBAC considered that the proposed measures of disease assessment were adequately addressed in the resubmission

The PBAC considered the potential for use of dupilumab outside the proposed restriction could be managed through a risk sharing arrangement



https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2020-03/files/dupilimumab-psd-march-2020.pdf

# End of report