CADTH

CADTH COMMON DRUG REVIEW

Patient Input

budesonide (Jorveza)

(AVIR Pharma Inc.)

Indication: Eosinophilic esophagitis, adults

CADTH received patient input from:

AEDESEO (Spanish Association for Eosinophilic Esophagitis)

American Partnership for Eosinophilic Disorders

ausEE Inc.

CURED (Campaign Urging Research for Eosinophilic Disease)

FABED (Families Affected by Eosinophilic Disorders)

Gastrointestinal Society

October 23, 2019

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**JORVEZA (bucodispersable budesonide)** **Treatment for patients with Eosinophilic Esophagitis**
Name of the Patient Group	**AEDESEO**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

AEDESEO (Spanish Association for Eosinophilic Esophagitis) is a non profit organization. Their main purposes are:

- To help patients and their families to learn about the eosinophilic esophagitis (EoE)
- To explain the different possible treatments
- To help dealing with diets
- To support psicologically patient and families
- To make contact with doctors expert in EoE
- To encourage and support investigation
- To represent patient needs in front of other patients, medical or state organizations

WEBSITE: www.aedeseo.es

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how**

many patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Jorveza is not commercialized at this moment in Spain; however, there are some patient taking this medicine. Jorveza is an orphan drug and it is being used as a compassionate treatment in those patients in which other alternatives have been unsuccessful.

We report the results based on personal interviews. Most patients are adults, although there are some teenagers non-respondant to other therapies with a quite affected aesophagus.

Patients using Jorveza report that the medicine is easy to take and, in contrast to viscose budesonide, it is ready to be used, and does not need any previous preparation. Most of them referes clinical improvement, although there are any patient with partial, but not complete, histological response.

Some of them have been using Jorveza for several months, and their doctors propose them to decrease those to see if can achieve remission with lowering it.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

EoE is a chronic disease that affects quality of life of patients and their families.

Talking about symptoms, disfagia and impaction are the symptoms that impair QoL mostly, specially the last one because it can happen sudden and unexpectedly. Impaction is hard, specially when happens in a public environment and it frequently needs emergent endoscopy. One of the main goals for patients to achieve is to be able to eat without difficulties.

Talking about treatment, diets are hard to follow; social life is impaired because of food restrictions, specially when restrictions are wery important. There are some schools that are not prepared for such diets and children have to carry their own food to school, instead of sharing school meals, which make them feel different from their mates. Besides, sometimes it is hard to find foods suitable at supermarkets, specially prepared meals. This situation makes cooking at home almost compulsory. This is an extra job for some families that do not how to cook.

Viscose budesonide needs to be prepared. It is time consuming and it needs the development of the adequate skills looking forward such preparation

Taking a chronic medicine is, sometimes hard for patients that can be anxious about long term side effects.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Proton pump inhibitors, as omeprazole, esomeprazole or lansoprazole. This is the first choosen medicine in aproximetely 2/3 of our patients. In Spain it is a cheap medicine easy to buy under medical prescription. There are pills to be swallowed by adults and for children there are either esomeprazole orodispersable tablets or a omeprazole syrup easy to swallow by toddlers. Patients are worried about eventual long term side effects as dementia or cancer.

We can use two different kind of corticosteroids: either budesonide or fluticasone:

- Budesonide is used mixed with a thickener, that can be sucralose or dextrinomaltose. The patient can prepare it at home or it can be prepared at the chemist. The adventages of preparing it at home is that you do not depend on the chemistry but, on the other hand, for some patients is difficult to make the mixture. Not all the chemistries have the thickener and , sometimes, you have to order it in advance. Patients ask to AEDESEO how thick the mixture must be: some of them prepared it not to tick enough and this point can impair effectiveness. If you order the chemistry to prepare the mixture, the price is higher and variable depending where you buy it .

  One budesonide pack costs 13 euros aprox and contains 20 phials. Dextrinomaltose tin, 500 gr. costs 13 euros aprox. Tha average cost for one month for an adult at the beginning of the treatment is approximately 85,8 euros, although there will be a dextrinomeltose left over to be used next month. At the chemist, 300 mililiters of budesonide syroup can cost 35 euros approximately, but its price can vary from one chemistry to another.
- Fluticasone: it is used now as phials. They are directedly swallow by patient. Some of them say thet they feel as if the amount of liquid was too small. It is well tolerated and easy to use.

  The cost of a box that contains 28 units is aproximetely 21 euros. For the initial treatment in an adult, the approximately monthly cost is 84 euros. There are some studies that demonstrate impairment in suprarrenal function in kids taking fluticasone. This patients need both, to be revised and to be taken a blood sample in order to reassure that suprarrenal function is preserved.

With any kind of treatment, patients need to be checked to see if there is, not only a clinical response, but a histological one. It means going periodically to the doctor and having periodic endoscopies done. As a matter of fact, endoscopies trigger the absence of work time, are invasive diagnostics tests and have costly procedures.

In AEDESEO we do not have experience with infusion lines treatments directly. We know that some first line EoE hospitals are trying Dupilumab.

Finally, it must be pointed that there is a group of non-respondant patients to either diets, PPI or swallowed corticosteroid, that needs a response of both, doctors and politicians.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Patients and their families need treatment that is easy to get at any chemistry, and that the National Health insurance can pay part of it. Not all the patients can afford expensive treatments, and as in Spain the National Health Service is universal, it would be mandatory that the system covers part of the expenditure.

Patients also need that the treatment be effective in terms of clinical improvement and histological response. Lack of symptoms stongly improves health related quality of life.

Patients also ask for a treatment lack, or at least, minimize, adverse side effects, due to long-lasting treatments. The possibility of these adverse effects can worsen patient quality of life.

It is also necessary that the treatment is easy to take, and to have it at home, meaning that oral intake is quite preferable that intravenous one, not only because the second one is painful for the patient, but also because is time and money consuming because you have to go to the hospital.

Whenever patients, families and caregivers choose this therapy they are looking forward to a complete clinical and histological remission that gathers the most economic treatment possible being as well the simplest and easiest to use.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (i.e clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

Initially, patients joined clinical trials. They were non PPI respondant patients. After that, gastroenterologists propose non-respondant patients to the current treatment lines, to try Jorveza.

The new drug has the following advantages: it does neither need to be prepared (as viscose budesonide) nor to be swallowed. Patients confirm good tolerability and good symptoms improvement. Almost all of them improve the histology as well. Some oral candidiasis had been reported.

Price is the main disadvantage. The box contain 90 tablets that lasts one and a half month for an adult initial treatment. The box costs 327 euros approximately. It is difficult for some patients to expend this amount of money at once.

Jorveza has been used as a compassionate use when other therapies, including PPI, swallowed corticosteroids and diets were no effective.

Although Jorveza was not commercialized, patients could get it through “foreing medication”, allowed by the Health Spanish ministry, but now this is not longer possible. This fact, put non-respondants to other therapies patients in a difficult situation.

Jorveza would be desierable to take viscose budesonide position. If it would not be possible, at least it is necessary for non-respondant patients. So to speak, the sequency of treatments could be as follows: PPI/swallowed corticosteriod/ diets, no matter this order, and, in case of non-response, it would be mandatory to try Jorveza.

IDEAL: PPI- JORVEZA- DIET or: DIET- PPI- JORVEZA or: JORVEZA- PPI- DIET
AT LEAST: NON RESPONDANT TO PPI- VISCOSE BUDESONIDE- DIET: TRIAL WITH JORVEZA

For patients and families Jorveza is important because:

- High rates of clinical response
- High rates of histological response
- Patients non-respondant to other therapies are respondant to Jorveza
- No preparation needed
- Not need to be swallowed
- Easier to take than intravenous medication

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

We can not respond to this point

8. Anything Else?

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

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.

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.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Dr Falk	2000			
Nestlé	14000			

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: Ruth García
Position: AEDESEO medical team leader
Patient Group: AEDESEO
Date:

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	
Name of the Patient Group	**American Partnership for Eosinophilic Disorders**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

The American Partnership for Eosinophilic Disorders (APFED) is a 501c3 nonprofit organization founded in December 2001 by a group of mothers of young children living with eosinophil-associated diseases. We are a patient advocacy group dedicated to improving the lives of those living with eosinophilic disorders. Our mission is to passionately embrace, support, and improve the lives of patients and families affected by eosinophil-associated diseases through education and awareness, research, support, and advocacy.

Apfed.org

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

The perspective we have provided in this questionnaire includes a combination of published studies, self-reported data that patients/caregivers have shared on APFED's online support

community (Eos Connection on the Inspire Network), and anecdotal stories shared by the patient to APFED.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Eosinophilic esophagitis (EoE) can significantly impact a patient and his/her family. In the United States, there is currently no therapy approved by the U.S. Food & Drug Administration that is indicated for the treatment of EoE. Presently, the disease is treated with dietary therapy, proton pump inhibitors, and/or corticosteroids that are used off-label. In some cases, the diet becomes so restricted that the patient must rely on special amino-acid based formulas for partial or full nutrition. For some of these patients, a feeding tube may be required.

Daily life can be impacted greatly for patients and their family. Difficulty swallowing, reflux, nausea, vomiting, fatigue, malnutrition, and other symptoms are common for patients. Missed school and work days due to symptom flares or ongoing medical treatment (as well as associated financial costs) add to patient/caregiver burden.

Dietary restrictions can be stressful for the entire family. It is time consuming to plan menus and cook; speciality foods or ingredients may be difficult to find in local grocery stores and often are expensive. These restrictions can/do impact activities such as holidays/family gatherings, social engagements, dining away from home, and travel.

A systematic review that was conducted and published in 2018 to evaluate the literature on the humanistic and economic burden of eosinophilic esophagitis on patients, their caregivers, and the health care system.[1] The authors concluded that EoE negatively impacts the health-related quality of life of patients and their families, and is also a burden to the health care system. Although data are sparse, currently available treatments appear to improve health-related quality of life.

Self-reports by pediatric patients, ages 2-18, indicate that nausea and vomiting strongly impact their quality of life; parents also report vomiting negatively impacts their children's quality of life.[2]

In another published study published in 2018[3], medical researchers and patient advocacy group partners examined the unmet needs and barriers to care perceived by individuals affected by EGIDs and if these varied between adult EGID patients and adult caregivers of children with EGID. The

following findings from the study shed light into the quality of life issues faced by patients with eosinophilic gastrointestinal diseases, such as eosinophilic esophagitis.

- Approximately 64% of respondents indicated that they did not have an easy access to dietitians or nutritionists who they felt understood the challenges faced by EGID patients.
- Approximately 62% had experienced food-related discrimination due to dietary restrictions to manage their EGID.
- Over half of the respondents (51%) indicated that they felt the need to seek professional help to manage emotional stress related to EGIDs, and 41% had actually sought professional help.
- Only 17% indicated that they had a local EGID support group in which they could participate.
- The majority of the participants indicated that their EGID had placed an emotional burden on family members (74%) and caregivers (75%), and 64% indicated that the out-of-pocket costs related to EGID had placed significant stress on them.

Regarding problematic symptoms, patients and caregivers that utilize APFED's online community (Eos Connection on the Inspire Network) commonly report their bothersome symptoms include nausea/vomiting, stomach pain, dysphasia/trouble swallowing or sensation of choking, reflux, chest pain, and fatigue.

1. Mukkada V, Falk GW, Eichinger CS, King D, Todorova L, Shaheen NJ. "Health-Related Quality of Life and Costs Associated With Eosinophilic Esophagitis: A Systematic Review." Clin Gastroenterol Hepatol. 2018 Apr;16(4):495-503.e8. doi: 10.1016/j.cgh.2017.06.036. Epub 2017 Jun 24.
2. M. Klinnert , W. Moore , J. Miller , D. Atkins , D. Fleischer, G. T. Furuta. "Impact of Eosinophilic Esophagitis (EoE) on Quality of Life (qol) for Youth and Their Families" J ALLERGY CLIN IMMUNOL FEBRUARY 2011. AB110 Abstracts
3. Girish Hiremath, et. al. "Individuals Affected by Eosinophilic Gastrointestinal Disorders Have Complex Unmet Needs and Frequently Experience Unique Barriers to Care." Clin Res Hepatol Gastroenterol. 2018 Oct; 42(5): 483–493.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

In the U.S., patients and caregivers manage EoE with diet management and medication prescribed off-label.

Diet management may include:

- Empiric Six-food Elimination Diet- This type of diet has shown success in some patients. Instead of basing dietary elimination on allergy testing results, patients eliminate common allergy-causing foods (milk, eggs, wheat, soy, peanuts/tree nuts, fish/shellfish).
- Elemental diet – All sources of protein are removed from the diet and the patient drinks only an amino acid formula. Sometimes, a feeding tube may be required.
- Food trial – Specific foods are removed from the diet, and then added back, one at a time, to determine which food(s) cause a reaction.

Disease surveillance/management involves repeat endoscopies with biopsies as foods/medications are introduced to determine tolerance and/or effectiveness.

Dietary therapy can be a highly effective treatment for many patients, however, it's daunting for many families to adhere to/comply with. Patients report feelings of social isolation as the result of dietary therapy.

For patients prescribed elemental formula, roughly 60% report not having insurance coverage for this medical food, and out-of-pocket costs become expensive.

Medications may include:

- Topical steroids – There are currently no FDA approved medicines available for the treatment of EoE. However, doctors have found that topical steroids are often successful in putting EoE into remission. Topical steroids (fluticasone or budesonide) are swallowed from an asthma inhaler or mixture to control inflammation and suppress the eosinophils. Systemic corticosteroids such as Prednisone are not used for chronic management of the disorder, but may be prescribed for acute situations and short periods of time.
- Acid suppressors – May also help relieve reflux symptoms in some patients in combination with dietary therapy or medications.

In some situations, both medications and dietary therapy may be used together.

For those using pharmacological treatment, treatments may not be covered by insurance as they are used "off-label" and are not specifically indicated for the treatment of EoE. The long-term safety profile of the medications used to treat EoE is also a concern that many patients and caregivers express.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers,

and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Patients have indicated that an effective therapy that resolves symptoms and long-term safety of a therapy is of high importance. Additionally, patients have also expressed a desire for convenience in medication administration, as well as therapies that are affordable and/or covered by insurance. For example, Oral Viscous Budesonide (OVB) requires the patient/caregiver to mix the liquid budesonide with a thickening agent (e.g., Splenda®, Neocate® Nutra) to achieve sufficient viscosity to coat the esophagus, a process which is not optimal for delivery/consistency.

One caregiver of a patient with EoE summed it up in an email message to APFED "…Convenience, cost, insurance coverage, accessibility, [the therapy's] effect on daily life such as work/travel/school, side effects, treatment effect on symptoms and scope results, ability to eat more foods with drug therapy, risks, research proof of concept and successful trials are things considered when choosing a therapy."

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

In the U.S., most patients currently have access via off-label prescription to topical steroids swallowed from an asthma inhaler or mixture, to control inflammation and suppress the eosinophils. Proton pump inhibitors (PPIs) may also be prescribed to reduce inflammation and control acid production.

A clinical trial of oral budesonide suspension (topical steroid) and in an oral form via a lollipop are currently ongoing. Patients that are currently mixing the budesonide to create a "slurry" report frustrations with having to compound this pharmaceutical or having to mix it at home. Patients frequently report confusion over mixing it at home (what to mix it with, timing of dose administration) which may contribute to compliance issues, and have expressed dissatisfaction with the options that they are given to mix it with (artificial sweeteners such as Splenda®, for example). Some patients have questioned if this medication contributes to behavior problems, particular in children. (anger, frustration, lack of motivation, poor concentration, and general moodiness are common behaviors that are noted by parents), and have expressed confusion as to

whether or not it is the pharmaceutical contributing to these behaviors or the artificial sweeteners it is being mixed with to create a slurry. Patients are also concerned about the impact of the drug on pediatric growth and adrenal suppression. Finally, some patients report cost as being a barrier to access, particularly if their insurance will not reimburse the therapy because it is being prescribed/used off-label.

A sampling of comments posted to APFED's Eos Connection support community on the Inspire Network that highlight these issues are as follows:

Sampling of Comments on Side Effects:

"My son was on .5 mcg of budesonide in a slurry twice a day for about 6 months, then we noticed that during that same time frame his height dropped from 85% to 35%. We cut back to once a day and his height has dropped now to 25% in the 10 months since. His weight is thriving but his height is dropping. We personally think it's due to the budesonide, but no doctor will say that. My son is also on inhaled Flovent twice a day for asthma. His back four molars are rotting. Pediatrician attributes it to swallowed and inhaled steroids, though both Pulmonologist and GI doc deny that as a possibility."

"I have been taking the viscous form of budesonide for more than a month now. I have noticed my mood trending toward being really cranky for no specific reason."

"Has anyone seen a slow down in the rate of growth, or seen overall height effected, while using swallowed Budesonide or Flovent to treat their EoE? I have 2 boys with EoE. My 16yr old has been on swallowed Flovent 220mcg for 2 and a 1/2 years and hasn't grown in height in over a year. He started falling off his growth curve at the age of 14 1/2 and has only grown about 1 inch since that time. He is also on Advair for his asthma. So he's getting more of the same steriod to treat his asthma. My 11yr old has been on swallowed Budesonide, 2 respules only (.5ml/mg each) daily, also for only 2 and a 1/2 years. While he is still growing, his growth velocity appears to be slowing down and seems to be struggling to stay on his curve. "

Sampling of Comments on Cost:

"My GI has prescribed the meds for slurries before but I never filled them because of cost."

"My husband has been dilated several times and has been prescribed budesonide to use as a slurry. Because this treatment is not approved by the FDA for this particular use, our insurance company will not pay for the drug. We have very expensive insurance which includes a drug plan. The doctor filed an appeal and they still denied it. The cost from our pharmacy, at a discounted rate, is $380 per month!"

Sampling of Comments on Mixing/Compounding:

"My boy has EoE and has been on the slurry mix [of budesonide] and 10 packers of artificial sugar to make the mix to drink every day. It has worked and his count is normal but I do not want to give it to him even if [the sugar] is the artificial type."

"His GI doctor prescribed budesonide to be mixed with Splenda. Is it possible that the Splenda is causing more stomach pain and or gas? Its a lot of Splenda for a 19 lb. baby."

"Our allergist wants to switch from swallowed Flovent to the Budesonide slurry to try to eliminate some of Spencer's throat pain. My main concern is the large amounts of artificial sweetener that comes with this treatment. Spencer has a history of not tolerating aspartame and Splenda--not to mention I don't allow any of my children to have artificial sweeteners. "

Sampling of Comments from Patients Who Report Good Successes:

"I'm 69, have EoE ….doctors gave me steroid medications to swallow with the intent of coating my esophagus but the medicine gave me laryngitis so I couldn't use it. I was also seeing a gastroenterologist who then suggested trying budesonide capsules. Budesonide gave me significant relief but didn't eliminate my symptoms….I put myself on an elimination diet and felt much better. As long as I take my budesonide and maintain a strict diet I feel fine. If not, the pain can come back rather quickly - it did one when I tried to decrease my level of budesonide."

"My son is 11 years old and has been on the slurry for almost 8 years now. He has not shown any side effects at all. He has always taken 2 of the .5mg/2ml budesonide respules in the morning, and 2 at night. (totaling 2 mg per day)

"My 14 year old son was diagnosed with EOE after suddenly not being able to swallow. His eosinophil count was over 100 with a tear and strictures in his esophagus. [He began therapy] 2 times a day with swallowed steroids and also an a daily antacid. He was scoped again six weeks later and his eosinophils count was completely down and his esophagus looked completely normal."

"My son was sick he was on Intermittent hospital homebound for several years. Once we started the budesonide slurry he got his life back. He is now in school all the time and plays football. He dates and has a normal life. You just have to keep pressing forward to find what works for your child. The Flovent did not help my son at all and the elimination diet and all the biopsies gave him a very poor quality of life."

"I am in a clinical trial for budesonide and have had great results."

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

A reliable biomarker has not yet been established.

8. Anything Else?

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

Appendix: Patient Group Conflict of Interest Declaration

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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 (Annual)			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbott Nutrition				x
Nutricia North America			x	
Celgene			x	
AstraZeneca			x	
Knopp	x			
Allakos			x	
Rare Patient Voice	x			
Takeda			x	
GlaxoSmithKline		x		
Sanofi Genzyme/ Regeneron			x	
Mead Johnson Nutritionals		x		
Pharmaceutical Research and Manufacturers of America		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: Mary Jo Strobel

Position: Executive Director
Patient Group: American Partnership for Eosinophilic Disorders
Date: 10/23/19

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Jorveza (budesonide) / eosinophilic esophagitis, adults**
Name of the Patient Group	**ausEE Inc.**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

Founded in 2009, ausEE Inc. is Australia's peak national support and patient advocacy organisation representing Australians living with an Eosinophilic Gastrointestinal Disorder (EGID) including Eosinophilic Oesophagitis (EoE).

We are a registered Australia wide charity whose mission is to improve the lives of those affected by EGIDs by providing support, evidence-based information, resources and campaigning to raise awareness and funds for further research in Australia.

ausEE Inc. is part of International alliances of like-minded organisations including being a patient advocacy group of the Rare Diseases Clinical Research Network (RDCRN) Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR) and the Coalition of Eosinophil Patient Advocacy Groups (C-EOS).

Run entirely by volunteers, ausEE strives to improve the quality of life for all people living with eosinophilic disorders.

For more information, please visit: www.ausee.org

2. Information Gathering

*CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.*

The information provided in this submission has been based on personal experience of ausEE Inc. President and Founder, Sarah Gray who is a parent of a 16 year old who was diagnosed with eosinophilic oesophagitis at 18 months of age and experiences and stories that have been shared with us by our members who are primarily based in Australia.

We have 1,181 members in our main support group which is for individuals, parents and carers of children living with an EGID and 429 members in our support group for adults living with an EGID. Both support groups do contain some International members.

Our member surveys, for which data has been shared in this submission are run through Survey Monkey and responses have been received from patients across all Australian states, with 3% of participants being from New Zealand and 6% from 3 other countries (United States, Canada and The Netherlands).

The current estimated prevalence of EoE is 1 in 2,000 individuals and rising.

3. Disease Experience

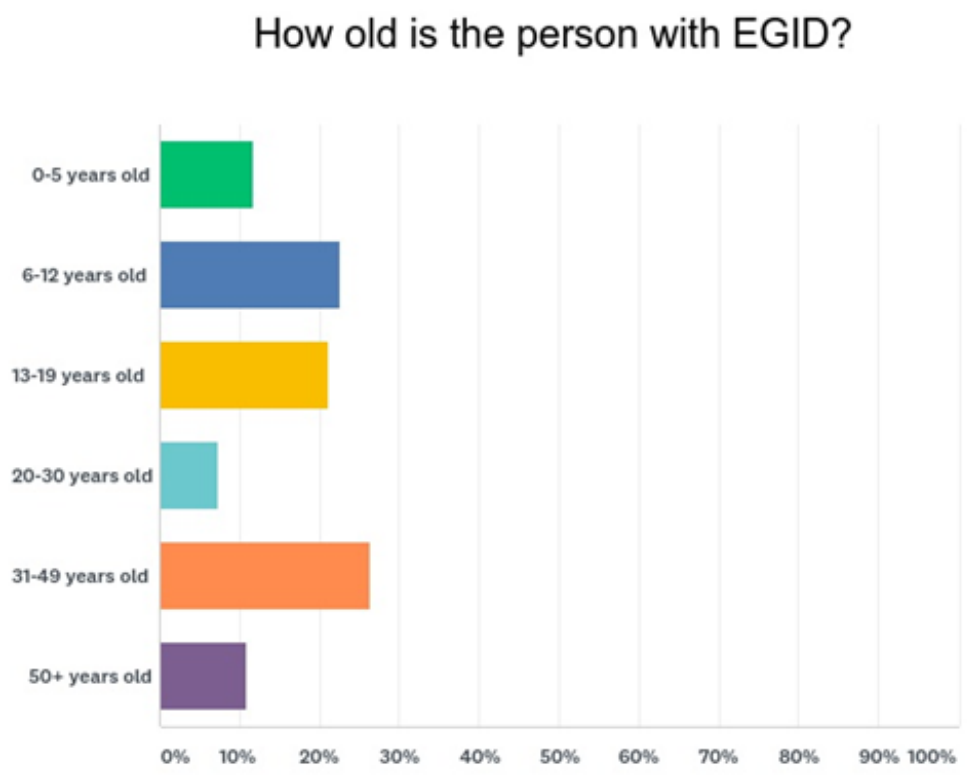
CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

We provide evidence-based information on EGIDs including EoE on our website[1] which explains the disease, common symptoms, diagnosis method and current treatment options.

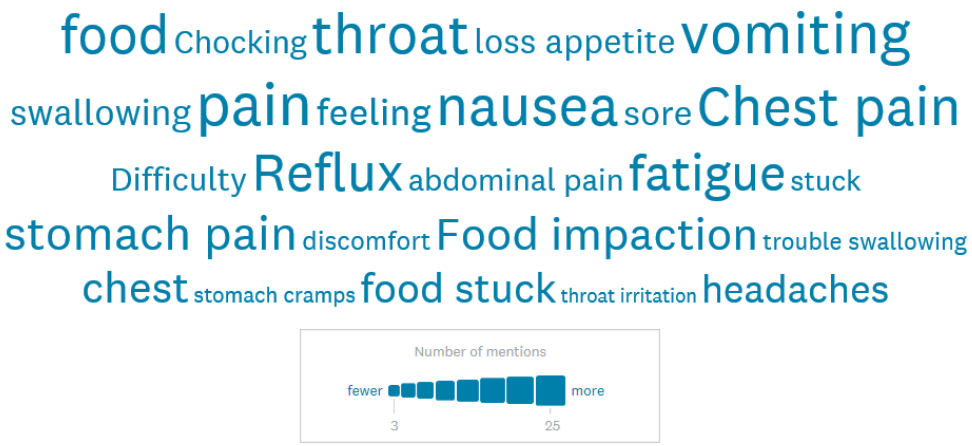
Living with EoE greatly impacts on quality of life; physically, socially and mentally. As EoE is a chronic disease that can be caused by an allergy to any food(s) and/or aero-allergens it can be very difficult for patients to find their triggers and it usually involves a lot of trial and error. If a patient undergoes an elimination diet as part of their treatment plan they are often having to undergo additional repeat endoscopies with biopsies whilst trying to find out these food triggers, as endoscopies with biopsies is currently the only way to effectively monitor EoE. This disease diagnostic and monitoring method is also required when a patient is trialing a medication. EoE requires ongoing monitoring and management and the treatment journey is often a long and very time-consuming process that is also costly for both the Government and the patient and impacts on overall wellbeing.

People with EoE can additionally live with other allergic diseases such as IgE (immediate) food allergies at risk of anaphylaxis, asthma, eczema and/or hay fever which further impact on their quality of life.

In April/May 2019 ausEE conducted a survey[2] of 157 people living with or caring for someone with an EGID. For 89% of respondents the diagnosis was EoE and the age at diagnosis ranged from 6 months to 66 years of age. We asked what the main symptoms were experienced by the person with an EGID during a flare. The ages of the patients living with the EGID and their responses to this survey question are presented in the word cloud below.



What are the main symptoms experienced by the person with an EGID during a flare?



Patient Story 1: I am an adult patient who is rurally based and I regularly choked on food and went undiagnosed and untreated for several years until I was diagnosed with what I know now to be EoE at 24 years of age. After initial diagnosis, even though I was placed on PPI medication and corticosteroid treatment I was not informed of the name of the condition or that it was related to allergies until 10 years later when I was 34 years of age. Recently I got a piece of pie meat stuck in my oesophagus on a weekend. I could not dislodge the meat and was bringing up blood and in immense pain. I called the ambulance for emergency treatment at my rural hospital where they performed a CT scan, and results indicated that there was air in my mediastinum. The next day I contacted my EGID specialist via my GP who advised that I should go to the nearest capital city hospital which is 5½ hours away for IV fluids, pain relief and antibiotics. At this hospital I have another CT scan and find out that I have a serious Boerhaave tear and I needed to stay in care at this capital city hospital for a week for monitoring and to be on IV antibiotics. My specialist has told me that my oesophagus is damaged and narrow and future scopes may be risky which is a consequence of 34 years of misdiagnosis and not being treated effectively.

Patient Story 2: I'm 23 years old and my whole life I've had to live with the struggles that come with being a child/person who has serious allergies and constant ill health. When I was a baby my Mum found out that I had anaphylaxis to peanuts when she gave me peanut butter for the first time. Along with peanuts, I'm also allergic to almonds, dust mites, dog dander, cat fur and soy. I am also seafood, gluten and lactose intolerant. I also have severe asthma and as a child I used to get sick quite often. I suffered severe anxiety while in high school and missed a lot of school due to being physically sick. However, this was just the start of many more health issues. As a young adult I was admitted to hospital for choking on some food at work during my lunch break and had to have an endoscopy to remove it. A few years later, on the day of my 22nd birthday party I choked on a piece of chicken and after 12 hours without it dislodging I went into the hospital in what can only be explained as the night from hell. After giving me 6 different drugs the chicken moved and I was able to go home the next day. About 2 months after that I was diagnosed with EoE. The gastroenterologist was explaining it and all I heard was disease and incurable. I just wanted to break down and cry, because every few years it feels like one thing after another. My next thought was I can't have anything wrong with my throat because I'm a singer. Four gastroscopies and four appointments later, I'm on Pulmicort (corticosteroid) and pantoprozole (PPI reflux medication) and even though I have days where it's a struggle I just keep going. I study music full time and there is nothing that means more to me than my music and singing. Some days I wake up and I'm so sick of feeling nauseous after I eat something, because it doesn't matter what I eat, it makes my stomach turn. Sometimes I'm in my singing lesson and my throat is so swollen that I can't move my larynx and it's hard to produce the sound I want. And sometimes I wake up during the night choking on my reflux because it's flaring up. But I want to be an Opera singer and I don't intend to let anything stop me.

Patient Story 3: I’m 20 years old and living with EoE. But you don’t look sick...? But I am, I have what you would call an invisible illness. I’m also what you would call a spoonie. I’m sick every day of my life. I complain a lot but also not enough and by looking at me you could never tell the stuff I’m going through. EoE affects my physical health as it restricts the foods I can eat, but it also affects my mental health just as much, having to go out with friends and not knowing if I can even eat anything. Is there water for me to drink if I choke? Where’s the closest bathroom? Does anyone know how to use my EpiPen? Is anyone ordering the shellfish...? I’ve had to leave before I’ve even ordered due to these things. I avoid social eating if I can. Knowing I can’t and shouldn’t eat my trigger foods hurts me mentally. I'm severely allergic to seafood and I do my best to avoid gluten, dairy and eggs but I also have many other allergies to things like oranges, strawberries, kiwis, lemon, lime and environmental ones likes grass, pollen, dust mite, perfumes and dogs to name a few. What’s scary is every year I’m developing more! I never know that

next time I eat something I might get very sick or have an anaphylactic reaction. Not all my allergies make me get immediate symptoms though, some just trigger my EoE and I'll choke on food later that day. I've had soooo many day surgeries to have an endoscopy for my EoE as my oesophagus is so small and narrowed and fragile due to this condition. I have endoscopies and dilation where they literally use a balloon to slowly stretch my oesophagus, it hurts but it's worth it. My oesophagus got down to the size of my pinkie finger in width, it should be about two fingers wide!

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Common treatment options for EoE include elimination diet, elemental formulas, antacid medications/proton pump inhibitors (PPIs), corticosteroid medications and oesophageal dilations.

There is no cure for EoE, but the goal of treatment is to eliminate the eosinophils in the affected area, thereby alleviating symptoms and reducing inflammation to minimal safe levels. Treating specialists discuss the treatment options with patients/families and tailor treatment to the individual.

In our April/May 2019 survey we asked what the treatments people used to manage their EoE during a flare and their responses to the question are presented in the word cloud below.

How do you treat/manage a flare?

One of the treatment options for EoE is following an elimination diet which is individualized patient to patient but commonly can mean a diet excluding top allergenic foods (milk, egg, fish, shellfish, wheat, soy, peanuts and tree nuts). Unfortunately, research has shown that there is no scientific based test (skin prick test, blood test or patch test) that can reliably indicate the specific food trigger(s) in EoE which is very frustrating for patients. Whilst some patients with EoE also already live with IgE (immediate) food

allergies at risk of anaphylaxis, research[3] has also reported that for patients with EoE that don't previously have any IgE food allergies there is an increased risk of them developing IgE-mediated food allergies including anaphylaxis to a previously tolerated food after a period of prolonged avoidance due to the patient being on an elimination diet for treatment of their EoE.

Patients often feel socially isolated due to following food restrictions and frustrated by the lack of available tests to determine triggers of their EoE.

A survey[4] in June/July 2019 of 108 ausEE members who live with or care for someone with an EGID focused on the impact of these allergic conditions and found that 90% felt that EGIDs impacted on their food budgets and 81% said that medicines and supplements for EGIDs also had a cost impact for them. 55% of respondents reported that having an EGID or caring for someone with an EGID also impacted on the number of hours they could work, and this is significant considering the additional costs families face with food, medicines and supplements. Additionally, 89% of respondents said they had difficulty going to a restaurant and 77% reported being anxious about attending social gatherings and 88% of people sadly found it difficult to go to social occasions/parties/celebrations because of their EGID.

Infants, kids, teenagers and even adults living with an EGID may require a prescribed elemental formula as part of their treatment plan to meet nutritional needs, either for short-term or long-term use depending on the individual and some may require feeding tubes for this and this also comes at additional significant costs and affects quality of life for the patient.

The main issues faced with the current corticosteroid medications used for EoE is that they are asthma medications used 'off label' and as they are not a specific targeted drug delivery indicated for EoE there are varied ways that patients report administering the medication as clinician advice around this can vary greatly. If a patient does not receive EoE remission whilst using the corticosteroid medication like budesonide (Pulmicort) there is left uncertainty if the reason for the treatment results was because of the drug delivery.

Side effects from medications currently used aren't commonly shared about in our support groups by adults living with EoE but some have expressed concerns about long term usage of reflux medication. They are also concerned about risk of long-term tissue damage and chronic inflammation if their EoE is left untreated as uncontrolled EoE can cause scar tissue/fibrosis in the oesophagus and the need for ongoing dilations.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Currently no medications are approved and listed on the Australian Pharmaceutical Benefits Scheme (PBS) for the specific treatment of EoE. Patients currently are needing to use corticosteroid medications typically used for asthma 'off label' for EoE at an increased out-of-pocket cost to patients.

Genetic/precision medicine is the subject of significant research globally and offers the promise of treatment and prevention for some people with rare diseases. This is another area we are following with interest for EGIDs and EoE.

Having a targeted drug delivery of budesonide, as being provided by Jorveza will help patients with EoE as it is a targeted drug delivery that has the potential to induce clinico-pathological remission in adults with EoE that would greatly improve quality of life for patients.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

No patients whose experiences have been shared in this submission have used the drug budesonide – Jorveza as it is not currently available in Australia. However, patients are commonly prescribed budesonide 'off label' in the form of Pulmicort and the liquid ampoules are mixed with sugar, Splenda, apple sauce or other various foods of suitable consistency and made into a slurry to coat the oesophagus.

7. Companion Diagnostic Test

If *the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.*

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- *Access to testing: for example, proximity to testing facility, availability of appointment.*
- *Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?*
- *Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?*
- *How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.*

Not applicable.

8. Anything Else?

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

We look forward to hearing the outcomes of this review as we understand that this product has the potential to be of great benefit to patients with EoE. We thank CADTH for the opportunity to provide our support in this submission process as Canada is 'leading the way' for what we hope will be available one day for Australian patients too.

References

1. What are Eosinophilic Gastrointestinal Disorders (EGIDs)? https://www.ausee.org/whatisegid.htm
2. Online survey completed by 157 people conducted by ausEE Inc. via Survey Monkey in April/May 2019 on EGIDs. https://www.ausee.org/survey-results
3. Cianferoni A, Shuker M, BrownWhitehorn T, Hunter H, Venter C, Spergel JM. Food avoidance strategies in eosinophilic oesophagitis. Clin Exp Allergy. 2019;49:269–284. https://doi.org/10.1111/cea.13360
4. Online survey completed by 108 people conducted by ausEE Inc. via Survey Monkey in June/July 2019 on the Social Impact of EGIDs. https://www.ausee.org/survey-results

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.

No – not applicable

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 – not applicable

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
Nil				

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: Sarah Gray
Position: President
Patient Group: ausEE Inc.
Date: 22 October, 2019

1. **About Your Patient Group (CURED Campaign Urging Research for Eosinophilic Disease)**

CURED is a not for profit foundation dedicated to those suffering from Eosinophilic Gastrointestinal Diseases (EGID), including eosinophilic esophagitis (EoE), eosinophilic gastritis (EG), eosinophilic colitis (EC) and other eosinophilic disorders.

CURED is committed to raising substantial funding to aid in research, advocating on behalf of EGID patients and their families, and working to educate and increase awareness about this complex group of diseases. It is our heartfelt belief that CURED can make a difference for the individuals and their families who are touched by these diseases.

In January 2003, our daughter, Jori, was diagnosed with Eosinophilic Disease.

It took a long time to make that diagnosis. Her red blood levels showed that she was malnourished. She had a lot of stomach aches and nausea. The doctors believed she had Celiac disease. She eventually had an endoscope and when they scoped her they found her stomach filled with inflammation, polyps and severe bleeding.

We had no idea where to turn to. So little was, and still is, known about the illness that we spent hundreds of hours researching where to go and what

to do. We have found some solace through support groups and our journey has brought some wonderful people into our lives.

The one thing we could not grasp was that there is no cure for Eosinophilic Disease. And there is little treatment. This has been the hardest part of all--feeling helpless and watching our daughter suffer. And so began our journey of starting a foundation. With energy and determination that we did not know we had, we elicited the help of family and friends. Within a year, CURED was founded. As it's name suggests, Campaign Urging Research for Eosinophilic Disease we are committed to finding a CURE for Eosinophilic Disease.

We are still amazed at the wonderful response we have gotten. We began CURED at our kitchen table in a northwest suburb of Chicago. We now operate fundraisers across the country. And we are still growing thanks to so many people who have shown how much they truly care.

2. CURED's information is gather from 16 years of speaking with patients and their families.

Hosting education conference with leading research, doctors and patients from around the world. Leading a support group with over 11,000 members. All of our data is collected from patients and families from around the world including Canada.

3. Disease Experience The symptoms and challenges that people experience as a result of Eosinophilic Esophagitis, fatigue, coughing, choking on food, wheezing, shortness of breath, stomach pain, chest pain, nausea, diarrhea, failure to thrive and weight loss. When asked whether this condition affected their day-to-day life, respondents indicated that it did indeed impact greatly their physical and leisure activities, and to a lesser extent, their work, ability to travel and socialize. A few direct quotes are: • "Living life without food is the biggest I have ever had to experience", "EoE affects all aspects of my day-to-day life. I struggle to keep my symptoms under control." • "I have to take many medications

daily. I watch my triggers. • " My quality of life is effect daily. Imagine living your life without food? Our world revolves around food no matter what the occasion is." • "I cough a lot when I am eating and always fearful of choking on my food or my food getting stuck in my esophagus" • "EoE severely affects my day to day life, restricting many activities and causing time off work. This disease is isolating to say the least." • "My allergies to environmental triggers cause wheezing, shortness of breath and all other symptoms mentioned above." The aspects of the condition that are most important to control for people living with it are first – damage to the esophagus, and second – discomfort and isolation. They would also like to be able to increase their diet and no longer have pain and suffering.

4. There is not current approved drugs for patients with EoE. Experiences With Currently Available Treatments - Treatments tried by the patients that have been diagnosed Floven, Budesonide mixed

with Splenda, Prednisone, Fesenra, Dipilumab and AK002. Current treatments do provide some relief for: damage of the esophagus and allowing patients to slightly increase their diet, but patients indicated they want to experience greater assistance with managing all of their symptoms. The cost burden is an issue, as was the time required to travel to health-care settings, the time required off work for these appointments and the changes to their daily routine to accommodate treatment. Another respondent indicated if their drug plan did not provide coverage, they would not be able to afford the medications.

5. Improved Outcomes Key treatment outcomes of EoE that patients would most like addressed are: reduced pain and nausea, reduced coughing, reduced fatigue and improved appetite. They would like an increased ability to fight infections and to have a higher energy level. Ideally, patients would experience an improved quality of life.

Administration of medication, side effects and cost burden were the three most commonly mentioned things that are evaluated when considering new therapies. “I am extremely fortunate that my insurance covers my medication, otherwise I would be unable to afford it. It has made a huge difference in my quality of life.” “It is disturbing to have to take 6 packets of Splenda with each dose of Budesonide. “I tried mixing it with other compounds and found myself getting sicker.” Now that I am taking more doses, an easier mechanism (a tablet, or something) would be preferable. I just find the taste not palatable as well as worrying about the intake of so much splenda.”

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. No – not applicable

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 – not applicable

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

GlaxoSmithKline, Knopp Biosciences - $0 to $5,000

Adare, Pfizer, Astra Zeneca, Lilly, Sanofi – Regeneron, Tekada - $5,001 to $10,000

Celgene, Allakos-$10,001 to $50,000

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: Ellyn Kodroff:

President & Founder:

CURED Nfp -

Date: October 21, 2019

Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it. We did not receive any external assistance in compiling 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. We did not receive any additional assistance in compiling this submission.

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Jorveza**
Name of the Patient Group	**FABED Families Affected by Eosinophilic Disorders**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	**fabedcharity@gmail.com**
Telephone Number	[redacted]

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

WWW.FABED.CO.UK

FACE BOOK Families Affected by Eosinophilic Disorders

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

[redacted] first set up a support group for Eosinophilic disorders in 2004 as I have 2 children with Eosinophilic Disease. The information provided is through both personal experiences where stated or through the experiences shared by our members and followers over the past 15 years.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

This disease has an impact emotionally, socially, physically and financially. To be able to eat without pain is a human function we take for granted. Eating and sharing food is the centre of all social events it brings us together in family and relationships, work meetings etc. It becomes isolating when you cannot eat the same food as your family friends, colleagues without difficulty i.e. problems swallowing food, choking, chest pain, regurgitation etc. These reactions can be to a known or previously unknown substance making it very difficult to manage. This affects everyone as the sufferer feels embarrassed upset and anti-social and the people around them feel embarrassed for them and awkward if they cannot share the same meal. The process of eating can be difficult and take longer than your eating companions because the sufferer is taking extra time to chew, it may be difficult for the person to talk whilst eating.

Often a sufferer's diet can become extremely restricted whilst trying to discover safe foods this becomes impossible for some to manage whilst others will withdraw from social activities in order to maintain their restrictions. Majority of sufferers will avoid eating out for fear of having a reaction and will choose to carry their own prepared food everywhere. For young children this impacts their daily social lives and friendship development i.e. absence from school, not being invited to sleep overs and Birthday parties etc. In addition to this for adolescents it makes what is already a challenging time feel impossible for anyone to understand what it is like to live with EOE. Throughout this time care givers are required to support them with special diets, emotional support and medical care. Into adulthood this condition impacts your work and social life as it can be very difficult to maintain a special diet or eating habits and when you are unable to manage your symptoms

you then can become unable to attend your normal daily commitments.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

- Restricted diets can leave you nutritionally incomplete unfortunately many patients struggle to access knowledgeable dieticians support.
- Elemental formula is not always prescribed and due to palatability often people will not tolerate the necessary quantity required or manage to maintain compliance of the restricted diet alongside the formula.
- NG tubes and Feeding Pumps MICI buttons etc. are only used in extreme nutritionally required circumstances but in the event, they are, this can have huge impact on daily life for patients and carers and can need 24 hour support.
- Using an asthma pump to deliver steroid treatment by swallowing instead of inhaling can be very tricky as is requires someone to not do what is on the instructions and there are no guarantees that the drug is delivered as needed to treat EOE.
- Using a slurry to deliver steroid treatment is open to many wrong administrations from mixing incorrectly to ingesting incorrectly.
- Many patients struggle to receive the treatments currently available as due to the above difficulties and lack of awareness they are not prescribed.

- Due to lack of awareness sufferers are often having to travel long distances to find appropriate care, this can sometimes take years.
- Lack of management and accessible treatments for EOE symptoms can result in multiple hospital visits, tests and loss of work and school attendance.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

- Patients need a treatment that is specifically designed and prescribed for eosinophilic oesophagitis.
- Patients need clear instructions for a treatment that is easy to administer to maintain compliance.
- Patients consider that unfortunately there may not yet be a magic treatment that cures their chronic condition, but they would hope for something that may improve their day to day quality of life i.e. eating, working and socialising.
- Patients accept that a treatment may only be part of managing their symptoms.
- Patients accept that steroids maybe needed but would prefer to know that they are getting the optimal treatment to the area that needs it i.e. the oesophagus.
- Patients would like to eat without fear of choking or pain.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

As this drug is awaiting HTA approval for funding by NHS we have a limited amount of feedback but as follows is a statement provided by an EOE adult patient who has been taking the drug Jorveza since December 2018

“I have felt a big improvement in my symptoms since taking the drug Jorveza, whilst it has not cured my disease it has made living with it easier. I feel this is due to the convenience and simplicity of taking the right dose of medication in a dispersible tablet, especially when away from home. I am still cautious about eating out in public due to my past experiences but I feel I have had less episodes of choking on food since taking Jorveza. I Know I have been fortunate to be put on this drug as its not widely available in the UK yet. I have had a long history of EOE for which my GP has experienced the difficulties in treating and therefore was able to prescribe it for me. I understand this is not the case for many other patients in the UK.”

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

8. Anything Else?

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

We would ask that in the future you consider this treatment to become available to adolescents and eventually children.

As described previously this condition has a huge impact especially on adolescents when they are trying to develop friendships and independence but sadly they cannot partake in normal social eating without feeling different or suffering the consequences of trying to eat the same foods as their companions.

Many patients will already will be using this medication budesonide or other steroid treatment through asthma pumps and will not be compliant with the swallowing or slurry technic. A dispersible tablet would be a simple alternative treatment that dramaticaly increases the chance of efficacy.

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.

   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.

   Not applicable

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.

   6th February 2018 Dr Faulk Pharma donated £250 towards travel expenses for myself to attend a patient advocacy training summer school by www.eurordis.org

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Dr Faulk at todays exchange rate	421			

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 Cordell
Position:
Trustee
Patient Group:
FABED Families Affected BY Eosinophilc Disorders
Date:
23/10/19

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Jorveza® (budesonide) for eosinophilic esophagitis in adults.**
Name of the Patient Group	**Gastrointestinal Society**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

As the Canadian leader in providing trusted, evidence-based information on all areas of the gastrointestinal tract, the GI (Gastrointestinal) Society is committed to improving the lives of people with GI and liver conditions, supporting research, advocating for appropriate patient access to health care, and promoting gastrointestinal and liver health.

Canadian health care professionals request more than 600,000 of our BadGut® Basics patient information pamphlets each year, and tens of thousands of Canadians benefit from our important quarterly publication, the *Inside Tract*® | *Du coeur au ventre*[MD] newsletter.

Our free BadGut® Lectures from coast to coast cover various digestive conditions for patients, caregivers, and other interested individuals. We also have dynamic websites in English (www.badgut.org) and French (www.mauxdeventre.org), which has had more than 4,600,000 *unique visitors* in the past 12 months. Organized on a number of topics, GI Society support group meetings offer a wealth of information for those newly diagnosed with a gastrointestinal disorder, as well as those who have lived with a condition for years.

Our highly trained staff and volunteers offer additional patient resources, including responding to information requests and participating in community initiatives. Staff and advisors work closely with health care professionals, other patient groups, and governments at all levels on behalf of GI patients. The GI Society, along with its sister charity, the Canadian Society of Intestinal Research (founded in 1976), has supported a number of significant clinical, basic, and epidemiological GI research.

2. Information Gathering

*CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.*

Data for this submission came from a variety of sources, including contact with patients and patient caregivers as well as the results of published studies.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Eosinophilic gastrointestinal disease (EGID) is a rare disease characterized by chronic inflammation in the gastrointestinal (GI) tract caused by a higher than normal number of eosinophils without evidence of other causes (e.g., infections, cancer). More information on our website here https://badgut.org/information-centre/a-z-digestive-topics/eosinophilic-gastrointestinal-disease/.

Physicians classify the disease according to the body tissue where the eosinophils accumulate. Each type of the disease requires long-term treatment. There is no cure for EGID. Eosinophilic esophagitis (EoE) is the most common type of EGID, where there are large numbers of eosinophils found in the esophagus, the tube that carries food from the mouth to the stomach. It can affect people of all ages and ethnic backgrounds, although there appear to be sex and genetic factors associated with the disease. Research has found that 75% of individuals with EoE are male and 70-80% have associated allergic disorders such as asthma, eczema, and seasonal and/or food allergies.

The symptoms of EoE vary for each and can include difficulty swallowing, vomiting, reflux, abdominal and/or chest pain, as well as a failure to thrive in the case of young children. Many individuals with EoE can unfortunately go for years without a proper diagnosis, as the symptoms are often similar to other well-known GI diseases, such as gastroesophageal reflux disease.

Untreated EoE may lead to malnutrition, poor growth, and anemia. In some patients, EoE is complicated by the development of narrowing in the esophagus (strictures) that can cause issues with swallowing and choking.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

There is currently no medication specifically approved by Health Canada for this disease. However, certain medications can reduce the number of eosinophils and improve symptoms and these are in widespread use. Treatment typically focuses on a combination of these medications and dietary therapy.

Individuals with EoE often have high rates of food allergies, and those allergies may be contributing to a high accumulation of eosinophils. Therefore, dietary therapy typically involves following some form on elimination diet. Some of these diets can be extremely restrictive, and the patient might require frequent nutrition counselling, which is often quite costly. These diets can be difficult to follow, and affect the individual's ability to eat in social situations.

When it comes to medications, there aren't many options. Physicians typically prescribe steroids to reduce the amount of eosinophils, but these drugs aren't currently approved for the treatment of EoE.

In cases where EoE can't be controlled with medication or elimination diets, and patients are severely symptomatic, physicians may recommend an "elemental diet", which essentially removes all regular foods and drink from the diet. Patients on this treatment receive nutrients by consuming a cocktail of amino acids, sugars, vitamins, minerals, and fats for approximately four to six weeks.

If an individual is not able to consume enough calories, or does not tolerate the elemental diet, then a feeding tube is required to manage EoE.

If an endoscopy shows that the esophagus has healed, then foods are gradually re-introduced in order to identify the culprits triggering EoE symptoms.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Currently, there are almost no treatments available to treat EoE. For patients, this means that they have little hope of having their disease-state improved. Jorveza®, is the first corticosteroid with an indication for EoE, and it can help those with EoE have a chance at reducing their symptoms and improving quality of life.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

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Studies find that budesonide is an effective treatment option for EoE. In one such study, budesonide treatment resulted in reduced symptoms as well as endoscopic and histologic improvement when compared with placebo. Other studies show similar results, as well as a considerable reduction in eosinophil count. We know that this medication is an effective option for a disease that has few, but it has not been approved for use in EoE until now. Jorveza® can offer patients a medicinal option that reduces symptoms and improves quality of life.

In addition, Jorveza® is an easy medication to take. Patients need to take one pill twice daily for six weeks (or up to twelve weeks if they do not respond adequately) in order to reduce eosinophil count to a more appropriate level.

7. Companion Diagnostic Test

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none				

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: Gail Attara
Position: Chief Executive Officer
Patient Group: Gastrointestinal Society
Date: 2019-10-22