CADTH

CADTH COMMON DRUG REVIEW

Patient Group Input Submissions

Eliglustat (Cerdelga)

(Sanofi Genzyme)

Indication: Gaucher Disease Type 1

eliglustat (Cerdelga) indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 poor metabolizers (PMs), intermediate metabolizers (IMs) or extensive metabolizers (EMs).

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.

The National Gaucher Foundation of Canada — permission granted to post.

CADTH received patient group input for this review on or before February 10, 2017

CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

CADTH

The National Gaucher Foundation of Canada

General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Cerdelga (eliglustat) for Gaucher disease type 1 (GD1).
Name of the patient group	The National Gaucher Foundation of Canada
Name of the primary contact for this submission:	[redacted]
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Website	www.gauchercanada.ca/
Permission is granted to post this submission	Yes

Submitting Organization

The National Gaucher Foundation of Canada is a voluntary group of individuals, families, health professionals and affiliated organizations with the purpose of providing support and information to those afflicted with Gaucher Disease, and their families and caregivers.

Conflict of Interest Declarations

a) *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements: In 2015 & 2016 The National Gaucher Foundation of Canada received unrestricted educational grants, to help fund our patient support efforts, from: Shire Canada, Actelion Pharmaceuticals Ltd, Genzyme Canada, and Pfizer Canada.*

b) *We have NO declaration(s) of conflict of interest in respect of those compiling this submission.*

Condition and Current Therapy Information

Information Gathering

To assess the challenges patients and caregivers face as a result of the disease, and to gain insight into their experiences with therapies used to treat Gaucher disease, The National Gaucher Foundation conducted an online survey of patients and caregivers from February 15 to March 21, 2016. Portions of the survey had a focus on Cerdelga (eliglustat). Additionally, the Foundation reached out to 2 treating clinicians to get their views on issues regarding existing treatments and unmet needs in treating Gaucher disease. This report reflects the results of the survey as well as the input from expert clinicians. A total of 37 individuals responded to the patient/caregiver survey. Respondents identified as "patient" n=32 (86.5%), "caregiver" n=4 (11%) or "other" n=1 (2.5%). The "other" respondent reported as second, non-prime caregiver spouse.

Respondents-by-Country: Canada n=31 (84%), Denmark n=1, Spain n=1, Slovenia n=1, Mexico n=1, Croatia n=1, Germany n=1. 22 of 31 Canadian Respondents identified their province of residence with their province of residence as follows:

BC:	2	MB:	1	QC:	1
AB:	4	ON:	13	PE:	1

We asked: **What type of Gaucher patient are you?** Total Respondents: 36. Thirty-three (33) respondents reported having Type 1 Gaucher disease, 1 reported having Type 2, and 1 reported having Type 3. 1 respondent was unsure. 7 survey participants (6 patients and 1 caregiver) had experience with Cerdelga (4 from Canada, 1 from Germany, 1 from Croatia and 1 from Denmark).

Additional background information about Gaucher disease was sourced from The National Gaucher Foundation of Canada website (www.gauchercanada.ca).

Impact of Condition on Patients

People with Gaucher disease, along with their families, must endure a wide range of emotional, social and physical challenges. Some individuals with Gaucher disease develop life-threatening conditions during childhood, while others do not experience symptoms until they are elderly. Nonetheless, Gaucher disease is progressive and, if left untreated, will usually become worse over time.

When Gaucher disease is diagnosed, frequently after a long diagnostic odyssey, there is often a feeling of uncertainty about the future because symptoms can vary so widely among patients, and can manifest at any time. For Gaucher patients who suffer from pronounced spleen and/or liver enlargement, body image can be a difficult challenge. Children (and adults) may be derided for appearing overweight, pregnant, or peculiar. For children, who can be very conscious of their appearance, the emotional and psychological toll can be significant.

Some Gaucher patients experience tremendous fatigue – resulting from anemia and an enlarged liver or spleen. Severely anemic patients may feel tired even after a full night's sleep, and regular activities may be very difficult and exhausting. Additionally, Type 1 Gaucher patients frequently experience severe bone pain which can often limit normal activities, make slight movements painful, make sleeping difficult, and may require hospitalization. For children, bone pain, and other physical manifestations of the disease, serve to limit their ability to participate in many activities and isolate them from their peers.

We asked patients in the survey: **What symptoms of Gaucher disease have had the most impact on you, or on the person under your care? (Select all that apply).**

Answer Choices	Responses	
Low red blood cells and platelet counts	**86.11%**	31
Bone pain & bone breaks/fractures	**66.67%**	24
Easy bruising	**66.67%**	24
Fatigue	**66.67%**	24
Aching joints	**55.56%**	20
Enlarged belly (from enlarged liver and spleen)	**52.78%**	19
Nose Bleeds	**47.22%**	17
Delayed growth (in children)	**16.67%**	6
Reduced appetite	**11.11%**	4
Total Respondents: 36		

***We asked*:** How has Gaucher disease had an impact on your life (or on the life of the person under your care)? Pick all that apply.

Answer Choices	Responses	
Impact of pain on work, career or recreational activities	**70.97%**	22
Psychological distress (mood changes and anxiety)	**45.16%**	14
Difficulty coping with diagnosis	**22.58%**	7
Total Respondents: 31		

Addition comments (other):

- *heavy nose bleeds*
- *The infusions have had the most impact on my schedule and budget.*
- *Total Hip Replacement by age 44*
- *No huge impact*
- *No real impact on my life*
- *I don't think it impacts my life.*
- *Realizing he is different from other kids*

We asked the open-ended question: ***How do symptoms and problems associated with Gaucher disease impact your day-to-day life and your quality of life? (For example, are you able to manage your family obligations? work? school? exercise? volunteer? etc.)*** Total Respondents: 28. Sample of responses:

"The many appointments and the time it took to go to the hospital every 2nd week for an afternoon of infusion, was the biggest impact on my life. It just took quite a bit of time. That said, I am grateful to be able to have infusions and thus, better health, so all the time taken was and is worth it."

"The most difficult aspect of this disease is its effect on my bones. I live with chronic bone pain. I have little stamina for either physical or social activities. My legs are weak and my mobility is restricted. The acute episodes of bone pain I experience are extremely difficult. I become lethargic and have little strength for basic daily activities."

"Pain (spleen) has sometimes curtailed activities. Risk of severe bruising/bleeding a constant concern and has limited physical activities."

"..osteoporosis and two fractured femurs--both problems associated with Gaucher disease--have dramatically affected my life. I used to enjoy hiking, golf, and biking and because of pain I have not been able to do these things (let alone take a brisk walk) for the past year. I've also cut back on a volunteer job that required a lot of walking. The worst impact has been psychological"

"… fear of bone pain, fear of breaking another bone. My doctor has recommended that I begin infusions a.s.a.p. because the best way to treat bones in Gaucher disease is to treat the Gaucher disease."

"Symptoms and problems have been reduced by enzyme replacement therapy, also replacement of both hips and both shoulders."

"Patrick does miss alot of school due to anxiety related issues with his disease"

"..on treatment, my symptoms associated with Gaucher Disease have no impact on my day-to- day life. without treatment i would be unable to continue in my current employment due to pain and fatigue"

"No impact, when i get medication I feel normal" He misses school a lot due to infusions and appointments. He can't participate in some things the other kids do, and if he does he is exhausted the next day.

Findings: Gaucher disease has many impacts on quality of life. Patients find IV infusions to be inconvenient and time-consuming, but recognize the value of treatment. Patients often report that despite therapy, they still experience residual bone disease.

Patients' Experiences With Current Therapy

Gaucher disease-specific treatments have the goal of reducing the amount of glucocerebroside in cells and to minimize the effects of the disease/slow down the worsening of symptoms. There are two main types of disease-specific therapies: enzyme replacement therapy (ERT) and substrate reduction therapy (SRT). ERT addresses the enzyme malfunction by replacing and/or providing additional enzyme (glucocerebrosidase) that a person with Gaucher disease needs, while SRT reduces the production and build-up of glucocerebroside by blocking the absorption of materials (certain carbohydrates) that are used by cells to make glucocerebroside. Drugs approved in Canada for the treatment of Gaucher disease are Cerezyme/imiglucerase (IV) and VPRIV/velaglucerase alfa (IV), both ERTS, and Zavesca (miglustat) - (oral administration) an SRT. Zavesca has limited use in Canada as CEDAC in 2004 had recommended it "*not be listed*". Both ERT therapies (imiglucerase and velaglucerase) require biweekly IV infusions over a lifetime, causing significant interference with school, careers, recreational and domestic activities. Further, current ERT therapies are associated with limited tissue distribution --- which may explain why bone manifestations, despite treatment with ERT, remain among the most painful and debilitating impacts of type I Gaucher.

We asked: **If your current treatment is with Enzyme Replacement Therapy (ERT), do you have residual bone disease or skeletal complications despite treatment? Including: bone pain, osteopenia (reduced bone mass), osteoporosis (bones become brittle/fragile), osteonecrosis (bones begin to break down) or joint collapse.** Total Respondents: 30. **50% of patients report residual bone diseases.**

Answer Choices	Responses	
Yes	**50.00%**	15
No	**40.00%**	12
Unsure	**10.00%**	3
Total		**30**

Eleven (11) patient offered comments:

- *honeycomb in bones*
- *from time to time joint pain in particular at left foot*
- *Chronic bone Pain, Osteoporosis*
- *bone pain*
- *I was put on bisphosphonate for osteopenia-- osteoporosis due to Gaucher disease. I suffered two Atypical Femur Fractures as a result of bisphosphonate.*
- *Osteoporosis*
- *Osteoporosis in lower spine and hips.*
- *Bone pain, rib fractures, osteopenia, aching limbs*
- *Fracture in spine*

- *bone pain still an issue*
- *At this point, not too severe*

We Further Asked: **With 1 being "not important" and 5 being "very important" - If you answered "Yes" to having residual bone disease, if a new therapy was available that had beneficial effect on the bone manifestations of Gaucher disease, how important would it be to have that treatment option available to discuss with your doctor?** Total Respondents: 28. 21 respondents answered "5". Weighted Average was 4.50.

	1 not important	2	3	4	5 very important	Total	Weighted Average
(no label)	**3.57%** 1	**3.57%** 1	**7.14%** 2	**10.71%** 3	**75.00%** 21	28	4.50

We Further Asked: **If your current or previous treatment for Gaucher disease was an infused therapy administered in a hospital or clinic setting, how inconvenient do you/did you find that process? With 1 being "not inconvenient" and 5 being "very inconvenient".** Total Respondents: 27. Weighted Average was 3.74. 63% (n=17) answered "4" or "5".

	1 not inconvenient	2	3	4	5 very inconvenient	Total	Weighted Average
(no label)	**3.70%** 1	**18.52%** 5	**14.81%** 4	**25.93%** 7	**37.04%** 10	27	3.74

We Further Asked: **In the treatment of your Gaucher disease, if you were to consider switching to an oral treatment (capsule) taken at home from an IV therapy administered in a hospital, please rank what your main motivations to switch would be? N=28.** 6 (randomized) options were provided. The following are the results in descending order along with weighted average (wa) scores:

- *I am seeking a more convenient treatment. wa = 4.43*
- *I find IV treatment to be disruptive in my life. wa=4.10*
- *I continue to have residual bone disease despite treatment with ERT. wa=3.75*
- *I am seeking a more effective treatment. wa=3.43*
- *I find the infusion/IV process to be stressful. wa=3.26*
- *I have an aversion to needles. wa=2.75.*

Findings: For patients with residual bone disease, a treatment option that offers the potential of having a beneficial effect on the bone manifestations of Gaucher disease is greatly needed. Also, many patients are seeking a much more convenient form of treatment that offers to improve their quality of life and lessen the burden of bi-weekly IV treatment.

Impact on Caregivers

We asked caregivers: **What is your caregiver experience with Gaucher disease? (a) How has Gaucher disease affected your daily routine or lifestyle? (b) What challenges have you had to deal with related to symptoms of Gaucher disease in the person under you care?**

- *Travelling to visit family abroad poses some difficulties due to getting the medication and supplies approved for transport. Other than that our daily routine or lifestyle is not affected. B) The patient could not walk for a period of time due to bone crisis during her childhood which was taxing on me emotionally and physically. I have had to deal with other symptoms early on in the diagnosis but not as much now.*
- *I am always fearful for my son. He feels like he sticks out in a crowd because he cannot participate in most things. We plan our schedule around his appointments, which take us out of province, hotel stay, bridge fees, car rental fees, food, etc...all out of pocket 2-3 times a year. This is not covered by government. Home infusions are handled by a visiting nurse who is afraid of our dogs, so an adult needs to be present with the dogs foe the few hours she is here biweekly.*
- *We have to live with knowing the outcome of our sons life, as he has type 3, We spend a lot of time researching new drugs and therapies. Our other children feel slighted sometimes, by the attention that is needed to care for the brother. Our son has neurological issues, which can lead to Behaviour issues. It's hard to watch your child in pain or going through tests that he doesn't understand, and not being able to do anything for them.*
- *My mother has Gaucher Disease. As she aged, she s able to do less. Therefore, I try to be available to help her physically.*

Information about the Drug Being Reviewed

Information Gathering

The National Gaucher Foundation conducted an online survey of patients and caregivers from February 15 to March 21, 2016. Portions of the survey had a focus on Cerdelga (eliglustat).

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

a) *Based on no experience using the drug, we Asked*: **With 1 being "not important" and 5 being "very important" - If your current or previous treatment for Gaucher disease was administered by IV infusion in a hospital or clinic setting, how important would it be for you to have a treatment option, to discuss with your doctor, that was a capsule/pill that you could take at home?** Total Respondents: 31. Weighted Average was 4.68. 84% (n=26) answered "5".

	1 not important	2	3	4	5 very important	Total	Weighted Average
(no label)	3.23% 1	0.00% 0	6.45% 2	6.45% 2	83.87% 26	31	4.68

b) *Based on* patients' *experiences with the new drug, we asked*: **What side effects (if any) have you experienced using Cerdelga? Pick all that apply.**

Answer Choices	Responses	
Nausea	**0.00%**	0
Back Pain	**0.00%**	0
Diarrhea	**14.29%**	1
Headache	**0.00%**	0
Fatigue	**0.00%**	0
Upper abdominal pain	**0.00%**	0
Pain in extremities	**0.00%**	0
No noticeable side effects	**85.71%**	6
Other (please specify)	**0.00%**	0
Total Respondents: 7		

We asked: **With 1 being "no improvement" and 5 being "significant improvement" please indicate how you feel Cerdelga has improved the management of your Gaucher disease.** 6 patients with Cerdelga experience answered the question. Weighted Average = 4.33

	no improvement 1	2	3	4	significant improvement 5	Total	Weighted Average
(no label)	**0.00%** 0	**16.67%** 1	**0.00%** 0	**16.67%** 1	**66.67%** 4	6	4.33

Some patients provided additional comments:

"Life is so much easier - take the capsule together with my vitamins - don't think about treatment as I did with ERT"

"I participated in the EDGE study out of Mt. Sinai Hospital in Toronto. Over the two years on the drug, my platelets and hemoglobin levels returned to normal. Diagnostic imaging showed shrinking of the size of liver and spleen. I have been off the study drug for 6 months and lab tests show that those hemoglobin/platelets and other markers have returned to pre-study levels."

We asked: **If your previous therapy was an infused (IV) treatment for your Gaucher disease, how important was it for you to switch to a take-home/oral drug. With 1 being "not important" and 5 "very important". Six (6) patients with Cerdelga experience answered the question. Weighted Average = 4.33.**

	not important 1	2	3	4	very important 5	Total	Weighted Average
(no label)	16.67% 1	0.00% 0	0.00% 0	0.00% 0	83.33% 5	6	4.33

***We asked*:** In making your decision to try, or switch to an oral, take-home treatment, what were your main motivators? (Select all that apply)

Answer Choices	Responses	
I found the infusion schedule and the infusion process to be inconvenient	85.71%	6
I was hoping a different treatment would be more effective	28.57%	2
The location for infusions was a long way from my home	28.57%	2
My physician suggested I try Cerdelga	28.57%	2
Enzyme Replacement Therapy is not an option for me	14.29%	1
I have an aversion to needles	14.29%	1
I continued to have residual bone disease despite treatment with Enzyme Replacement Therapy	14.29%	1
I was not responding well to previous treatment	0.00%	0
Total Respondents: 7		

We asked the open-ended question: **Are there any other benefits/Quality of Life improvements as a result of taking Cerdelga?** Five patients offered comments:

"Life is so much easier - take the capsule together with my vitamins - don't think about treatment as I did with ERT. Easier to bring when travel - don't need to be at hospital or at home for treatment"

"Freedom!!! Not living life in 2 weeks intervals... "

"I realize that both the ERT and the oral SRT are very expensive, as is too often the case with rare disorders and orphan drugs. However, mindful of the rising costs of healthcare, I can't help but think that compliant patients like me will cost the health care system much less money over time taking the pills than if I have to get my treatment in a hospital. …"

" my fatigue and bone pain stopped as a result of taking Cerdelga " "Less time spent in hospital environment "

We also asked: **Is there anything else about your experience with Cerdelga that you would like us to know and include?** Two patients offered comments:

"Eliglustat (aka Cerdelga) worked for me and I am distressed that I can't keep getting it having been on the EDGE study for two years. I also realize that patients on the oral drug regime have to be responsible and compliant."

"it greatly helped with my fatigue and bone pain, but gradually my spleen and liver volumes increased and my platelet counts decreased."

Conclusions:

With Gaucher disease patients frequently reporting that existing IV therapies are inconvenient and disruptive to their lives, and additionally reporting residual bone disease despite treatment along with fatigue due to existing treatment, it is clear that effective treatment options are greatly needed.

Patient experience with Cerdelga indicates that this new treatment likely has a beneficial effect on the bone manifestations of Gaucher disease, and that this treatment seems to cause less fatigue. Also, many patients indicate that there is a significant improvement in their quality of life due to the elimination of the burden of bi-weekly IV treatment.