Stakeholder Input

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Appendix 2: Stakeholder Input - Patient

Name of Drug: Eltrombopag
Indication: For the treatment of adult patients with severe aplastic anemia (SAA).
Name of Patient Group: Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC)
Author of Submission: Adam Waiser (consultant) in cooperation with Cindy Anthony of AAMAC

1. About Your Patient Group

In 1987, the concerned parent of a child with aplastic anemia founded the Aplastic Anemia Family Association of Ontario. One of the very first goals of the Association was to advocate for the formation of a national bone marrow donor registry in Canada. Today, the Aplastic Anemia and Myelodysplasia Association of Canada (AAMAC) is a federally incorporated and a registered national charity with the ambitious goal of providing a seamless support network for every Canadian patient, family member, friend and concerned healthcare provider dealing with aplastic anemia, myelodysplasia or PNH.

Led by a volunteer board of directors and a distinguished team of medical advisors from across Canada, the Association has a number of provincial chapters. The Association relies heavily on the generosity of individual donors and volunteers, including chapter coordinators, to provide an array of essential programs and services.

AAMAC Website

2. Information Gathering

AAMAC collected the data for this submission from an online patient survey combined with telephone interviews of patients with eltrombopag experience. Links to the survey were sent via e-mail to people registered through the AAMAC database. The survey had a combination of multiple choice, rating and open-ended questions. The questions asked about the impact of severe aplastic anemia (SAA) on the lives of patients and the efficacy of current treatments. The survey also posed questions specifically directed to patients with eltrombopag treatment experience. Comments reflecting the majority sentiment are included to provide a deeper understanding of patient perspectives.

A total of 11 patients with SAA completed the survey between May 2 and June 20, 2023.. All 11 respondents were from Canada, representing British Columbia, Alberta, Manitoba, Ontario and Quebec. Of the 11 respondents, 9 had treatment experience with eltrombopag. Five (5) respondents with eltrombopag experience agreed to participate in telephone interviews with the consultant to discuss their treatment experience and elaborate on their feedback.

3. Disease Experience

The most commonly cited symptoms of SAA were fatigue (100%, n=11), unexplained or easy bleeding (82%), shortness of breath (64%), dizziness (46%) and rapid or irregular heart rate (46%).

Several respondents also described brain fog associated with SAA:

- “When you have low hemoglobin, you’re not as mentally sharp. If you have to rush with something, you get confused.”

- “I was making mistake. I was sometime walking into walls.”
- “I don’t stay in social situations. I can’t keep up with them, so I avoid social situations.”

General comments about living with SAA included:

- “Your quality of life is significantly impacted. You’re completely dependent on the healthcare system for support to live.”
- “Perform monthly blood test to monitor counts causes anxiety and worry. Constant stress and concern of other diseases manifesting from underlying condition.”
- “Fearful because you don’t know what going to happen in the future because of the limited treatment options in the future.”

4. Experiences With Currently Available Treatments

All 11 respondents provided information about the treatments that they have received since their diagnosis. A large majority of respondents were treated with cyclosporine, anti-thymocyte globulin (ATG) and blood transfusions. No other treatment was reported by more than 2 respondents.

Treatments Received	n	Treatments Received	n
Cyclosporine	11	Leukine (sargramostim)	1
Anti-thymocyte globulin	10	Neulasta (pegfilgrastim)	1
Blood transfusion	9	Epogen (epoetin alfa)	1
Tacrolimus	2	Platelet transfusion	1
Bone marrow transplant	2	Danazol	1
Neupogen (filgrastim)	2		

A plethora of side effects were reported as a result of these treatments: increased hair growth (73%, n=11), hand or foot numbness (73%), headache (64%), hives (64%), nausea (55%), vomiting (46%) and high blood pressure (46%).

Nausea and headaches were most commonly cited as the side effects that were most difficulty to tolerate.

Cost of treatment was the most commonly cited difficulty for accessing treatment, followed by the travel distance to access treatment and the unavailability of treatment in Canada. Fifty-five percentof respondents needed financial assistance to deal with the costs associated with SAA or its treatment.

When asked about their overall experience with treatment for SAA, these were some of the responses:

- “Very hard on the body, both physically and mentally. Pain and discomfort. Quality of life severely decreases.”
- “Les effets secondaires de la cyclosporine étaient énormes et très très fort.”
- “The bone marrow transplant was very difficult due to the high doses of chemotherapy and the full body radiation. Neupogen causes me extensive bone pain. Epo I found gave me energy and made me feel like I had been topped up with an infusion.”

5. Improved Outcomes

AAMAC asked patients to evaluate the importance of different outcomes for their SAA treatment on a scale of 1 (not important) to 5 (very important). Every outcome received an average score of 4.5 or higher. However, limiting long-term disease consequences and preventing relapse were both given the highest possible rating by every respondent. This would suggest that patients prioritize these health outcomes over quality of life considerations like reducing symptoms or managing side effects.

Importance of outcome	Average (n=89)
Limiting long-term disease consequences	5.00
Preventing relapse	5.00
Improving complete blood count (CBC) and reticulocyte count	4.82
Improving quality of life	4.64
Reducing SAA symptoms	4.55
Managing treatment side effects	4.50

Respondents were also asked if they would be willing to tolerate new side effects from therapies that can reduce SAA symptoms and limit long-term disease consequences. On a scale of 1 (will not tolerate side effects) to 10 (will tolerate significant side effects), respondents gave an average score of 7.18, supporting a conclusion that patient values prioritize health outcomes in SAA treatment.

6. Experience With Drug Under Review

Of the 11 respondents, nine had treatment experience with eltrombopag. At the time of the survey, five respondents had received eltrombopag for 0-6 months, 1 respondent had received it for 6-12 months and three had received it for more than one year.

Four of the respondents are still being treated with eltrombopag, three completed the course of treatment, one stopped treatment because the clinical trial in which they were participating had ended, and one ended the treatment because it didn't work.

Respondents sometimes received eltrombopag in combination with other drugs, including cyclosporine, tacrolimus, danazol, anti-thymocyte globulin and everolimus.

Quality of Life

Patients were asked to rate the change to their quality of life on eltrombopag compared to other treatments they had received on a scale of 1 (much worse) to 5 (much better). The average scores indicate that respondents believe that

eltrombopag had positive impact on all aspects of their life. However, the largest beneficial change was to their complete blood count (CBC) and reticulocyte counts, one of the health outcomes identified as a patient priority.

Change to quality of life on eltrombopag	1 – much worse	2	3	4	5 – much better	Average
Complete blood count (CBC) and reticulocyte count	0.00% 0	0.00% 0	11% 1	11% 1	78% 7	4.679
SAA symptoms	0.00% 0	11% 1	11% 1	11% 1	44% 4	4.147
Treatment side effects	0.00% 0	22% 2	22% 2	0.00% 0	22% 2	3.336
Quality of life	0.00% 0	0.00% 0	22% 2	11% 1	67% 6	4.449
Ability to work	0.00% 0	0.00% 0	22% 2	11% 1	56% 5	4.388
Ability to sleep	0.00% 0	0.00% 0	44% 4	0.00% 0	44% 4	4.008
Ability to care for children	0.00% 0	0.00% 0	22% 2	0.00% 0	44% 4	4.336

Side Effects

Muscle aches (43%, n=7) was the most commonly reported side effects of eltrombopag, followed by liver problems, diarrhea and nausea (29% for all). However, respondents overwhelmingly described these side effects as tolerable.

When asked how much they could tolerate the side effects associated with eltrombopag on a scale of 1 (completely tolerable) to 10 (completely intolerable), the average score was 8.6 with no respondent giving a score lower than 5.

It should be noted that some patients reported that they were not always sure which side effects were due to eltrombopag and which were due to other drugs they were concurrently receiving.

Overall Experience

When patients were asked to describe their positive and negative experiences with eltrombopag, these were some of their comments:

- Positive in that my platelet count has improved, blood sugar and pressure are stabilized. Fatigue and chest tightness have dissipated and I have begun trying to regain my previous ability to resume activities. Nothing negative that I can't tolerate.
- Within three weeks or so, it really picked everybody up because they saw my results and they saw a change in my demeanor.
- I'm not normal, but pretty close to normal.

- If I had to, I'd do it all over again.

7. Companion Diagnostic Test

n/a

8. Anything Else?

Caregivers

One section of the survey asked the caregivers for SAA patients to describe the effect of eltrombopag on the person for whom they were caring. These were some of the comments:

- "The totality of the medications my husband received were very effective and continue to be so. I am aware of the effect of Eltrombopag on outcome results so was extremely grateful he was able to receive it."
- "He got his life back, no more awful side effects and regained energy, interest, positive outlook and ability to return to activities. Hard to watch an active person just sit without energy."

Patient Recommendation

When asked if they would recommend eltrombopag to other patients with SAA, eight respondents said that they would and one said that they would not.

Asked to elaborate, respondents commented:

- "I believe Elrombopag reduced my recovery time from when I started ATG therapy and to when my bone marrow was able to start producing red/white blood cells without the need of blood transfusions. Approx three weeks after ATG/Cyclo therapy and starting Eltrombopag, I no longer need blood transfusions."
- "If patients were allowed treatment to this medication, it would greatly improve a lot of individuals' lives."
- "Hard to assess question as I was not on it long and it didn't help me at all."
- "I do firmly believe that it supports and had a benefit to my treatment journey and allowed me to go into full remission."

Key Points

1. Eighty-nine percent of respondent who received eltrombopag said that they would recommend it to other patients with SAA.
2. Current SAA therapies have extensive side effects.
3. Patient values prioritize long-term health outcomes.
4. The outcomes reported by respondents who received eltrombopag were overwhelmingly positive.
5. Eltrombopag improved the average quality of life for respondents in every listed category.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, 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.

   Adam Waiser, an independent consultant, completed this submission with assistance and oversight from AAMAC staff.

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.

Adam Waiser, an independent consultant, created the surveys, conducted the telephone interviews and analyzed the data for this submission with assistance and oversight from AAMAC staff.

List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis		X		
Taiho		X		
Takeda		X		
BMS			X	
Alexion			X	
Sobi			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: Cindy Anthony
Position: Executive Director
Patient Group: Aplastic Anemia & Myelodysplasia Association of Canada
Date: June 19, 2023