

CADTH COMMON DRUG REVIEW

Patient Input

TELOTRISTAT (Xermelo)

(Ipsen Biopharmaceuticals Canada Inc.)

Indication: carcinoid syndrome

CADTH received patient input from:

Carcinoid Neuroendocrine Tumour Society – Canada

October 19, 2018

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1. About Your Patient Group

CNETS Canada is a registered Patient Group with CADTH. CNETS Canada is widely recognized by patients and the medical community across Canada as an organization that helps improve the quality of life and survival for NET patients by raising awareness of the disease and the latest available diagnostics and treatments; making sure that patients, caregivers, health care professionals and others have the information they need in the areas of medical and scientific research, treatment and support; and by supporting patients and helping them navigate the best care options.

CNETS Canada provides support and education for Canadians on all aspects of NeuroEndocrine Tumours (NETs). We help Canadian NET patients seek and obtain personalized diagnostic and therapeutic options. We also advocate on behalf of individual patients and for policies to support NET patients. The organization does its work in collaboration with medical and scientific experts, stakeholders and partner associations.

2. Information Gathering

CNETS Canada used an online questionnaire (SurveyMonkey) to collect both qualitative and quantitative information from NET patients for our submission to CDR on Telotristat for the treatment of refractory carcinoid syndrome, primarily diarrhea (in patients inadequately controlled by SSA therapy alone), as an adjunct to somatostatin analogue (SSA) therapy.

The online survey was promoted on the CNETS Canada website, Facebook page and Facebook closed support group. Survey responses were confidential and anonymous.

The online survey for patient feedback on Telotristat was open from September 3, 2018 to September 29, 2018.

Demographics:

- **10** Neuroendocrine cancer (NET) patients and **1** caregiver provided input to CNETS Canada's submission on Telotristat.
- **7** male and **3** female NET patients
- Age range: 30-39 (3), 40-49 (0), 50-59 (1), 60-69 (2), 70-79 (4)
- **10** patients were treated or currently being treated with Telotristat.
- Patients are from British Columbia (0), Saskatchewan (0), Alberta (2), Manitoba (1), Ontario (4), Quebec (1), Nova Scotia (0), New Brunswick (1), Newfoundland (0), Outside of Canada (1)

3. Disease Experience

Impact of NETs on Quality of Life

The majority of NET cancer patients report a negative impact on their quality of life.

Background (Global NET Patient Survey)

The International Neuroendocrine Cancer Alliance (INCA) and Novartis Pharmaceuticals Corporation collaborated on the first global survey to gather data on the NET patient experience. The goal of the Global NET Survey was to "increase understanding of the experiences, needs and challenges of NET patients, and to provide insights and learnings among countries and regions to advance NET care." 1928 NET patients responded to the survey worldwide. The study found that most NET patients' quality of life was negatively affected.

The study results showed that decreased energy levels and emotional health issues were very common among respondents. Patients also had to make necessary lifestyle changes around diet, physical activity, and spend more time and money on appointments. Their work life was also negatively affected. 80% of those patients not working were not able to work because of their NET. A further 50% of those patients working had to often miss work because of their disease.

Disease Impact on Quality of Life

The 10 patients who completed the online survey were asked to **rate how symptoms and the disease impacts their day-to-day life and overall quality of life on a scale of 1 - No impact to 7 - Extremely large impact.**

The weighted average rating on: **Impact of NET symptoms on Quality of Life:** Diarrhea (**5.8**), Fatigue/weakness (**4.8**), Flushing/rash (**4.3**), Abdominal Pain (**3.5**), Sweating/ headaches (**3.2**), Anxiety (**2.6**), Breathlessness (**1.7**). Patients rated **Diarrhea** as the symptom that has an extremely large impact on their Quality of Life.

The weighted average rating on: **Impact of the disease on Quality of Life:** Finances (**5.0**), Ability to Work (**4.6**), Energy (**4.5**), Travel (**4.4**), Emotional (**3.9**), Participation in Leisure (**3.6**), Social Life (**3.9**), Relationships (**3.7**).

Patients rated **Finances and Ability to Work** as having the largest impact on their quality of life.

Patients were asked what aspects of the disease are more important to control than others?

90% of the patients who completed the online survey indicated the most important aspect of their disease to control is **diarrhea**. **70%** of patients said that second most important aspect to control is **disease progression and flushing**. **50%** of patients indicated **fatigue** as an important aspect of their disease to control.

4. Experiences With Currently Available Treatments

The 10 patients were asked what therapies / treatments they used to manage NET cancer?

Telotristat (**100%**), Somatostatin Analogs (**100%**), Surgery (**90%**), Liver Embolization (**30%**), Ablative Techniques (**10%**), Chemotherapy (**0%**), Other: alternative therapies (**30%**).

Patients were asked to describe challenges and benefits of current therapies?

Patients described a wide range in both challenges and benefits of the current therapies for patients. At the very best, some patients said the treatments have helped to control symptoms. On the down side, patients indicated the treatments cause long recovery times, debilitating side effects, and complications. No patient reported that the current therapies cured or stopped progression of their NET cancer.

Selected quotes from the online survey:

General challenges with currently available treatments:

- Disease is still progressing
- I have a N.B. Health card which covers the cost. I would be unable to have treatments without it.

Challenges with available treatments excluding Telotristat:

- Not enough control of diarrhea
- 2 mid gut surgeries (2008 and 2011). Still had progression. Went on Sando (2011), then Lanreotide (2016). Needed liver ablation and embolization this year (2018). Ablation and 1st embo seem to have reduced liver tumor load. 2nd embo scheduled for this November to address other side of liver.

Challenges with available treatment including Telotristat:

- Liver embolizations are the hardest to endure, but they provide the most relief. However, that relief

sometimes only lasts a few months. Somatostatin treatment is necessary every 2 weeks to keep my flushing and diarrhea to a minimum. Over time the injection sites have suffered, and there is regular pain due to this. Telotristat has helped with the urgency and consistency of my bowel movements, helping to keep them under control.

- Lanreotide works on symptoms but is inconvenient to have it injected every 3 weeks. The Telotristat also helps the symptoms but to take 6 250mg pills per day is also very inconvenient.

5. Improved Outcomes

The 10 patients who are on or have taken Telotristat were asked why they were prescribed Telotristat?

- Severe diarrhea
- Flushing and diarrhea
- To help manage symptoms, which were medium to high and weren't reduced by other treatments
- To control diarrhea
- Continuing diarrhea

The 10 patients were asked what outcomes were important in evaluating Telotristat?

100% of patients said the most important outcome for treatment with Telotristat was symptom (diarrhea) control. All patients also said that with improved diarrhea control, this would also improve their quality of life.- .e. ability to function socially, more energy, self-esteem.

The 10 patients treated or currently on treatment with Telotristat were asked what were the benefits they received from treatment with Telotristat?

90% - 9 of 10 patients said the Telotristat helped to control the severe diarrhea

The 10 patients were asked what were the negative effects they experienced from treatment with Telotristat?

10% - 1 of 10 patients experienced a rash/hives and had to stop taking Telotristat

10% - 1 of 10 patients said it was inconvenient to carry the pills around with them and pill burden.

The 10 patients were asked to describe the overall impact treatment with Telotristat has had on their health and well-being?

Selected quotes and impact statements from the online survey and patient interviews:

- Huge, I wasn't able to go out for long periods, and was getting very depressed
- Life is much better "bathroom" wise
- Overall it has been a positive impact.
- Feel very positive about daily life. And, partic. in the 3 yr. Clinical Trial assisted certification in Canada (feels very good)
- Improved ability to function socially
- Quality of life has improved
- Not afraid to go out anymore because of an "accident"

6. Experience With Drug Under Review

90% (9 of 10 patients) treated or currently on treatment with Telotristat said they accessed the treatment through a clinical trial. 1 patient said they were forced to pay out of pocket when they did not qualify for a trial.

90% (9 of 10 patients) treated or currently on treatment with Telotristat said they were able to tolerate or manage the side effects of the treatment, having little or no impact on their quality of life. **10%** (1 patient) had to stop Telotristat because they developed a rash.

The benefits and disadvantages of treatment with Telotristat were described in previous sections. **90%** (9 of 10 patients) said the biggest advantage for treatment with Telotristat, that they did not get from other treatments was improved symptom (diarrhea control) and improved quality of life and wellbeing.

7. Companion Diagnostic Test

There is no companion diagnostic test for treatment with Telotristat.

8. Anything Else?

Carcinoid syndrome is caused when neuroendocrine tumours (NETs) release excessive amounts of certain hormones (for example serotonin) into the bloodstream. Typical symptoms of carcinoid syndrome include diarrhea and flushing.

Telotristat works by reducing the action of an enzyme which is involved in the production of serotonin within the tumour. The reduction in the amount of serotonin made by the tumour reduces the number of episodes of diarrhea that patients experience.

Carcinoid syndrome diarrhea, can be extremely debilitating, significantly affecting a patient's quality of life – and many find it to be the most difficult syndrome related symptom to control.

Telotristat has shown effective and is it different from other medicines currently available in reducing Carcinoid syndrome diarrhea, which has a huge negative effect on a patient's quality of life. The lack of symptom control affects patients physically, emotionally and socially in their day to day life.

CNETS Canada respectfully requests that the CDR Canadian Drug Expert Committee (CDEC) issues a positive recommendation for treatment with Telotristat for the treatment of refractory carcinoid syndrome, primarily diarrhea (in patients inadequately controlled by SSA therapy alone), as an adjunct to somatostatin analogue (SSA) therapy.

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
Novartis				✓
Ipsen				✓
Sanofi Genzyme			✓	
Pfizer		✓		
BTG		✓		
AAA		✓		

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: Jackie Herman

Position: President

Patient Group: Carcinoid Neuroendocrine Tumour Society of Canada (CNETS Canada)

Date: October 19, 2018