Common Drug Review
Patient Group Input Submissions

Pasireotide (Signifor) for Cushing's Disease

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
Canadian Pituitary Tumours & Related Diseases Network (PTN) — permission granted to post.

CADTH received patient group input for this review on or before August 28, 2014

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.

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Canadian Pituitary Tumours & Related Diseases Network (PTN)

1. General Information

Name of the drug CADTH is reviewing and indication(s) of interest		Pasireotide (Signifor) for Cushing's Disease
Name of the patient group		Canadian Pituitary Tumours & Related Diseases Network (PTN)
Name of the primary contact for this submission:		[redacted]
Position or title with patient group		[redacted]
Email		[redacted]
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Patient group's contact information:	Email	info@raredisorders.ca
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	Website	
Permission is granted to post this submission		Yes

1.1 Submitting Organization

The Canadian Pituitary Tumours & Related Disorders Network (PTN) is a newly registered not-for-profit organization. It held its first meeting in 2014 under the auspices of the Canadian Organization for Rare Disorders, which continues to provide administrative support. The group will elect a full board and enrol additional members in October and is currently operating under the founding board.

1.2 Conflict of Interest Declarations

The Canadian Pituitary Tumours & Related Disorders Network has no conflict of interest to declare with respect to any corporate members, working partnerships, sponsorship, or funding arrangements.

The Canadian Organization for Rare Disorders, which provides administrative support to TPN, receives unrestricted education grants and conference support from corporations and organizations with general and specific interest in this area, including BIOTECanada, Rx&D, Canadian Institutes for Health Research, Care for Rare Research Program, PRISM (a CIHR-funded project at University of Alberta), Novartis and Pfizer.

[redacted] are employees of the Canadian Organization for Rare Disorders. [redacted] has received travel support and an honorarium from Novartis to present at the Global Pituitary Network meeting in 2013.

2. Condition and Current Therapy Information

2.1 Information Gathering

Information was gathered through focus groups, individual interviews, and a survey provided on Survey Monkey. The participants were recruited from an inaugural meeting of the Canadian Pituitary Network, from support groups in Halifax, Toronto, Calgary/Edmonton, and Vancouver, and through endocrine and oncology clinics. In addition, a request targeted at Cushing's patients with experience using Signifor was posted in two (US-based) websites, The Pituitary Network Association and Cushing's Support & Research Foundation. This was deemed necessary because we knew of no patients in Canada who had accessed Signifor either through clinical trials or early access programmes.

Information was received from 22 Cushing's patients in Canada and six Cushing's patients in the USA. The majority (44%) were between the ages of 40 and 60, with one-third between the ages of 30 and 40 and the remainder evenly split between those over 60 years of age and under 29 years old. Among respondents, 95% identified as having Cushing's Disease (result of pituitary tumour) and the remainder, Cushing's syndrome (not the result of a tumour or adenoma).

2.2 Impact of Condition on Patients

Overall, the Cushing's patients who responded tended to be those who were seriously or very seriously affected. When asked to rate the severity of their symptoms, 100% said they currently or in the past had experienced severe weight gain, with about 60% reporting that the weight gain was "very severe." Moreover, between 50 and 60% said they currently or in the past had experienced "very severe" symptoms of bruising, menstrual or sexual dysfunctions, fatigue or weakness, mood disorders, and cognitive difficulties (thinking or memory). An additional one-third reported these symptoms as "severe." In addition, many had developed secondary conditions; more than half said they had severe high blood pressure, and nearly half said they had moderate to severe bone loss leading to fractures. About one-third had developed mild or moderate hyperglycaemia.

Their ratings of symptoms underscored their descriptions of the impact of their condition. Almost all patients described Cushing's Disease as having had a major and "devastating" impact on their "entire" lives", affecting them physically, psychologically, socially, and financially. "It has ruined my life in many ways. It has changed the way my body looks and how I feel about my body in a very negative way. I struggle everyday not to let this disease get the best of me." "I can no longer drive, go to school, maintain my artistic practice, earn a living, etc. and those are just a few of the pragmatic issues." Even those who have undergone "successful" surgery continue to struggle with the aftermath of the surgery.

"It took over 3-1/2 year's post-bilateral adrenalectomy to see and feel a significant change. The quality of life has not returned to what it was before Cushing's. Today I live steroid dependent and adrenal insufficiency, with a lung tumour, chronic pain on a daily basis; cognitive disabilities (e.g. constantly searching for words, lack of concentration. Short-term memory is a continual battle."

Prior to treatment, almost all experienced tremendous challenges in getting an accurate diagnosis while struggling with the symptoms. "From the time I was 16 to 27, I dealt with the symptoms, not know what was wrong. Weight gain, amenorrhea, acne, striae, depression, HTN, kidney stones, lethargy, dysglycemia. It wasn't until I got into diabetes education as a Nurse Educator that I was able to get to the bottom of it by persisting with a new Endocrinologist." "I gained 180 lbs in 8 months. I was diagnosed with polycystic ovarian syndrome, pre-diabetes, then eventually Cushing's."

About one-third of the patients reported they were no longer able to work, and one-third said they had considerably changed what they did or how much they did.

2.3 Patients' Experiences With Current Therapy

All the patients who responded had undergone surgery to remove their pituitary tumour and/or their adrenal glands. Slightly more than 60% said they had had more than one surgery. In addition, about one-third had received radiation therapy. Almost all (88%) had received medication to control cortisol production, mitotane (Lysodren) and/or metyrapone (Metopirone). Most had or were currently taking medication to control blood pressure and about 12% were receiving medication to manage their glucose levels. More than two-thirds had or were currently receiving medication to manage mood disorders, while about 12% reported receiving medication to treat sexual disorders. None of the Canadian patients had received Signifor (pasireotide), while the six non-Canadian participants had taken Signifor at least once. About 75% had or were currently receiving hydrocortisone (replacement therapy) and a small number (5%) were receiving growth hormone therapy

In terms of effectiveness, slightly more than one-third said surgery was very effective (resolved symptoms) while one-fourth said it was "not at all" effective. The remainder said surgery was "little" or "somewhat" effective. The downside for most was the need for cortisone therapy to treat the resultant (pan)hypopituitarism. About two-thirds of those receiving radiation therapy said it was "effective" or "very effective." Conversely, less than half perceived medication to reduce cortisol levels (when surgery was not successful) as being effective. In terms of secondary symptoms, about half said that their medication to treat high blood pressure was effective while less than half found the drugs to treat mood disorders to be effective and drugs to improve glucose levels or sexual functioning to be mostly ineffective.

About three-fourths of the patients reported serious or very serious side effects to the surgery, and two-thirds experienced the same negative reactions to radiation therapy.

Overall, surgery was considered the most (only truly) effective therapy, often accompanied by radiation therapy, but these procedures were experienced as terrible ordeals. Moreover, they did not work for everyone, and the effects were not necessarily long-lasting.

2.4 Impact on Caregivers

Interestingly, the respondents to the survey all self-identified as patients; there were no caregivers who responded (unusual for a rare and severe condition). This is probably due to the fact that most Cushing's patients are women (used to giving rather than receiving care), and most are in their 30's or 40's (and not able to rely on their children to provide care).

There were some caregivers who did participate in the focus groups (a couple of whom were women whose male partners had Cushing's). They spoke about the tremendous impact on the whole family. "Normal family life and social relationships were just not possible. We never knew from day to day what to expect." "We used to go out a lot but after the Cushing's, my wife was very self-conscious about her appearance and just didn't want to be around other people. I told her it didn't matter but gradually people just stopped asking."

In addition to supporting the patient through the physical and emotional symptoms, family members experienced their own concerns about the future with Cushing's Disease. "Looking back, I don't know how we survived those 10 years not knowing what the problem was. The doctors kept coming up with different diagnoses, but we knew that none of these could be right." Families under these long sieges of uncertainty gradually change. "We had hoped that things would go back to normal once she had

surgery but that never happened." Sadly, about one-fourth to one-third (of the women) had separated from their spouses or partners following the onset of the disease. Many had recreated single lives or were coping as single mothers in addition to dealing with their condition.

3. Information about the Drug Being Reviewed

3.1 Information Gathering

Information was gathered through the same sources as described in Section 2.

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

None of the Canadian patients who responded had experience in using Signifor, but most were aware of the drug and quite realistic about its possible benefits. Most understood it would be used only for those for whom surgery is not an option or not effective. "It would not be applicable to my situation, but one of my friends from the support group would possibly greatly benefit from it as the alternative ketoconazole (antifungal) that she is taking to suppress her cortisol potentially comes with long term risk to her liver." Most are also aware of the very serious potential side effects, egg, "…very good chance of developing diabetes, needs liver toxicity monitoring." However, the comments also spoke to its potential benefit as an alternative to the more drastic adrenalectomy, sometimes performed as a last resort when pituitary surgery or medication doesn't work. "I have hope that it will help to treat the tumour enough so that we don't need adrenalectomies."

Among the six patients from the USA who had experience with Signifor, the experience varied. Two patients reported that they had stopped taking the drug during the first six months because they did not experience a drop in cortisol levels. A third patient stopped because of severe adverse effects, which included stomach pains, diarrhea, and nausea as well as very high glucose levels. Three other patients had been on therapy from six to 18 months and reported a significant impact on both their physical and psychological status. They reported weight loss and/or "loss of fatty tissue" deposits throughout their body. They all said they had more energy and less fatigue as well as a "more positive" outlook. And because they felt better and looked better, they were also "more up for socializing, which contributed to their overall sense of well-being."

4. Additional Information

Most of the respondents did not think Signifor was the right therapy for them; however, 89% said it was "very important" that the remainder said it was "important" that Signifor be available as an option. Ba [Signifor] "provides an alternative for those who cannot have surgery to provide relief of suffering." Similarly, it is necessary "so people who were not "cured" or have no other option can be treated before it's too late." "I think that those with full blown Cushing's, in whom surgery is not an option, need drug options. As many as possible, as safely as possible."

Finally, "Signifier may be one of the last resorts for some people living with Cushing's disease. From what I understand the only thing left would be adrenalectomy. This alone comes with a higher mortality rate just on it's own let alone coupled with Cushing's disease."

Overall, patients are modest in their expectations but nevertheless feel that with a disease with such severe symptoms and so many challenges to treat effective, having a drug that provides another option gives some patients one more chance. Appropriate patients should be given the chance to try the drug under monitored conditions to see if it works and whether they can handle the side effects.