



Section 1 — General Information

Name of the therapeutic review	Pulmonary Arterial Hypertension Therapeutic Review
Name of patient group	British Columbia Pulmonary Hypertension Society (BCPHS)
Patient Group's contact information	BC Pulmonary Hypertension Society 6032 Canada Avenue Duncan, BC V9L 1V3 www.bcpchs.org
Date of submission	October 2, 2013

1.1 Submitting Organization

The British Columbia Pulmonary Hypertension Society (BCPHS) is a charitable foundation that was founded by PH patient Elizabeth McCall in 2001. The mission of the Society is to advocate for those living with pulmonary hypertension, to promote public awareness of PH through education, to provide support to patients and caregivers affected by PH, to support research and education of healthcare professionals, and to raise funds to meet the objectives set by the Society.

1.2 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:**
We do not have any conflicts to declare in this regard.
- b) **We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:**
We do not have any conflicts to declare in this regard.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

Information used to complete this section was gathered by requesting that a number of patients and caregivers living in the Province of British Columbia (aiming to encompass all the various therapies currently available) to respond to questions in sections 2.2, 2.3, and 2.4. Additional information has been added based on the experience gained by volunteering within the PH community for the past ten years and gathering the stories from patients and caregivers, which we have gathered and heard during that time.

2.2 Impact of Condition on Patients

Pulmonary hypertension has a significant impact on the lives of patients. For the most part, it is a disease which most patients have never heard of until their diagnosis. It is a shock and life changing experience for patients and their families to go from being generally healthy, to learning that they have a rare and terminal illness. As diagnosis often occurs in the already late stages of the disease's progression, patients are generally forced to undergo immediate and drastic lifestyle changes. This is a shock to both the patient and their caregivers and surrounding community.

Symptoms and challenges posed by pulmonary hypertension include, but are not limited to:

- Difficulty breathing with exertion
- Dizziness with chest constriction (i.e. bending forward) and with sudden exertion (i.e. standing up)
- Fatigue
- Syncope
- Shortness of breath

The following aspects are those most important to control:

- Breathing ability
- Dizziness and syncope

With pulmonary hypertension, daily life becomes a struggle. Shortness of breath, fatigue, headaches, sleep disturbances, and a low tolerance for physical exertion of any kind make regular household chores and daily events difficult. As this disease affects people of all ages from children to older adults and every age group in between, patients are affected in different ways. Children may be prevented from attending regular school, and adults may not be able to work even part time. Pursuit of even leisure activities can be challenging due to low energy and stamina. The life course of PH patients is interrupted and adapted by the disease, as certain dreams cannot be pursued. As PH affects more women than men, and generally women in their childbearing years, many women must give up their desire to build their own families. This is because pregnancy with PH is dangerous for both the health of the patient and infant, and thus strongly contraindicated. Adults with PH struggle with simple day to day activities such as climbing stairs, walking short distances, carrying things (groceries, children, etc.) Simple activities can lead to exhaustion, shortness of breath and in some cases loss of consciousness for PH patients.

It is impossible for people suffering from PH to plan ahead as they do not know from one day to the next how they will be feeling. Many patients live in fear of what lies ahead for them knowing that they are dealing with a progressive and life-threatening illness. This can lead to further stress and anxiety as it is not known what the future holds. Patients' lives are also largely dictated by the appointments they must keep as there are frequent trips to see the doctor, hospitalizations and routine tests that all take up a great deal of time for patients and often their caregivers as well. Many patients must travel significant distances to see their specialists, which puts an additional burden, physical, emotional and financial on them.

Another major source of frustration for patients living with PH is that it is often times a very "invisible disease" that is not readily apparent to others. Some patients do not look sick and therefore must also deal with social stigmas and are often accused of being "lazy" or of "abusing the system". Because the disease is so unknown, patients are often faced with the need to explain their condition at length to family members, friends, co-workers and even health care professionals who may not be familiar with the illness.

2.3 Patients' Experiences With Current Therapy

There are currently seven (Riociguat for patients with inoperable or residual chronic thromboembolic PH was approved on Thursday, September 19, 2013, as such we do not yet have data from patients on this drug), approved therapies. Approved therapies include: Sildenafil; Ambrisentan; Bosentan; IV epoprostenol (Flolan); Treprostinil; Thermostable epoprostenol (Caripul); Tadalafil

Unfortunately with this disease, the effectiveness of the therapies can vary greatly from patient to patient and most of the different treatments come with a number of adverse side effects. None of the therapies offer cures, however, they do lessen the severity of many of the symptoms and allow many patients to have more quality of life. The effectiveness of therapy varies drastically from patient to patient, with some experiencing a great deal of improvement on a particular therapy while others continue to experience severe symptoms and deterioration of their condition on one or a combination of the available therapies. For this reason, it is extremely important for PH specialists to have the discretion with regards to prescribing therapies for this disease as each patient will have unique reactions to the therapies that are currently offered.

The patients who responded to our request stated for the most part that the effectiveness of the therapies that they are on was fair and was allowing them to “remain somewhat stable” without offering the opportunity to live a normal life/accomplish the tasks that they should be able to do for their ages.

Experience with therapy is generally positive: one of the main benefits is the reduction in lung pressures, decrease in workload demand on the heart and delay of disease progression.

Most patients on therapy also saw an increased ability for light physical activity: for example now able to make the bed, which was impossible before treatment. The medications (particularly IV therapies) help to keep the PH stable and do play a role in increasing the quality of life of the patient.

In addition to the PH-specific treatments they are on, most patients also take diuretics and blood thinners as well as anti-nausea medication in order to control one of the side-effects of PH treatment.

The adverse effects of currently approved medications include:

- Nausea (stated by all patients who provided feedback – most end up having to take anti-emetics to control this)
- Gastrointestinal discomfort and pain
- Diarrhea (particularly IV epoprostenol)
- fatigue
- Insomnia
- Bruising
- Weight gain
- Early onset menopause
- Osteopenia
- Headaches
- Cataracts
- Skin flushing, redness and spots on the skin (IV epoprostenol)

One of the main hardships people discussed as far as accessing therapy was the cost as many were only partially covered or had to fight to get coverage for the therapies they are on. Difficulty in gaining approval for more than one therapy was also an issue. The additional stress of having to fight for coverage adds an additional burden to patients and their families. Some patients have taken the risk of signing up for drug trials in order to take a chance of possibly receiving the drug rather than a placebo as this is their only hope for accessing therapy.

Although a cure is the main need that many patients have described, they are other needs that are not met by many of the current therapies. Many patients find that dealing with therapies requiring 24 hour continuous infusion is very difficult and that the opportunity for new therapies that may alleviate this is very promising and would greatly improve their quality of life. Even on therapy, most patients still experience a number of symptoms and are slightly to greatly limited in their daily lives.

2.4 Impact on Caregivers

Caring for a person living with PH is drastically life-changing for the caregiver as well. Many suddenly find themselves in situations where they are now in need of fulfilling roles to which they were not accustomed or were used to sharing such as: dealing solely with household chores, being responsible for the children, being the sole wage earners for their household and often times needing to mix complicated medications either on their own (in the case of the parents of a child dealing with PH) or assisting their loved one with this difficult task.

In addition, caregivers support patients by attending appointments, helping with managing side effects, mixing medications, and many other duties, such as being responsible for making sure there is back up medication. Caregivers often become the only breadwinners, as well as the main source of support both with housekeeping and childcare duties. In addition to these very demanding roles, caregivers also act as a psychological support base for the patient. They often give up their personal time, and are also living with the disease. In addition, they must live with the very grave reality that there is no cure and that at some point they will likely lose the patient to this disease. Caregivers often face burnout and need many reminders to also care for themselves, something that tends to get forgotten. Relationships, particularly marriages are sometimes victims to the strains of a patient/caregiver dynamic.

Parents who are caregivers to small children affected by this disease live in constant fear. Paediatric PH is often very aggressive and these caregivers do whatever they can to alleviate the impact of the disease on their children. All paediatric medications are used off-label and most of the most effective treatments are extremely invasive (iv epoprostenol for example). These caregivers face not only the regular challenges of raising a child but also worry about things like site pain, swelling, site changes, tape, blood draws and worry about their child progressively getting worse until a transplant is the only option.

Section 3 — Information about New Drugs

3.1 Information Gathering

Information used to complete this section was gathered by requesting a large cross-section of patients and caregivers (aiming to encompass all the various therapies currently available) to respond to questions in section 3.2. Additional information has been added based on ten years of volunteering within the PH community and the stories from patients and caregivers, which we have gathered and heard during that time.

3.2 What Are the Expectations for New Drugs or What Experiences Have Patients Had to Date With New Drugs?

a) Based on no experience using new drug(s):

The patients we have spoken with or received submissions from are for the most part, very hopeful about new drugs and new developments in the field of pulmonary hypertension. They believe that with more studies, trials and new drugs on the market one day the adverse effects of this illness and its side

effects from medications or the symptoms of the illness itself will be narrowed and hopefully a sick person can live better than is possible now, and with a more normal life.

Many of the new therapies that are coming on the market will make life easier for patients in many ways as there are now options that will allow patients more freedom as they may be able to get away from mixing medications daily, from having to carry ice packs all the time and from living with the fear of what could result if there were any complications with medications having very short half-lives.

Patients are looking forward to options that will allow them to live without the need for IV therapies as well as to the development of more improved therapies that will allow them to live life more fully with less complicated treatments, less side effects and ultimately, better quality of life.

b) Based on patients' experiences with new drug(s) as part of a clinical trial or through a manufacturer's compassionate supply:

We have heard from or spoken to a small number of patients who have been or are currently part of clinical trials. They felt that the new drugs were helping to decrease pressures, and delay progression of the disease; they had increased ability to perform daily tasks and an increased ability for light physical activity.

Side effects were rated from mild (nasal congestion, skin flushing) to more severe such as nausea, loss of appetite.

Generally the mild side affects are tolerable, while those that cause severe discomfort and physical reactions (such as nausea etc.) are not. Patients who experienced severe side effects had mentioned not continuing on the drug(s) and/or opting for something else

The new drugs are generally thought of as being easier to use because they were either in oral form or provided other benefits (such as no ice packs, not needing to mix twice a day etc.).

All of the patients who had participated in trials for new drugs believed that they would make significant improvements on their health (mostly from the point of view of delay of progression of the disease) as well as their well being, particularly in light of being able to take on new activities, and feel less shortness of breath and other symptoms. Patients are enjoying every day as a gift, which they would not be able to do without pharmaceutical advancements and the availability of new drugs.

Section 4 — Additional Information

It would be very good to have more time to gather input from patients in order to be able to provide greater feedback. We are a small organization driven solely by volunteers and while we are working closely with other organizations such as PHA Canada to spread the word and gather submissions, with the time constraints we have faced, we have not been able to gather as many submissions as we would have liked.