



## Patient Group Input to CADTH

from: **Pulmonary Hypertension Association of Canada (PHA Canada)**

### Section 1 — General Information

<b>Name of the therapeutic review</b>	Pulmonary Arterial Hypertension Therapeutic Review
<b>Name of patient group</b>	Pulmonary Hypertension Association of Canada (PHA Canada)
<b>Patient group's contact information</b>	1311 Howe Street, Suite 208, Vancouver BC V6Z 2P3 604-682-1036 <a href="http://www.phacanada.ca">www.phacanada.ca</a>
<b>Date of submission</b>	October 3, 2013

#### 1.1 Submitting Organization

The Pulmonary Hypertension Association of Canada (PHA Canada) is a charitable organization established by patients, caregivers, parents and family members collectively referred to as “Canadians living with PH”. PHA Canada aims to end isolation, provide education, support PH patients and their caregivers and create a united Canadian PH community. We strive to connect the PH community from coast to coast to bring awareness to this rare disease. Our membership consists of patients, caregivers, family members and health care workers who are directly affected by and/or involved in the care of patients with and the treatment of pulmonary hypertension.

#### 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:**

PHA Canada has a standing Corporate Committee, where all members of industry involved in research and development and distribution of drugs that which treat pulmonary hypertension are invited to participate. Current members are: Actelion Pharmaceuticals, Bayer Inc, GlaxoSmithKline, McKesson Specialty Pharmacy, Pfizer Canada, Shoppers Drug Mart Specialty Health and Unither Biotech. These members pay yearly dues and participate in discussions at regular, typically semi-annual meetings surrounding the areas of common interest within our community. These members also provide sponsorship funds (in the form of unrestricted grants) which support our programs and campaigns. We feel that bringing all members to the table jointly allows us to eliminate bias in favouring any one company and/or medication.

Our stance is that we support access to any and all medications that have received a Notice of Compliance through Health Canada based on clinical trials demonstrating they are safe and effective in the treatment of pulmonary hypertension. PHA Canada does not favour or recommend any specific treatment, as the critical decision of what course of treatment is best for each individual patient should be determined by his or her PH treating specialist in conjunction with the patient.

**b) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:**

This submission has been reviewed and approved by the Chair of our Board of Directors who has received consulting and speaking fees (Actelion, Bayer, GSK), research grant support (Actelion), and

investigator fees for participation in pharmaceutical clinical trials (Actelion, Bayer, Gilead, GSK, Ikaria, Lilly, United Therapeutics).

## Section 2 — Condition and Current Therapy Information

### 2.1 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 sections 2.2, 2.3, and 2.4. Additional information has been added based on PHA Canada's history of five years of working within the PH community and the stories from patients and caregivers, which we have gathered and heard during that time. *(Please see appendix 1 for a compilation of some of the patient answers to specific questions we posed them)*

### 2.2 Impact of Condition on Patients

Pulmonary hypertension has a significant impact on the lives of patients. Pulmonary hypertension is most often a disease of which the newly diagnosed patient has never heard until the time of diagnosis. It is a shock and life-changing experience to learn that one has a rare, usually progressive and typically terminal illness. Patients and their caregivers go through often abrupt life changes as a result.

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

- Difficulty breathing with any little exertion
- Dizziness with chest constriction (i.e. bending forward) and with sudden exertion (i.e. standing up)
- Fatigue
- Swelling of feet and ankles
- Syncope
- Chest pain

The following aspects are those most important to control:

- Breathing ability
- Peripheral edema
- Dizziness and syncope

With pulmonary hypertension, day-to-day life is made difficult, exhausting and challenging. Activities which many patients cannot do include (depending on the severity/progression of the disease and how effective treatments are): walking any more than short distances without experiencing symptoms; walking inclines or a few steps upstairs at a normal pace; carrying heavy objects (such as laundry, grocery bags etc); lifting medium weight loads (such as a toddler); household chores (such as cutting grass, vacuuming, shovelling); walking long distances (e.g. through an airport); dancing; and exercise (moderate to high intensity). Indeed, patients can struggle with even basic tasks such as bathing, dressing, and in some instances completing simple household chores such as preparing meals, or making a bed.

Planning ahead for activities and tasks is nearly impossible: as pulmonary hypertension symptoms and the related heart failure can fluctuate from day to day, patients may never be certain of how they will feel. Sometimes even getting out of bed is a struggle because of a lack of strength and physical symptoms such as aching legs. Patients learn to cope and look after their necessary daily activities, but at a significantly slower pace. Many patients must travel significant distances to see their specialists, which puts places additional physical, emotional and financial burdens on them.

On a daily basis, patients struggle with the physical symptoms of shortness of breath, fatigue, and a low tolerance for physical exertion of any kind. However, some also experience other general medical symptoms, such as headaches and sleep disturbance. Patients also suffer with a loss of ability to care for themselves and fulfill their roles as caregivers for others. Some struggle with a new limited ability to care for their children. Many patients have to give up careers in the prime of their lives. Women must often give up dreams of themselves becoming parents, as pregnancy in women diagnosed with pulmonary hypertension is often fatal, and thus strictly contraindicated. There are increasing reports from patients and growing recognition in healthcare providers about psychological issues related to PH. Patients commonly experience depressed mood, anxiety, feelings of helplessness and hopelessness as they are faced with a serious illness with a high risk of death within a few years. Although patients often improve physically in response available therapies, side effects and complexities of current therapies contribute to these negative feelings.

An additional major frustration for patients is the fact that pulmonary hypertension most often is an invisible disease. Patients do not look sick when resting or seated, and thus often have to face social stigma. This is exemplified when parking in a handicapped spot and receiving comments of “abusing the system”. As the disease is unknown and misunderstood, many patients struggle with the additional challenge of having to explain their disease due to a lack of understanding from even close family members.

Facing such pronounced challenges in so many aspects of regular day-to-day living results in a severely compromised quality of life for pulmonary hypertension patients.

### **2.3 Patients’ Experiences With Current Therapy**

Patients in Canada with PH are fortunate in that 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 the oral agents: Sildenafil (Revatio); Tadalafil (Adcirca); Ambrisentan (Volibris); Bosentan (Tracleer); and the infusion therapies: IV epoprostenol (Flolan); IV and SC Treprostinil (Remodulin); and IV Thermostable epoprostenol (Caripul).

We have received feedback from patients on most of the above-mentioned medications and of note; all patients were on combination therapy. One person was participating in a clinical trial (AMBITION study), as she was unable to have combination therapy for Tadalafil/Ambrisentan funded in her province. The trial is double-blind, so it is unclear with which exact PH therapy she is currently being treated.

Experience with therapy is generally positive; one of the main benefits is the reduction in the severity of pulmonary hypertension, as measured by reduced pulmonary artery pressures, a resulting decrease in workload on the heart associated with improved cardiac function and blood flow, and some evidence of a delay of disease progression.

The effectiveness of therapy varies drastically from patient to patient, based on many factors: a patient’s age, gender, type of PH, severity of PH, and underlying medical conditions. Some patients experience a dramatic improvement on a particular therapy, with less shortness of breath and other disease-related symptoms, improved ability to function and exercise, and some return to work, caregiver roles, and other social involvement. However, patients with PH are rarely “cured” of their disease. Despite responding to current PH therapies, many patients with PH treated with current PH therapies remain

quite ill with moderate-severe PH and significant ongoing right-ventricular heart failure. As well as patients remaining physically limited with severe symptoms as above, they have to deal with the prospect of more complex medications, possible lung transplantation, and high risk of progressive PH with shortened survival.

Responses to PH monotherapy (single medication) are often limited, such that many patients require consideration of use of two different PH medications con-currently (combination PH therapy). This is especially true for patients with more advanced, moderate-severe PH, which is the stage at which more than half of patients are currently being diagnosed. However, not all patients currently have access to PH combination therapy across Canada, and thus many are still only treated with PH monotherapy with inadequate improvement in their disease. **For this reason, PHA Canada strongly believes that it is extremely important for Canadian PH specialists to have the discretion with regards to prescribing therapies for this disease, as each patient will have unique responses and side effects to the PH therapies that are currently offered.**

Most patients stated that they would consider the effectiveness of current therapies in controlling the condition as being “fair”. While the medication is helping to keep them alive and delaying the progression of the disease, as well as alleviating some of the symptoms and making certain tasks easier, it is not a cure. Patients often remain quite symptomatic and limited, and people continue to die from this disease despite the current available therapies.

Patients also saw an increased ability to carry out 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.

Aside from taking PH-specific treatments, 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-emetic medications to control this)
- Gastrointestinal discomfort and pain
- Diarrhea (particularly IV epoprostenol)
- Fatigue
- Insomnia
- Bruising
- Weight gain
- Headaches
- Skin flushing, redness and spots on the skin (IV epoprostenol)

One of the main hardships people discussed as far as accessing therapy was the initial approval for combination dual therapies, and cost associated with the medicines. Initial approvals were often difficult to obtain and caused hardship and additional stress on the patients and their families. One patient enrolled herself in a double-blinded trial in order to have at least a chance of receiving combination therapy for which she could not get coverage. Additionally, the supplements and treatments needed for dealing with the side effects of the PH medications are not covered and costly.

The main need that patients described, as not being met by current therapies, was a cure for the disease. Additionally, they stated that dizziness and breathing continue to be issues even when on medication. Their daily activities continue to be limited and they are certainly not physically capable of doing many of the things they could prior to their disease. Most patients even when on treatment are unable to work or are limited to very part time work. The difficulties of managing some medications such as IV epoprostenol and the limitations and impact on quality of life that such medications put on the lives of patients was also seen as a need that is not being met.

## **2.4 Impact on Caregivers**

One patient who provided us with feedback best described the impact on caregivers by stating: “If PH patients are suffering from an invisible disability, then their caregivers are even more invisible victims”.

Caregivers are often the main support for the patient. As PH primarily affects women, their husbands and partners are often thrown into very difficult roles: they are financial providers (especially when the patient cannot work, which is more often than not); they take on the bulk of the work around the home (household chores are often a great difficulty for patients); and in many instances, they become the main care provider for any children. In addition, caregivers support patients through attending doctors’ appointments, helping with managing side effects, mixing medications and many other duties.

Not only do caregivers take the brunt of the work around the home and financial responsibilities, they also become psychological support systems for these patients. They often give up their personal time, and are also living with the disease. In addition, they face the very grave reality that there is no cure and that at some point they will likely lose their loved one 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 typically 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 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 PHA Canada’s history of five years of working 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):**

Most PH patients realize that there is no cure for PH, which remains a serious, progressive, and often fatal illness. Although many patients have received the benefit of currently available PH medications,

most of the benefits are limited, such that patients still have moderate-severe PH with significant right-sided heart failure. Most patients realize that research is progressing, and that new medications are being developed, and they are hopeful of more significant benefits.

**b) Based on no experience using new drug(s):**

In general, patients are 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 will be reduced, and hopefully all PH patients will experience improved quality of life.

With the new therapies coming on the market, there are many things that will make life easier for patients. New intravenous infusion medications such as Caripul that have a longer half-life will allow patients who have previously been on intravenous medications requiring daily mixing and constant refrigeration a little more freedom, as they will now be able to avoid mixing their medications daily and will not have to constantly keep their medications on ice.

Patients are looking forward to development of new drugs that will eliminate the need for IV Epoprostenol therapy (oral Epoprostenol analogues, for example). They look forward to new drugs extending the lives of patients, allowing them to have fewer hospital visits and experience fewer side effects.

Most patients are hopeful that new drugs will allow them to return to work, be able to play with their children, be alive long enough to watch their children grow and be have both quality and quantity of life.

Patients also noted that a large expectation they have for new drugs coming to the market was the ability to have more choices in treatment. As patients with this disease all react quite differently to medications, therefore having more options and being able to work with their specialists on finding the right choice and/or right combination of choices, is very important to them. One caregiver stated “He [the patient] has gone through a couple of treatments already, we are getting to the end of options, which is very scary. Options equal hope, and without hope, we have nothing”.

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

Several of the patients who provided their feedback had been and/or were currently part of clinical trials. These patients had often been previously treated with currently available PH medications, but with either minimal or transient response, as the disease eventually progressed, required additional treatment options. Patients felt that the new drugs were helping to decrease pulmonary artery pressure, improve heart function, and delay progression of the disease. They had an increased ability to perform daily tasks and an increased ability to undertake light physical activity.

Side effects were rated from mild (nasal congestion, skin flushing) to more severe such as nausea and loss of appetite). Generally the mild side effects are tolerable, while the more severe discomfort and physical reactions 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. One patient stated that these new drugs are giving her a new lease on life: without the new therapies available to her as part of a trial, she would be packing up her affairs and waiting for death. New advances and technologies give her hope that she will see her son grow up and the continuing research into pulmonary hypertension and new treatments allow her to hope for even more in the future. 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

One of the suggestions that we would have with improving the patient input process is for longer lead times and more time for submissions. We are interested in giving input from as large of a cross-section of our patient population as possible and this often takes time to coordinate.

PHA Canada is currently in the process of seeking patient and caregiver input through a PH-specific formal burden of illness survey. The survey closes on October 25, 2013. We anticipate having high-level preliminary data in early November, followed by a full report in early 2014. The results of this survey will surely be of interest to CADTH as they continue with the therapeutic review of this treatment area.