



Patient Group Input to CADTH

from: **Edmonton P.A.H. (Pulmonary Arterial Hypertension) Society**

Section 1 — General Information

Name of the therapeutic review	Pulmonary Arterial Hypertension Therapeutic Review
Name of patient group	Edmonton P.A.H. (Pulmonary Arterial Hypertension) Society
Patient group's contact information	14412 – 65 Street, NW, Edmonton, Alberta, T5A 2C7
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1.1 Submitting Organization

The Edmonton P.A.H. (Pulmonary Arterial Hypertension) Society also known as EPAHS is a charitable organization formed by a group of patients and caregivers. EPAHS vision is to enhance the life of a patient/caregiver affected by pulmonary hypertension. Our mission is help provide support by way of support group meetings, education forums, healthy recreation for patients and families, to provide emotional support to patients and anyone else affected by PH. We also hold awareness activities to increase the public awareness of this disease. Our members are typically patients and caregivers but also sometimes include other family members, medical professionals, yoga instructors involved in PH, and anyone else affected by PH.

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 have no conflict of interest with any other group or company.

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

We have no conflict of interest in respect of those playing a significant role in compiling this submission.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The information gathered for this submission was gathered from patients and caregivers through a focus group gathering, one to one conversations, and personal experiences.

2.2 Impact of Condition on Patients

The condition related symptoms and problems that impact the day to day life of a patient are difficulty breathing with or without exertion, palpitations or pounding of the chest, chest pain, ankle, leg, and abdomen swelling due to fluid retention, dizziness, syncope (fainting), tingling of hands and feet due to low oxygen levels. PH is a devastating disease and most likely patients are mis-diagnosed with other lung disease like asthma for many years until the right diagnosis is found. This leads to end stage PH and once finally diagnosed the patient has already began experiencing very dangerous symptoms. Every patient is different. The key is early diagnosis.

The following aspects are those most important to control are breathing, peripheral edema, dizziness, syncope, and chest pain.

The condition affects day to day life as follows:

- Lack of energy;
- Unable to take part in activities such as sporting activities which could include soccer, baseball, tennis, walking long distances, walking short distances, swimming, and any other sport activity that involves exertion;
- Taking care of your daily hygiene which could include showering, bathing, and washing hair;
- Unable to do heavy household chores like vacuuming, laundry, washing floors, etc.
- Unable to do light household chores including washing dishes, making beds, dusting and any other activity not included in this list;
- Unable to take part in social gatherings;
- Unable to do errands like shopping for groceries;
- Unable to carry heavy objects like grocery bags, laundry;
- Unable to shovel walks or cutting grass;
- Unable to climb one set of stairs;
- Unable to prepare meals;
- Unable to lift children;

The life of a patient depends on the day. Planning activities and tasks is impossible: PH symptoms and sometimes the patient experiences right side heart failure which could lead the patient to being on bed rest. Patients never know how they are going to feel from one day to the next. It takes a lot of energy to plan your day especially if you have young children. Some patients need to bring in extra help by hiring a nanny. It is a very hard disease to live with and as a result this puts a hardship on the family. Some patients do not have access to PH specialists and as a result require traveling long distances to see a PH specialist which increases the burden of financial, emotional, and physical burdens on the family and patients.

Everyday a patient tolerates with shortness of breath, low energy, limited physical activity, unable to do errands. Some patients experience other general symptoms, such as headaches, muscle aches, and problems sleeping. Some 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 to available therapies, side effects and complexities of current therapies contribute to these negative feelings.

One other aspect to a patient is that patients know they are living with 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. Many patients, on a weekly basis (myself) get rude comments from the general public wanting to know if I was stupid enough to fall asleep in the sun as I look sunburned which is one major side effect to a medication.

2.3 Patients' Experiences With Current Therapy

Patients in Canada with PH can be on one or in most cases is combo therapy which includes the following medications:

- Riociguat (which is for inoperable or residual chronic thromboembolic PH which was just approved on September 19, 2013)
- Sildenafil (Revatio);
- Tadalafil (Adcirca);
- Ambrisentan (Volibris);
- Bosentan (Tracleer);
- IV epoprostenol (Flolan)
- IV and SC Treprostinil (Remodulin); and
- IV Thermostable epoprostenol (Caripul).
- Oxygen and blood thinners
- Diuretics
- Other high blood pressure medications. Please note this doesn't work in every patient and is quite slim.

We have received information from patients who are on the above mentioned medications. I am a patient on Flolan, Revatio and other medications. Most patients are on combo therapies which include three of the medications. Most people have positive feedback and some patients (not all) have some reduced pressures. Some patients also have experienced their heart going back to normal size. However, we still have severe symptoms of PH and although the treatments are good, they are not perfect. The medications have helped patients live longer lives but with much difficulty. No patient is ever cured of the disease. Most patients never are unable to go back to work. This disease is a progressive disease and even with current therapies no one knows for sure how long a patient will survive. Some patients are able to do a bit of exercise however; it takes a patient longer to recover from any sort of physical activity. For instance travel is very hard as a patient who goes away for a few days may take a week or 10 days to fully recover.

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. Most patients with PH who are treated with current PH therapies remain quite ill with moderate-severe PH and significant ongoing right-ventricular heart failure. Many patients will one day need a double lung or double lung and heart transplant. Transplantation is a high risk procedure and has limited chance for survival.

Combination therapy is currently the best option for a patient as it has been proven in patients I have spoken too to prolong their life. Life after all, is the most important and precious gift. We believe that it should be up to the PH specialist on what treatments the patient should be on even if it is a combination of all of the above mentioned medications. We still are not up to standards that USA and Europe have for treating their patients living with pulmonary hypertension.

Some patients consider themselves to be doing okay on the current medications however, some patients did say that they have not seen much improvement. The medication on the most part keeps us alive but is in no way a cure or a good quality of life. Patients do continually decline as the disease progresses and eventually patients die from the disease.

The problem is the current therapies are that most of the medications cause several side effects resulting in the patient taking other medications to combat those new problems. For instance, most patients develop stomach problems resulting in the patient having to take acid reflux medication, develop ulcers, get nausea, severe diarrhea, body aches resulting in the patient taking pain medications, sleep disturbance resulting the patient taking sleeping pills, anti-depressants due to emotional health, and many other medications. Please keep in mind that each patient is different. Some patients develop severe skin conditions requiring prescription creams while others develop condition affecting the other major organs.

Some patients mentioned that they feel the drugs keep us alive while other new therapies come to market and do give us some quality of life.

The adverse effects of currently therapies are:

- Nausea
- Gastrointestinal discomfort and pain
- Diarrhea (particularly IV epoprostenol)
- Fatigue
- Insomnia
- Bruising
- Weight gain
- Headache. Most patients mentioned that headache are migraines
- Bone pain
- Muscle weakness
- Muscle pain
- Jaw pain (epoprostenol)

Costs of medications are expensive and waiting for approval of combined therapies takes too long for a patient who is extremely sick. Normally patients have an extra expense due to all the side effects associated with current therapies. Patients are still in need of better therapies with less side effects and hopefully one day a cure.

2.4 Impact on Caregivers

Caregivers are the means to support of the patient. Without a caregiver most patients would need to have assistance either by living in a continuing care centre or help from a loved one or friend. Caregivers can experience any of the following:

- Stress as to whether or not your partner is going to die;
- Always checking to see if the patient is breathing;
- Helping and mostly maintaining to all household chores, grocery shopping, banking, and other errands;
- Meal planning
- Helping with preparation of medications;
- Picking up medications

- Getting oxygen supplies and making sure there are sufficient supplies at home;
- Many caregivers are absent from work because they need to be at appointments or at home helping their partner;
- Increased stress;
- Lack of looking after self;
- Anxiety;
- Life style change
- Financial hardship
- Raising children

Caregivers get burnt out from all the work at their own jobs, work around the home and financial responsibilities; they also become psychological support systems for these patients. They 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. I have heard of many instances where spouses have not been able to handle the stress of the illness and as result left the marriage. Without the caregiver most patients would have difficulty living on their own.

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 speaking with patients and caregivers (aiming to encompass all the various therapies currently available).

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.

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. We are all hopeful for a cure.

Hopefully, with new therapies it will make life much easier for the patient and caregiver. There is a new intravenous drug called Caripul and as a flolan patient it will make it easier to manage with the day to day mixing of the medication. This medication will allow patients to have a little more freedom in planning activities. The new medication will not require being mixed on a daily basis and ice packs won't be an issue. Everyday a flolan patient must mix the medication and ensure they have adequate ice packs to keep the medication cold at all times.

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 up 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 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".

b) 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

We acknowledge that PH is an orphan disease that affects only a small number of Canadians who are disadvantaged because of expensive treatments. There are only a handful of medications available and patients need to have access to all of them. There is still much research that needs to be done on using these medications that are available and in developing new ones. Any restrictions of access to medications may have a severe consequence for patients and could be life threatening, patients could die. We need all the medications to be approved so that all patients living with PH have a chance for a longer life with less symptoms, less additional medications due to side effects, and for the new patients that will be diagnosed to have a chance at life, so that we can have the same quality life of the rest of Canadians.