

## IN BRIEF A Summary of the Evidence

# Drugs for Pulmonary Arterial Hypertension

## Key Messages

- For people with Functional Class (FC) II or III pulmonary arterial hypertension (PAH), all single-drug therapies appear similarly effective at preventing the disease from worsening. Sildenafil or tadalafil generally provide the best value, so these are preferred first-line treatments for most patients. For people with FC I or IV PAH, there is not enough evidence to make a recommendation.
- Add-on therapy should be offered to patients whose PAH is not controlled with single-drug therapy. Consider the balance of potential benefits versus potential increases in adverse events.
- The decision to change or add therapies should be based on patient-specific factors and response, and should be made by a PAH specialist working in one of Canada's designated pulmonary hypertension centres.

## Condition

Pulmonary arterial hypertension (PAH) is a complex and progressive disease characterized by increased pressure in the pulmonary artery (the blood vessel that carries blood from the heart to the lungs). Patients commonly experience shortness of breath, swelling of ankles and legs, dizziness, or fainting. On average, patients live about five to seven years after diagnosis.

The disease most commonly affects people between 20 and 40 years of age, and is more common in women than men. There are estimated to be between 313 and 767 Canadian adults with PAH.

The World Health Organization has developed a classification system for PAH based on level of function and symptoms. Patients may have Functional Class (FC) I through IV, with increasing numbers reflecting increased severity.

## Drugs

Supportive therapy includes oxygen, diuretics to reduce fluid accumulation, anticoagulants to prevent blood clots, and other measures aimed at treating symptoms. Most patients will require advanced therapy – drugs that aim to treat the disease itself. Eight such drugs are approved in Canada. They belong to four classes:

- prostanoids (injectables: epoprostenol, treprostinil)
- endothelin receptor antagonists (oral: bosentan, ambrisentan, macitentan)
- phosphodiesterase type-5 (PDE-5) inhibitors (oral: sildenafil [both oral and injectable], tadalafil)
- soluble guanylate cyclase (sGC) stimulator (oral: riociguat)

Patients whose disease is not well controlled with a single drug (monotherapy) are usually offered combination therapy with a second drug.

## Issue

PAH is treated in specialized clinics by experts who often need to intervene aggressively against a severe and fatal disease. However, with large variations in practice, and new treatments available, a review of clinical effectiveness, safety, and cost-effectiveness will help to inform decisions about PAH therapy.

## Methods

An expert committee made recommendations based on a systematic review of the scientific evidence for these drugs and an economic analysis.

## Results

The systematic review included 20 unique studies. None of the studies provided direct (“head-to-head”) comparisons of advanced therapies, so a network meta-analysis was conducted to allow indirect comparisons. Most studies measured changes in six-minute walk distance, a measure that does not reliably reflect more important outcomes such as hospitalization or death.

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