

Tadalafil for pulmonary arterial hypertension

Product:

TADALAFIL (Adcirca®)

Class of drugs:

phosphodiesterase inhibitor

Indication:

pulmonary arterial hypertension

Manufacturer:

Eli Lilly Canada Inc.

Highlights of Recommendation:

- ♦ Tadalafil is an oral drug indicated for the treatment of pulmonary arterial hypertension (PAH), a disease characterized by high blood pressure in the artery that carries blood from the heart to the lungs.
- ♦ A clinical study comparing tadalafil to placebo in patients with PAH found that tadalafil 40mg per day improved patients' functional capacity and quality of life.
- ♦ Tadalafil costs \$26.14 per day. Sildenafil, a comparator product in the same drug class, is available at a lower cost.
- ♦ **Overall, the Committee acknowledged that tadalafil provides clinical efficacy in the treatment of PAH but recommended that the drug cost be assessed.**

Background:

Pulmonary arterial hypertension (PAH) is a serious, progressive disorder characterized by abnormally high blood pressure in the pulmonary artery, which carries blood from the heart to the lungs. PAH occurs when the small blood vessels in the lungs narrow, causing pressure to build and back up. Over time, the heart becomes unable to keep up with the extra work needed to pump blood through the lungs, and patients develop right-sided heart failure.

PAH can occur on its own due to unknown causes (known as primary or idiopathic PAH), or as a secondary complication of other conditions such as congenital heart disease, HIV, and connective tissue diseases. Symptoms of PAH include fatigue, dizziness, shortness of breath, chest pain, and a racing heartbeat. As the disease worsens, symptoms may severely limit physical activity.

The goals of treatment are to slow disease progression, relieve symptoms, improve exercise capacity, prevent blood clots, and prolong survival. Standard treatments consist of lifestyle modifications, supplemental oxygen therapy, and conventional medications (e.g. oral anticoagulants, digoxin, calcium channel blockers, and diuretics). In the last several years, drugs specifically developed to treat PAH have become available. These include: prostanoids (epoprostenal, treprostinil); endothelin type A receptor antagonists (bosentan, ambrisentan, sitaxsentan); and phosphodiesterase inhibitors (sildenafil, tadalafil).

CED Recommendation

The CED recommended that tadalafil (Adcirca®) be funded if the drug cost could be assessed, on the basis that tadalafil has shown clinical benefits in the treatment of pulmonary arterial hypertension but a less expensive comparator product is available.

Executive Officer Decision

Based on the CED's recommendation and a cost agreement with the manufacturer, the Executive Officer decided to fund tadalafil (Adcirca®) through the Exceptional Access Program for the treatment of pulmonary arterial hypertension according to specific criteria.

Status

Funded through the Exceptional Access Program.

continued...

Detailed Discussion:

- ◆ In a 16-week, double-blind randomized controlled study (*Galie et al. Circulation 2009*), tadalafil (in various doses) was compared with placebo in 405 patients with primary or secondary PAH. Approximately half of the patients in the study were on background therapy with bosentan.
- ◆ The study showed that tadalafil, administered at a dose of 40mg per day, was superior to placebo at improving patients' six-minute walk distance (a surrogate measure of functional capacity commonly used in clinical studies for PAH). The placebo-adjusted treatment effect in patients taking tadalafil 40mg per day was 26 meters. Patients on tadalafil 40mg per day also demonstrated improvements in several quality of life measures.
- ◆ Response to tadalafil was greater in patients who did not receive background treatment with bosentan. The placebo-adjusted change in six-minute walk distance was 44 meters in patients who received tadalafil without bosentan compared with 23 meters for patients on background bosentan. It was noted that bosentan may increase tadalafil metabolism, thereby reducing tadalafil levels and its treatment effect.
- ◆ Treatment response to tadalafil was similar between patients with primary PAH and those with secondary disease. This is the first clinical study to provide evidence that phosphodiesterase inhibitors are equally effective in both the primary and secondary forms of PAH.
- ◆ The daily cost of tadalafil is \$26.14. Although tadalafil is considerably less expensive than several other PAH treatments, it is more costly than the generic version of sildenafil.
- ◆ **Overall, the Committee noted that tadalafil has been shown to provide clinical benefits in the treatment of PAH but recommended that the drug cost be assessed.**

EAP Funding:

Based on the CED's recommendation and a cost agreement with the manufacturer, the Executive Officer decided to fund tadalafil (Adcirca®) through the Exceptional Access Program (EAP) for the treatment of pulmonary arterial hypertension according to specific criteria.

The EAP criteria can be found at: http://www.health.gov.on.ca/english/providers/program/drugs/eap_criteria.html



Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

For more information, please contact:

Ministry of Health and Long-Term Care

Ontario Public Drug Programs
Hepburn Block, 9th Floor
80 Grosvenor Street, Queen's Park
Toronto, Ontario M7A 1R3
or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html