**Emerging Drug List**

**Bosentan**

**Generic (Trade Name):** Bosentan (Tracleer®)

**Manufacturer:** Actelion

**Indication:** For the treatment of pulmonary arterial hypertension in patients with WHO functional class III and IV primary pulmonary hypertension, or pulmonary hypertension secondary to scleroderma.

**Current Regulatory Status:** Tracleer received a Notice of Compliance on November 30, 2001 and has been marketed in Canada since December 14, 2001.

**Description:** Bosentan is a dual endothelin receptor antagonist with affinity at both the A and B subtypes of receptors. Bosentan decreases both pulmonary and systemic vascular resistance resulting in increased cardiac output without increasing heart rate. Bosentan is available as 62.5 mg and 125 mg tablets. It is initially dosed at 62.5 mg twice daily for four weeks and then increased to the maintenance dose of 125 mg twice daily.

**Current Treatment:** In general, the treatment of pulmonary hypertension consists of an initial vasodilator challenge with prostacyclin, nitric oxide or adenosine to determine whether a patient is a “responder” or “non-responder”. Oral calcium channel blockers are then initiated in patients deemed as “responders”. Treatment with continuous intravenous epoprostenol is reserved for patients deemed as “non-responders” or in “responder” patients that do not attain an optimal response with maximal doses of calcium channel blockers. If intravenous epoprostenol fails to produce improvement, the only options are either a lung or heart-lung transplantation.

**Cost:** The cost for Bosentan is $3,594 for a bottle of 60 tablets (either strength). Therefore, the annual cost of treating pulmonary hypertension with bosentan is $43,128.

**Evidence:** Researchers evaluated the efficacy of bosentan in 32 patients with pulmonary hypertension in a 12 week, blinded, randomized, placebo controlled trial. Patients on bosentan started at a dose of 62.5 mg bid for four weeks followed by 125 mg bid. The primary endpoint was a change in exercise capacity as measured by a six minute walk. At 12 weeks, the distance walked in six minutes improved by 70 m in the bosentan group versus a worsening of 6 m in the placebo group. There was also a significant improvement in the cardiac index, pulmonary vascular resistance, pulmonary artery pressure, pulmonary capillary wedge pressure and mean right atrial pressure compared to placebo (p<0.05 for all). Seven of the 11 placebo patients and 20 of the 21 bosentan patients continued treatment until week 20. At 20 weeks the distance walked in six minutes improved by 77 m in the bosentan group versus a worsening of 15 m in the placebo group. Bosentan treatment was associated with an improvement in NYHA functional class from III to II in nine of 21 patients, with no patients deteriorating.
BOSENTAN

With placebo, one patient of 11 had an improvement from class III to class II and two deteriorated to class IV. The rest did not change.

Commentary:
Bosentan represents a new therapeutic option to parenteral epoprostenol (Flolan®) for the treatment of pulmonary hypertension. The major short coming of epoprostenol is the increased risk associated with the need for long-term intravenous access. Also, patients on long-term epoprostenol appear to develop tolerance to the medication, requiring dosage increases over time.

References:
Tracleer® (bosentan) [product monograph]. Laval (QC): Actelion Pharmaceuticals; 2001 November 16.


This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

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