

Tiotropium for COPD

Tiotropium is a new drug that promises to be a useful addition to current treatments for COPD. This bulletin summarises current evidence and recommendations. It should be read in conjunction with the COPD POEM.

Main Points

- Tiotropium (Spiriva) significantly improves clinical outcomes (dyspnoea, health related quality of life, frequency of exacerbations) compared with placebo and ipratropium.
- It is a convenient once daily bronchodilator that causes a prolonged increase in FEV₁.
- Once daily tiotropium produces a significantly greater increase in trough FEV₁ than ipratropium 4 times daily.
- Tiotropium is at least as effective and may be superior to long acting beta-2 agonists (LABA) in improving clinical outcomes in COPD.
- Trials have mainly involved patients with moderate to severe COPD.
- Spiriva is fully subsidised by Pharmac on special authority according to set criteria.

Tiotropium (Spiriva) Special Authority for Subsidy

Initial application only from a general practitioner or relevant specialist. Approvals valid for 2 years for applications meeting all of the following criteria:

1. To be used for the long-term maintenance treatment of bronchospasm and dyspnoea associated with COPD; and
2. In addition to standard treatment, the patient has trialed a dose of at least 40 mcg ipratropium q.i.d for one month; and
3. The patient's breathlessness \geq grade 4 according to the Medical Research Council (UK) dyspnoea scale. Grade must be stated on the application; and
4. FEV₁ $<$ 40% of predicted (copy of actual result and predicted value to be included in application, or values to be stated on form); and
5. Either:
 - 5.1 Patient is not a smoker; or
 - 5.2 Patient is a smoker and been offered smoking cessation counseling; and
6. The patient has been offered annual influenza immunisation.

The role of tiotropium in the treatment of COPD

Tiotropium (Spiriva) is a long acting anticholinergic bronchodilator that is chemically similar to the short acting bronchodilator ipratropium. Two important features differentiate it from the latter; it is selective for the specific muscarinic receptors that mediate smooth muscle contraction of the airways, and its effects are long acting making it suitable for once daily administration.

In a recent Cochrane systematic review the results of nine RCTs involving over 6,500 patients were pooled (Barr et al, 2005). The trials compared tiotropium with placebo, ipratropium bromide, or long-acting beta-2 agonists (LABA) for a duration of greater than or equal to one month.

In patients with moderate to severe COPD tiotropium reduced COPD exacerbations (OR 0.74; 95% CI 0.66 to 0.83) and related hospitalisations (OR 0.64; 95% CI 0.51 to 0.82) compared with placebo or ipratropium. Based on a 45% baseline risk of exacerbation and a 10% risk of hospitalisation, the NNT with tiotropium for one year was 14 (95% CI 11 to 22) to prevent one exacerbation, and 30 (95% CI 22 to 61) to prevent one hospitalisation compared with placebo and ipratropium. When compared with LABA, reductions in these endpoints were similar.

Tiotropium significantly increased FEV₁ and FVC from baseline compared with placebo, ipratropium and LABA over 6-12 months, and also improved health-related quality-of-life and symptom scores. Tiotropium has a flat dose response curve and doses greater than the standard 18 micrograms per day do not give additional benefits (Gross, 2004).

Comparisons with LABA (not currently funded for COPD in New Zealand) are inconclusive. Two trials found that tiotropium improved FEV₁, and health related quality of life compared with salmeterol over six months. However, another trial found no significant difference between the same treatments in health related quality of life or exacerbation rates at six months. (Clinical Evidence, 12:2004). Further studies are required to assess the effect of tiotropium in mild to moderate COPD and in combination with inhaled corticosteroids and LABA.

Warnings and adverse effects

Tiotropium is contraindicated in patients with a history of hypersensitivity to atropine or its derivatives including ipratropium. It should not be used for the initial treatment of acute episodes of bronchospasm, i.e. rescue therapy, where short acting bronchodilators are indicated.

Dry mouth is the most frequently reported adverse effect and may be slightly more frequent than with ipratropium. Other adverse effects possibly linked to tiotropium include tachycardia, urinary retention and constipation. Patients should be advised to avoid getting the powder in the eye as conjunctivitis and local irritation can occur. As with other anticholinergic drugs, tiotropium should be used with caution in patients with narrow-angle glaucoma, prostate hyperplasia or bladder-neck obstruction.

For more information please refer to the Spiriva medicines data sheet.
<http://www.medsafe.govt.nz/profs/Datasheet/s/Spirivacap.htm>

References

- Barr R, Bourbeau J, Camargo C, Ram F. Inhaled tiotropium for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD002876.
- Kerstjens HA, Postma DS. COPD. Clinical Evidence, 12; 2004.
<http://www.clinicalevidence.com> (Accessed March 2005).
- Gross NJ. Tiotropium Bromide. Chest 2004;126:1946-53.