PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
APC BOARD DATE: 31 OCT 2018
PENDING CCG APPROVAL

NHS Pan Mersey Area Prescribing Committee

TIOTROPIUM inhaler (Spiriva® Respimat®) in adults with asthma

GREEN

The Pan Mersey Area Prescribing Committee recommends the prescribing of TIOTROPIUM inhaler (Spiriva® Respimat®) as an option for patients with poorly controlled asthma who are already on a maintenance dose of inhaled corticosteroid plus a long-acting beta$_2$ agonist inhaler.

Tiotropium 2.5 micrograms/dose inhaler (Spiriva® Respimat®) is not recommended for routine use as add-on maintenance bronchodilator treatment in adult patients with asthma. It may be considered as an alternative to other options for patients with poorly controlled asthma despite using a medium dose inhaled corticosteroid (ICS) and a long acting β_2 agonist inhaler[1,7].

Tiotropium 2.5 micrograms/dose inhaler (Spiriva® Respimat®) is licensed in patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (ICS) (≥800 micrograms budesonide/day or equivalent) and long-acting β_2 agonists (LABA) and who have experienced one or more severe exacerbations in the previous year.

Compared to placebo, tiotropium statistically significantly improved lung function measures and reduced the rate and time to first severe exacerbations in patients with poorly controlled asthma and persistent airflow obstruction who were already treated with an ICS. However, these did not translate into clinically relevant improvements in asthma control or patient quality of life and did not significantly reduce asthma symptom-free days, or use of rescue medication, or asthma-related hospitalisations[2].

The trials excluded patients with COPD, but all patients enrolled in the trials were required to have FEV1 <80% predicted and a ratio of FEV1/FVC <70%, which would place them in the same category of persistent airflow limitation as patients with COPD.

A systematic review and meta-analysis (n=1326) investigated the efficacy associated with long-acting muscarinic antagonists (LAMAs) as add-on therapy to inhaled corticosteroids in patients with uncontrolled, persistent asthma[3]. It concluded that LAMA use was associated with a lower risk of asthma exacerbations compared with placebo. However, adding LAMA, compared with adding LABA was not associated with significant improvements in exacerbation risk. Triple therapy (ICS+LABA+LAMA) was not associated with a lower risk of exacerbations.

Patients with this level of disease severity or instability should be receiving regular reviews of their treatment. Adherence, inhaler technique and discussion of potential trigger factors should be assessed before initiating additional agents in patients who remain symptomatic on ICS and LABA therapy[4].

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

Version: 4.0
Review date: October 2020
(or earlier if there is significant new evidence relating to this recommendation)

TIOTROPIUM inhaler (Spiriva® Respimat®) in adults with asthma

EFFECTIVENESS

Tiotropium was compared against placebo as add-on therapy to high dose ICS and LABA in two, replicate 48-week, randomised, placebo-controlled trials in asthma patients with persistent airflow limitations, who had experience of at least one severe exacerbation in the last year [2].

The changes from baseline in peak and trough FEV1 were statistically significantly greater with tiotropium; however, the improvements were smaller than those normally considered to be clinically meaningful in asthma patients with baseline airways obstruction (e.g. 12% or 200mL). There were no statistically significant improvements for secondary endpoints of symptom-free days or use of rescue medication, and no clinically meaningful improvement in asthma symptom control or patient quality of life. Tiotropium significantly increased the time to first severe exacerbation (needing initiation or doubling of systemic corticosteroids), and significantly reduced the proportion of patients experiencing a severe exacerbation and the number of severe exacerbations per patient year. Number-needed-to-treat to avoid one severe exacerbation was 15. Tiotropium did not significantly reduce asthma-related hospitalisations.

SAFETY

Dry mouth is the most common side-effect of antimuscarinic bronchodilators; also gastro-intestinal motility disorder (including constipation and diarrhoea), cough, and headache; less commonly nausea, gastro-oesophageal reflux disease, dysphagia, tachycardia, palpitation, atrial fibrillation, throat irritation, pharyngitis, dysphonia, bronchospasm, including paradoxical bronchospasm, urinary retention, mydriasis, angle-closure glaucoma, blurred vision, and nasopharyngitis can occur. Dental caries due to dry mouth, and dry skin have occurred rarely [5].

Refer to product SmPC for further information

COST

Drug	Cost per Year (Drug Tariff July 18)
Tiotropium	£276
Montelukast	£14
Theophylline SR	£45 - £107
Double inhaled steroid dose	£54 - £306

Based on an asthma prevalence of 6.5%, 79% of asthma patients being adults and assuming 5-10% of patients may have difficult to treat asthma, there may be as many as 259 - 518 adults with asthma potentially eligible for treatment with tiotropium per 100,000 population. Likely uptake is unknown, however based on an acquisition cost of £276 per patient per year and 10% to 50% of eligible patients receiving tiotropium the potential cost per 100,000 is £7,149 - £71,484.

PATIENT FACTORS

The efficacy and safety of tiotropium in children and adolescents has not yet been established. It should be used with caution in patients with narrow-angle glaucoma, prostatic hyperplasia or bladder-neck obstruction, recent myocardial infarction, unstable or life-threatening cardiac arrhythmia, or hospitalisation due to heart failure within the past year. Plasma levels may be increased in moderate-severe renal impairment [6].

PRESCRIBING INFORMATION

Spiriva Handihaler dry powder device, Braltus® inhalation powder and Spiolto® Respimat® inhalation solution are not licensed in asthma.

IMPLEMENTATION NOTES

Tiotropium may be prescribed where a patient has a diagnosis of COPD as per NICE CG101 COPD and Pan Mersey guidelines on COPD inhaled drug therapy, as well as for patients requiring additional add-on therapies as stated in the British guideline on the management of asthma.

Green drugs are appropriate to be prescribed in primary and/or secondary care.

REFERENCES

1. BTS/SIGN British Guideline on the Management of Asthma, September 2016 (accessed 09/07/2018)
2. Kerstjens HAM, Engel M, Dahl R, et al. Tiotropium in Asthma Poorly Controlled with Standard Combination Therapy. N Engl J Med 2012; 367: 1198-207.
3. Sobieraj DM, Baker WL, Nguyen E, et al. Association of Inhaled Corticosteroids and Long-Acting Muscarinic Antagonists With Asthma Control in Patients With Uncontrolled, Persistent Asthma. A Systematic Review and Meta-Analysis JAMA 2018; 319(14): 1473-1484
4. PrescQIPP Tiotropium bromide (Spiriva Respimat® 2.5 microgram, inhalation solution) in asthma. February 2016 (accessed 12/07/218)
5. British National Formulary (accessed 09/07/2018)
6. SmPC Spiriva Respimat® http://www.medicines.org.uk/emc/ (accessed 12/07/2018)
7. NICE NG80 Asthma: diagnosis, monitoring and chronic asthma management November 2017 (accessed 09/07/2018)
8. NICE ESNM55 Asthma: tiotropium (Spiriva Respimat) March 2015 http://www.nice.org.uk/advice/esnm55 (accessed 12/07/2018)