

**South East London Area Prescribing Committee
Formulary recommendation**

Reference	048
Intervention:	Tiotropium Respimat 2.5 micrograms inhalation solution (Spiriva Respimat®) for the treatment of asthma in adults (Tiotropium is a long acting muscarinic agonist [LAMA])
Date of Decision	February 2016
Date of Issue:	March 2016
Recommendation:	Amber – Initiation by respiratory specialist/ can be initiated in primary care on the recommendation of a respiratory specialist
Further Information	<ul style="list-style-type: none"> • Tiotropium Respimat is accepted for use within South East London as an add-on option for the treatment of adults with asthma at step 4 of the BTS/SIGN treatment algorithm in line with its licensed indication*. • Tiotropium Respimat will be initiated by a respiratory specialist or initiated in primary care on the advice of a respiratory specialist in line with the SEL guideline for asthma. • The alternative add-on options at step 4 of the BTS/SIGN algorithm are: <ul style="list-style-type: none"> - An inhaled corticosteroid at a dose of up to 2000 micrograms per day - A leukotriene receptor antagonist - Theophylline modified release - A slow release beta-2 agonist tablet • Tiotropium has demonstrated statistically significant improvements in FEV1 and reduced exacerbations when compared with placebo at BTS/SIGN step 4 therapy, although the clinical effect was not large. • There are no comparative data between tiotropium and other add-on options recommended at BTS/SIGN step 4. The alternative add-on treatments recommended at BTS/SIGN step 4 currently do not have a strong evidence base for this particular stage of therapy. The recommendations for these agents are mainly based on extrapolation from trials of add-on therapy to inhaled corticosteroids. • Educational and supporting resources for managing patients with asthma in primary care will be developed and made available by the SEL Responsible Respiratory Prescribing Group. These will include resources to support healthcare professionals in primary care to step down asthma treatment when appropriate. <p>*Tiotropium Respimat is licensed for use as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 µg budesonide/day or equivalent) and long-acting beta-2 agonists and who experienced one or more severe exacerbations in the previous year.</p>
Shared Care/ Transfer of care required:	Not necessary – inhalers for asthma are already routinely prescribed in primary care without shared care
Cost Impact for agreed patient group	<ul style="list-style-type: none"> • Based on a budget impact model referred to in the evidence evaluation, direct drug costs for adopting at this stage in therapy might approximately be in the region of £15,000 to £25,000 per 100,000 population. • This equates to between £270,000 to £450,000 for the population of SEL. • Data on exacerbation rate improvement suggests that addition of tiotropium to a therapeutic regimen may reduce the need for hospital admissions and potentially reduce the need for more expensive subcutaneous therapy (e.g. omalizumab), however the incremental benefit of adding this treatment to the options currently available in this regard is not possible to quantify.
Usage Monitoring &	<ul style="list-style-type: none"> • Trusts to monitor and submit usage and audit data on request to the APC.

Impact Assessment	<ul style="list-style-type: none"> • CCGs to monitor EPACT data. • Exception reports from GPs if inappropriate prescribing requests are made to primary care.
Evidence reviewed	References (from evidence evaluation) <ol style="list-style-type: none"> 1. Summary of Product Characteristics, Spiriva Respimat. Available here <accessed 10.01.2016> 2. British Thoracic Society/Scottish Intercollegiate Guidelines Network 2014. British Guideline on the Management of Asthma. Available here. <accessed on 10.01.2016> 3. Global Initiative for Asthma (GINA) 2015. Global Strategy for Asthma Management and Prevention. Available here. <accessed on 10.01.2016> 4. National Institute for Health and Care Excellence, 2015. ESNM 55: Asthma: Tiotropium Respimat. Available here. <accessed on 10.01.2016> 5. Drug and Therapeutics Bulletin September 2015 53 (9) p102-104. Tiotropium – what role is asthma? 6. Royal College of Physicians 2014. Why asthma still kills: the National Review of Asthma Deaths (NRAD) Confidential enquiry report. Available here. <accessed on 10.01.2016> 7. Kerstjens H, Engel M, Dahl R et al. Tiotropium in Asthma Poorly Controlled with Standard Combination Therapy. NEJM 2012 367 (13) p1198-1207 8. Lee S, Kim H, Yoo K et al. Long-acting anticholinergic agents in patients with uncontrolled asthma: a systematic review and meta-analysis. International Journal of Tuberculosis and Lung Diseases 2014 18 (12) p1421-1430. 9. Tian J, Chen J, Chen R et al. Tiotropium versus placebo for inadequately controlled asthma: a meta-analysis. Respiratory Care 2014 59 (5) p654-666 10. Peters S, Kunselman S, Ictovic N et al. Tiotropium Bromide in Step-Up Therapy for Adults with Uncontrolled Asthma. NEJM 2010 363 (18) p1715-1726 11. Price D, Fromer L, Kaplan A et al. Is there a rationale and role for long-acting anticholinergic bronchodilators in asthma? Primary Care Respiratory Medicine. 2014 24 doi:10.1038/npjpcrm.2014.13 12. Ullah MI, Newman GB, Saunders KB. Influence of age on response to ipratropium and salbutamol in asthma. Thorax 1981; 36 p523–529. 13. Connolly MJ. Ageing, late-onset asthma and the beta-adrenoceptor. Pharmacological Therapy 1993; 60 p389–404. 14. Partridge MR, Saunders KB. Site of action of ipratropium bromide and clinical and physiological determinants of response in patients with asthma. Thorax 1981; 36 p530–533 15. Berry M, Morgan A, Shaw DE, Parker D, Green R, Brightling C et al. Pathological features and inhaled corticosteroid response of eosinophilic and noneosinophilic asthma. Thorax 2007; 62: 1043–1049. 16. Pavord ID, Brightling CE, Woltmann G, Wardlaw AJ. Non-eosinophilic corticosteroid unresponsive asthma. Lancet 1999; 353: 2213–2214. 17. Bradding P, Green RH. Subclinical phenotypes of asthma. Curr Opin Allergy Clin Immunol 2010; 10: 54–59. 18. Lazarus SC, Chinchilli VM, Rollings NJ, Boushey HA, Cherniack R, Craig TJ et al. Smoking affects response to inhaled corticosteroids or leukotriene receptor antagonists in asthma. Am J Respir Crit Care Med 2007; 175: 783–790. 19. Chaudhuri R, Livingston E, McMahon AD, Lafferty J, Fraser I, Spears M et al. Effects of smoking cessation on lung function and airway inflammation in smokers with asthma. Am J Respir Crit Care Med 2006; 174: 127–133. 20. Ohta K et al. Long-term once-daily tiotropium Respimat is well tolerated and maintains efficacy over 52 weeks in patients with symptomatic asthma in Japan: a randomised, placebo-controlled study. PLoS One 2015; 10: e0124109. 21. Medicines and Healthcare products Regulatory Agency. Tiotropium: Safety studies of Spiriva Respimat. Drug Safety Update 2011; 4(4): H2 [online]. Available: https://www.gov.uk/drug-safety-update/tiotropium [Accessed 10 January 2016]. 22. Medicines and Healthcare products Regulatory Agency. Tiotropium delivered via Respimat compared with Handihaler: no significant difference in mortality in TIOSPIR trial. Drug Safety Update 2015; 8 (7): 1 [online]. Available here. [Accessed 10 January 2016]. 23. All Wales Therapeutics and Toxicology Centre 2015. Tiotropium (Spiriva Respimat) 2.5 micrograms solution for inhalation. 24. Scottish Medicines Consortium 1028/15. Tiotropium 2.5microgram solution for inhalation.

NOTES:

- a) Area Prescribing Committee recommendations and minutes are available publicly on member CCG websites.
- b) This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
- c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS**