NICE advice

Chronic obstructive pulmonary disease: aclidinium bromide

Evidence summary
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Overview

The content of this evidence summary was up-to-date in January 2013. See summaries of product characteristics (SPCs), British national formulary (BNF) or the MHRA or NICE websites for up-to-date information.

Key points from the evidence

Aclidinium bromide (Eklira Genuair) is an inhaled long-acting muscarinic antagonist (LAMA) for maintenance bronchodilator treatment to relieve symptoms in adults with chronic obstructive pulmonary disease (COPD). It received a European marketing authorisation in July 2012 and was launched in the UK in September 2012.

In people with stable COPD who remain breathless or have exacerbations despite using short-acting bronchodilators as needed, the NICE guideline on Chronic obstructive pulmonary disease: Management of chronic obstructive pulmonary disease in adults in primary and secondary care (partial update) (NICE clinical guideline 101) advises that maintenance therapy can be provided by the following (alone or in combination, with choice depending on several factors; see guideline for details):

- a long-acting beta$_2$ agonist (LABA)
- a LAMA

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- a LABA with an inhaled corticosteroid (ICS) in a combination inhaler.

Evidence from 2 phase III placebo-controlled trials (ACCORD COPD I [n=561, 12 weeks] and ATTAIN [n=828, 24 weeks]) in patients with moderate to severe COPD showed that aclidinium bromide improved disease-oriented measures of lung function over 12 and 24 weeks compared to placebo. A statistically significant improvement was seen in the primary end points; ACCORD COPD I 12-week trough FEV_1 (forced expired volume in 1 second) least squares mean difference 124 ml, ATTAIN 24-week trough FEV_1 least squares mean difference 128 ml, with 400 micrograms aclidinium bromide compared with placebo (both $p<0.0001$). These differences are around the level considered to be clinically relevant (minimum clinically important difference 100 ml).

In the 24-week study, more patients had clinically significant improvements in the patient-orientated secondary outcomes of health status and dyspnoea with aclidinium bromide than with placebo.

The number of anticholinergic adverse events seen with aclidinium bromide (such as dry mouth and constipation) was low, and similar across all groups.

The publication of longer term studies comparing patient-orientated outcomes for aclidinium bromide with other active treatments for COPD would enable its place in therapy to be more clearly established. Local decision makers will need to consider the evidence for aclidinium bromide alongside that for the other treatments for COPD. Individual patient factors and the costs and safety profile of each treatment will need to be taken into account.

Key evidence

Kerwin EM, D'Urzo AD, Gelb AF et al. (2012) Efficacy and safety of a 12-week treatment with twice-daily aclidinium bromide in COPD patients (ACCORD COPD I). COPD: Journal of Chronic Obstructive Pulmonary Disease 9: 90–101

Jones PW, Singh D, Bateman ED et al. (2012) Efficacy and safety of twice-daily aclidinium bromide in COPD patients: the ATTAIN study. European Respiratory Journal 40: 830–6

About this evidence summary

'Evidence summaries: new medicines' provide summaries of key evidence for selected new medicines, or for existing medicines with new indications or formulations, that are considered to be of significance to the NHS. The strengths and weaknesses of the relevant evidence are critically reviewed within this summary to provide useful information for those working on the managed entry of new medicines for the NHS, **but this summary is not NICE guidance**.

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Relevance to NICE guidance programmes

Aclidinium bromide was not considered appropriate for a NICE technology appraisal and is not currently planned into any other work programme.

Introduction

Chronic obstructive pulmonary disease (COPD) is characterised by airflow obstruction that is usually progressive and not fully reversible; it is predominantly caused by smoking[1]. COPD is a common cause of death and long-term disability. According to GP registers, there were nearly 900,000 patients with COPD in England in 2010/11[2]. During the same period there were approximately 120,000 hospital admissions in England in which COPD was the primary diagnosis[3].

The NICE clinical guideline on COPD defines COPD as follows:

- Airflow obstruction is defined as a reduced FEV_1/FVC ratio (where FEV_1 is forced expired volume in 1 second and FVC is forced vital capacity), such that FEV_1/FVC is less than 0.7.
- If FEV_1 is at least 80% predicted normal, a diagnosis of COPD should only be made in the presence of respiratory symptoms, for example breathlessness or cough.

Classification of severity of airflow obstruction in COPD according to NICE guidance is shown in table 1.

Table 1 Classification of severity of airflow obstruction in COPD

Severity of airflow obstruction		
Post-bronchodilator FEV_1/FVC	FEV_1 % predicted	Post-bronchodilator
<0.7	≥80%	Stage 1: Mild[a]
<0.7	50–79%	Stage 2: Moderate
<0.7	30–49%	Stage 3: Severe
<0.7	<30%	Stage 4: Very severe[b]

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Abbreviations: COPD, chronic obstructive pulmonary disease; FEV_1, forced expired volume in 1 second; FVC, forced vital capacity.

[a] Symptoms should be present to diagnose COPD in people with mild airflow obstruction.

[b] Or FEV_1 <50% with respiratory failure.

The NICE clinical guideline on COPD advises that all patients who are still smoking should be encouraged to stop, and offered help to do so, at every opportunity. The guideline recommends the following inhaled treatments for managing people with stable COPD. The list is not comprehensive but does include the key recommendations that relate to this evidence summary and the likely place in therapy of aclidinium bromide.

- Short-acting bronchodilators, as necessary, should be the initial empirical treatment for the relief of breathlessness and exercise limitation.
- In people with stable COPD who remain breathless or have exacerbations despite using short-acting bronchodilators as required, offer the following as maintenance therapy:
    - if FEV_1 is at least 50% predicted: either long-acting $beta_2$ agonist (LABA) or long-acting muscarinic antagonist (LAMA)
    - if FEV_1 is less than 50% predicted: either LABA with an inhaled corticosteroid (ICS) in a combination inhaler, or LAMA.
- In people with stable COPD and an FEV_1 of at least 50% who remain breathless or have exacerbations despite maintenance therapy with a LABA:
    - consider LABA+ICS in a combination inhaler
    - consider LAMA in addition to LABA where ICS is declined or not tolerated.
- Offer LAMA in addition to LABA+ICS to people with COPD who remain breathless or have exacerbations despite taking LABA+ICS, irrespective of their FEV_1.
- Consider LABA+ICS in a combination inhaler in addition to LAMA for people with stable COPD who remain breathless or have exacerbations despite maintenance therapy with LAMA irrespective of their FEV_1.
- The choice of drug(s) should take into account the person's symptomatic response and preference, and the drug's potential to reduce exacerbations, its side effects and cost.

See the NICE pathway on COPD for more information.

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[1] National Institute for Health and Clinical Excellence (2010) Chronic obstructive pulmonary disease: Management of chronic obstructive pulmonary disease in adults in primary and secondary care (partial update). NICE clinical guideline 101

[2] NHS Information Centre (2011) QOF prevalence data tables 2010/11

[3] NHS Information Centre. HESonline. Inpatient statistics, primary diagnosis: 3 character 2010-11

Product overview

Drug action

Aclidinium bromide (Eklira Genuair) is an inhaled LAMA administered using a breath-actuated, multi-dose, dry powder inhaler (the Genuair inhaler)[4].

New therapeutic indication

Aclidinium bromide received a European marketing authorisation in July 2012 and was launched in the UK in September 2012. It is indicated as a maintenance bronchodilator treatment to relieve symptoms in adults with COPD[4].

Course and cost

The recommended dosage is 1 inhalation of 322 micrograms aclidinium twice daily. Each delivered dose (the dose leaving the mouthpiece) contains 375 micrograms aclidinium bromide equivalent to 322 micrograms of aclidinium. This corresponds to a metered dose of 400 micrograms aclidinium bromide (the dose referred to in the clinical studies) equivalent to 343 micrograms aclidinium.

Aclidinium bromide is available in an inhalation device preloaded with 60 unit doses (1 month of treatment) at a cost of £28.60 (excluding VAT; costs taken from MIMS, December 2012). Based on this, the cost per patient per year is £343.20. The breath-actuated device has an end-of-dose lock-out system to prevent use of an empty inhaler, an audible click and colour change window to confirm correct inhalation[4].

[4] Almirall Limited (2012) Eklira Genuair summary of product characteristics

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Evidence review

This evidence review is based on 2 published phase III studies of aclidinium bromide in adults with moderate to severe COPD: the 12-week study ACCORD COPD I and the 24-week study ATTAIN (see tables 2 and 3). Other phase III studies of aclidinium bromide in COPD have been completed but are not published in full. These include the 12-week ACCORD COPD II study (with a 40-week open-label extension)[5], a 52-week extension study to ACCORD COPD I[6], a 52-week safety study[7], and a 6-week study with aclidinium bromide, tiotropium and placebo arms[8].

ACCORD COPD I Kerwin et al. 2012

- Design: 12-week, randomised, double-blind, placebo-controlled, parallel-group study (with 2-week run-in).
- Population: 561 patients (40 years and over) who were current or former cigarette smokers with moderate to severe COPD (post-bronchodilator FEV_1/FVC less than 0.7 and FEV_1 between 30% and 79% of predicted). At baseline, mean age was 64 years and mean FEV_1 was 47% of predicted. Before screening, most patients in all treatment groups used COPD medications (64% used short-acting $beta_2$ agonists (SABAs), 38% used a LABA+ICS, 30% used a LAMA, 8% used ICS, 5% used a LABA, and 5% used short-acting muscarinic antagonists (SAMAs). SABAs and ICS could be continued throughout the study but SAMAs, LAMAs and LABAs were stopped.
- Intervention and comparison: twice-daily aclidinium bromide 200 micrograms, 400 micrograms or placebo, all using a multiple-dose dry powder inhaler (Genuair).
- Outcome: the primary efficacy end point was change from baseline to week 12 in morning pre-dose (trough) FEV_1. The secondary efficacy end point was change from baseline to week 12 in peak FEV_1 (within 3 hours of morning dose). Both analyses were based on the intention to treat population. Health status (St George's Respiratory Questionnaire [SGRQ]) and dyspnoea (Transitional Dyspnoea Index [TDI]) were also assessed.

Table 2 Summary of the ACCORD COPD I study: Kerwin et al. 2012[9]

	Aclidinium bromide 200 micrograms bd	Aclidinium bromide 400 micrograms bd	Placebo	Analysis
Randomised	n=185	n=190	n=186	

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Safety population[a]	n=184	n=190	n=186	
ITT population[b]	n=184	n=190	n=185	
Completed study	n=152	n=166	n=149	
Efficacy (ITT population)				
Primary outcome: change from baseline to week 12 in morning pre-dose (trough) FEV_1	LS mean 62 ml (SE 15 ml)[c]	LS mean 99 ml (SE 15 ml)[c]	LS mean −25 ml (SE 15 ml)[c]	LS mean difference over placebo 86 ml (95% CI 45 to 127 ml, p<0.0001) for 200 microgram; 124 ml (95% CI 83 to 164 ml, p<0.0001) for 400 microgram
Selected secondary outcomes:				
Change from baseline to week 12 in peak FEV_1	Not reported[d]	Not reported[d]	Not reported[d]	LS mean difference over placebo 146 ml (95% CI 101 to 190 ml, p<0.0001) for 200 micrograms; 192 ml (95% CI 148 to 236 ml, p<0.0001) for 400 micrograms
Safety (safety population)				
Patients reporting serious adverse events	4.3% (8/184)	3.2% (6/190)	2.2% (4/186)	The study did not state whether there was a statistically significant difference between groups

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COPD exacerbations	9.2% (17/184)	7.4% (14/190)	12.4% (23/186)	The study did not state whether there was a statistically significant difference between groups

Abbreviations: bd, twice daily; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expired volume in 1 second; ITT, intention to treat; LS, least square; SE, standard error.

[a] Patients who took at least 1 dose of study treatment.

[b] Patients in the safety population who had baseline and at least 1 post-baseline FEV_1 assessment.

[c] European Medicines Agency (2012) European public assessment report: Eklira Genuair

[d] Change from baseline to week 12 in peak FEV_1 not reported in paper or EPAR.

ATTAIN (Jones et al. 2012)

- Design: 24-week, randomised, double-blind, placebo-controlled, parallel-group study (with 2-week run-in).
- Population: 828 patients (40 years or over) who were current or former cigarette smokers with moderate to severe COPD (post-bronchodilator FEV_1/FVC less than 0.7 and FEV_1 less than 80% of predicted). At baseline, mean age was 62 years and mean FEV_1 was 52% of predicted. Before screening, most patients in all treatment groups used COPD medications (50% used a SABA, 38% used a ICS, 30% used a LABA, 27% used a LAMA, 16% used a SAMA, 14% used a LABA+ICS, 11% used a SABA+SAMA). SABAs and ICS could be continued throughout the study but SAMAs, LAMAs and LABAs were stopped.
- Intervention and comparison: twice-daily aclidinium bromide 200 micrograms, aclidinium bromide 400 micrograms or placebo, all using a multiple-dose dry powder inhaler (Genuair).
- Outcome: the primary efficacy end point was change from baseline to week 24 in morning pre-dose (trough) FEV_1. Secondary efficacy end points were change from baseline to week 24 in peak FEV_1 (within 3 hours of morning dose), and the percentages of patients achieving clinically significant improvements in SGRQ total score and TDI focal score at week 24. All analyses were based on the intention to treat population.

Table 3 Summary of the ATTAIN study: Jones et al. 2012[10]

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	Aclidinium bromide 200 micrograms bd	Aclidinium bromide 400 micrograms bd	Placebo	Analysis
Randomised	n=280	n=272	n=276	
Safety population[a]	n=277	n=269	n=273	
ITT population[b]	n=277	n=269	n=273	
Completed study	n=253	n=252	n=232	
Efficacy (ITT population)				
Primary outcome: change from baseline to week 24 in morning pre-dose (trough) FEV_1	LS mean 26 ml (SE 16 ml)[c]	LS mean 55 ml (SE 16 ml)[c]	LS mean −73 ml (SE 16 ml)[c]	LS mean difference over placebo 99 ml (SE 22 ml, p<0.0001) for 200 micrograms; 128 ml (SE 22 ml, p<0.0001) for 400 micrograms
Selected secondary outcomes:				
Change from baseline to week 24 in peak FEV_1	LS mean 206 ml (SE 17 ml)[c]	LS mean 231 ml (SE 17 ml)[c]	LS mean 22 ml (SE 17 ml)[c]	LS mean difference over placebo 185 ml (SE 23 ml, p<0.0001) for 200 micrograms; 209 ml (SE 24 ml, p<0.0001) for 400 micrograms
Percentage of patients achieving clinically significant improvement[d] in SGRQ total score at week 24	56.0%	57.3%	41.0%	OR 1.83 for 200 micrograms vs. placebo (p<0.001) OR 1.87 for 400 micrograms vs. placebo (p<0.001)

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Percentage of patients achieving clinically significant improvement[e] in TDI focal score at week 24	53.3%	56.9%	45.5%	OR 1.47 for 200 micrograms vs. placebo (p<0.05) OR 1.68 for 400 micrograms vs. placebo (p<0.01)
Safety (safety population)				
Patients reporting serious adverse events	4.3% (12/277)	5.6% (15/269)	5.5% (15/273)	The study did not state whether there was a statistically significant difference between groups
COPD exacerbations	15.9% (44/277)	14.1% (38/269)	20.5% (56/273)	The study did not state whether there was a statistically significant difference between groups

Abbreviations: bd, twice daily; COPD, chronic obstructive pulmonary disease; FEV_1, forced expired volume in 1 second; ITT, intention to treat; LS, least square; OR, odds ratio; SE, standard error; SGRQ, St George's Respiratory Questionnaire; TDI, Transitional Dyspnoea Index.

[a] Patients who took at least 1 dose of study treatment.

[b] Patients in the safety population who had baseline and at least 1 post-baseline FEV_1 assessment.

[c] European Medicines Agency (2012) European public assessment report: Eklira Genuair

[d] Decrease of at least 4 units.

[e] Increase of at least 1 unit.

Clinical effectiveness

Both ACCORD COPD I and ATTAIN found that aclidinium bromide improved disease-oriented measures of lung function compared with placebo in people with moderate to severe COPD.

In ACCORD COPD I, after 12 weeks of treatment, compared with placebo, aclidinium bromide 200 micrograms and 400 micrograms twice daily statistically significantly improved the primary outcome of change from baseline in trough FEV_1 by 86 ml and 124 ml respectively (both p<0.0001).

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In ATTAIN, 24 weeks of treatment with the same doses of aclidinium bromide also statistically significantly improved the change from baseline in trough FEV_1 over placebo by 99 ml and 128 ml respectively (both p<0.0001). Both studies also found aclidinium bromide statistically significantly improved the change from baseline in peak FEV_1 (see tables 2 and 3 for details).

The full NICE guideline on COPD considers 100 ml to be a clinically important difference in FEV_1. Both studies report changes in trough FEV_1 greater than 100 ml for the recommended licensed dosage of 400 microgram twice daily.

Both studies reported results related to health status (SGRQ and TDI). However, only the results from the ATTAIN study, which was powered to detect a treatment difference in these endpoints are discussed here. At week 24 in the ATTAIN study, aclidinium bromide 200 micrograms and 400 micrograms twice daily produced statistically significant improvements over placebo in baseline-adjusted mean SGRQ total score (−3.8±1.1 units, p<0.001 and −4.6±1.1 units, p<0.0001 respectively). A clinically significant improvement in SGRQ total score of at least 4 units on a 100-point scale was achieved in 56.0% of the aclidinium bromide 200 microgram group, 57.3% of the 400 microgram group and 41.0% of the placebo group (odds ratio [OR] 1.83 and 1.87 compared with placebo respectively; p<0.001 for both).

At week 24, aclidinium bromide 200 micrograms and 400 micrograms twice daily also produced statistically significant improvements over placebo in baseline adjusted mean TDI focal score (0.6±0.3 units, p<0.05 and 1.0±0.3 units, p<0.001 respectively). A clinically significant improvement in TDI focal score of at least 1 unit (on a scale that ranges from −9 to 9) was achieved in 53.3% of the aclidinium bromide 200 microgram group, 56.9% of the 400 microgram group and 45.5% of the placebo group (OR 1.47, p<0.05 and OR 1.68, p<0.01 compared with placebo respectively).

In ATTAIN, the rate of COPD exacerbations of any severity was lower with aclidinium bromide than with placebo. Rate ratios were 0.72 (95% confidence interval [CI] 0.52 to 0.99, p<0.05) for 200 micrograms twice daily compared with placebo and 0.67 (95% CI 0.48 to 0.94, p<0.05) for 400 micrograms twice daily compared with placebo. The rate of moderate to severe exacerbations (needing treatment with antibiotics or corticosteroids or resulting in hospitalisation) was not statistically significantly reduced with aclidinium bromide. However, in a pooled efficacy analysis of results from ATTAIN and ACCORD COPD I, a statistically significant reduction in the rate of moderate to severe exacerbations was seen with aclidinium bromide 400 micrograms twice daily compared with placebo (rate per patient per year: 0.31 compared with 0.44 respectively, p=0.0149)[11]. These studies did not have the statistical power to detect a difference in exacerbations, and these results need to be confirmed in further trials.

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Safety

The percentage of patients reporting adverse events was similar between all groups in both studies. In ACCORD COPD I, adverse events were reported in 50.5% of the aclidinium bromide 200 microgram group, 44.7% of the aclidinium bromide 400 microgram group and 52.2% of the placebo group. These percentages were 54.5%, 53.5% and 57.1% respectively in ATTAIN. The proportions of patients reporting serious adverse events were also similar across the 3 groups in both studies (see tables 2 and 3 for details). The studies did not state whether there were statistically significant differences between groups in these events.

In both studies, the incidence of anticholinergic-related adverse effects (for example, dry mouth and constipation) was low and similar across groups. The most common adverse event was COPD exacerbation (see tables 2 and 3 for details).

Patients with unstable cardiac conditions were excluded from the studies, and these conditions may be affected by the anticholinergic mechanism of action of aclidinium bromide. Therefore, the summary of product characteristics cautions use in patients with a myocardial infarction during the previous 6 months, unstable angina, newly diagnosed arrhythmia within the previous 3 months, or hospitalisation within the previous 12 months for heart failure (New York Heart Association classes III and IV)[8].

Evidence strengths and limitations

Both studies demonstrate that aclidinium bromide has beneficial effects on lung function in people with moderate to severe COPD. However, the studies had several limitations that affect their usefulness in assessing the place in therapy of aclidinium bromide within the NHS.

Firstly, the primary end point in both studies was the disease-orientated outcome of change in FEV_1 levels over either 12 or 24 weeks. ATTAIN did have patient-orientated secondary outcomes of health status (SGRQ score) and dyspnoea (TDI focal score), and was sufficiently powered to detect treatment differences in these. Both studies also reported on COPD exacerbations. However, the publication of further longer term studies designed to measure these outcomes and assess long-term safety would be useful.

Secondly, the comparator in these studies was placebo. There are no fully published phase III studies comparing aclidinium bromide with other active treatments for COPD, for example a LAMA or a LABA (with or without an ICS). Results from studies comparing aclidinium bromide with an

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active comparator on clinically important outcomes, such as COPD exacerbations, would enable its place in therapy to be more clearly established.

Caution is needed when translating phase III trial results to clinical practice in a diverse population of people with COPD. Patients in these trials had moderate to severe COPD; no published data are available on patients with mild or very severe disease. Patients were excluded from ACCORD COPD I and ATTAIN if they had experienced a recent COPD exacerbation. There was also a 2-week run-in phase to assess disease stability, after which 47% of patients were excluded in ACCORD COPD I and 22% of patients were excluded in ATTAIN. In addition, between 6% and 20% of patients in each group did not complete the studies and so the method of last observation carried forward was used to fill in the missing data. For both studies allocation concealment was unclear, which may have introduced bias.

[5] US National Institutes of Health (2012) ClinicalTrials.gov Identifier: NCT01045161 [online; accessed 19 November 2012]

[6] US National Institutes of Health (2012) ClinicalTrials.gov Identifier: NCT00970268 [online; accessed 13 November 2012]

[7] US National Institutes of Health (2012) ClinicalTrials.gov Identifier: NCT01044459 [online; accessed 13 November 2012]

[8] US National Institutes of Health (2012) ClinicalTrials.gov Identifier: NCT01462929 [online; accessed 13 November 2012]

[9] Kerwin EM, D'Urzo AD, Gelb AF et al. (2012) Efficacy and safety of a 12-week treatment with twice-daily aclidinium bromide in COPD patients (ACCORD COPD I). COPD: Journal of Chronic Obstructive Pulmonary Disease 9: 90–101

[10] Jones PW, Singh D, Bateman ED et al. (2012) Efficacy and safety of twice-daily aclidinium bromide in COPD patients: the ATTAIN study. European Respiratory Journal 40: 830–6

[11] Almirall Limited (2012) Eklira Genuair summary of product characteristics

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Context

Treatment alternatives

In people with stable COPD who remain breathless or have exacerbations despite using short-acting bronchodilators as needed, maintenance therapy can be provided by the following (alone or in combination, with choice depending on several factors, see the NICE clinical guideline on COPD for details):

- a LABA
- a LAMA
- a LABA and an ICS in a combination inhaler.

Costs of treatment alternatives

Drug	Usual dosage[a,b]	30-day cost excluding VAT
Aclidinium bromide (Eklira Genuair)	322 micrograms twice daily	£28.60[c]
Glycopyrronium bromide (Seebri Breezhaler)	50 micrograms once daily	£27.50[c]
Tiotropium (Spiriva HandiHaler)	18 micrograms daily	£34.87 (refill £33.50)[d]
Tiotropium (Spiriva Respimat)	5 micrograms daily	£35.50[c]
Formoterol (Formoterol Easyhaler, Atimos Modulite, Foradil, Oxis Turbohaler)	12 micrograms twice daily	£11.88 to £24.80[c,d]
Salmeterol (Serevent Accuhaler, Serevent Evohaler, Neovent)	50 micrograms twice daily	£29.26[c,d]
Indacaterol (Onbrez Breezhaler)	150 micrograms daily	£29.26[d]

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[a] Doses taken from the relevant summary of product characteristics.

[b] The doses shown do not represent the full range that can be used and they do not imply therapeutic equivalence.

[c] Costs taken from MIMS December 2012.

[d] Costs taken from Drug Tariff December 2012.

Estimated impact for the NHS

Likely place in therapy

The choice of treatment for a person with COPD depends on drug efficacy, tolerability to treatment, possible adverse events and the suitability of different inhaler devices to the person. Inhaled long-acting bronchodilators have an important role to play in managing COPD; and the manufacturer expects aclidinium bromide to be used as an alternative to the established LAMA, tiotropium.

Currently, published efficacy and safety data for aclidinium bromide are limited to short-term, placebo-controlled trials with disease-orientated primary outcomes. Published trial data for the alternative maintenance treatments, LABAs and the established LAMA tiotropium, show they significantly reduce the risk of patient-orientated outcomes, such as COPD exacerbations[12]. There is limited data on exacerbations with aclidinium bromide. Similar data from longer term clinical outcome trials comparing aclidinium bromide (and the other recently marketed LAMA, glycopyrronium bromide) with active comparators are needed for local decision makers to be able to determine their place in therapy.

Aclidinium bromide is less expensive than tiotropium, at £28.60 for 30 days treatment (compared with between £33.50 and £35.50 for tiotropium), but more expensive than glycopyrronium bromide (£27.50 for 30 days treatment). Aclidinium bromide is administered twice daily, compared with once daily for tiotropium and glycopyrronium.

Estimated usage

The manufacturer stated that aclidinium bromide is anticipated to be used in newly diagnosed COPD patients needing LAMA therapy, and in those patients who need additional therapy with a LAMA after an annual review. The manufacturer estimates that up to 184 people per 100,000 of the primary care population may require initiation of treatment with a LAMA each year[13]. During

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the financial year 2011–2012, over 4 million items of tiotropium were prescribed in primary care in England, at a cost of nearly £155 million[14].

[12] Chong J, Karner C, Poole P (2012) Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews issue 9: CD009157

[13] Almirall Limited: personal communication October 2012

[14] NHS Business Services Authority: personal communication December 2012

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