

Chronic obstructive pulmonary disease: umeclidinium/vilanterol combination inhaler (Anoro Ellipta)

Evidence summary

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[nice.org.uk/guidance/esnm49](https://www.nice.org.uk/guidance/esnm49)

Key points from the evidence

The content of this evidence summary was up-to-date in November 2014. See [summaries of product characteristics \(SPCs\)](#), [British national formulary \(BNF\)](#) or the [MHRA](#) or [NICE](#) websites for up-to-date information.

Summary

Anoro Ellipta is a combination inhaler containing umeclidinium bromide (a long-acting muscarinic antagonist [LAMA]) and vilanterol (a long-acting beta₂ agonist [LABA]). Umeclidinium/vilanterol is the first LAMA/LABA combination inhaler available in the UK for the treatment of COPD. It is licensed as a maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD. The combination inhaler has been compared in randomised controlled trials (RCTs) with its individual components, tiotropium monotherapy and placebo. Studies suggest that there are benefits for forced expired volume in 1 second (FEV₁) with the umeclidinium/vilanterol combination inhaler. However, the clinical relevance of these benefits is unclear. There is limited evidence on patient-orientated outcomes such as shortness of breath, quality of life outcomes or exacerbation rates.

Effectiveness	Safety
<ul style="list-style-type: none">• Statistically significant improvement from baseline in trough FEV₁ of 0.090 litres with umeclidinium/vilanterol 62.5/25 micrograms compared with both vilanterol alone and tiotropium 18 micrograms (1 RCT; n=846; 24 weeks).• Statistically significant improvement from baseline in trough FEV₁ of 0.112 litres with umeclidinium/vilanterol 62.5/25 micrograms compared with tiotropium 18 micrograms (1 RCT; n=905; 24 weeks).• Statistically significant improvement from baseline in trough FEV₁ with umeclidinium/vilanterol 62.5/25 micrograms of 0.052 litres compared with umeclidinium 62.5 micrograms and 0.095 litres compared with vilanterol 25 micrograms (1 RCT; n=1532; 24 weeks).• Statistically significant improvement in transition dyspnoea index (TDI) score with umeclidinium/vilanterol compared with placebo of 1.2 units. No statistically significant difference in TDI score compared with umeclidinium or vilanterol monotherapy (1 RCT; n=1532; 24 weeks).	<ul style="list-style-type: none">• The summary of product characteristics (SPC) states that cardiovascular effects, such as cardiac arrhythmias, atrial fibrillation and tachycardia, may be seen after the administration of muscarinic receptor antagonists and sympathomimetics, including umeclidinium/vilanterol.• The SPC states that umeclidinium/vilanterol should be used with caution in people with severe cardiovascular disease. In addition, it states that consistent with its antimuscarinic activity, umeclidinium/vilanterol should be used with caution in people with urinary retention or with narrow-angle glaucoma.• The SPC lists urinary tract infection, sinusitis, nasopharyngitis, pharyngitis, upper respiratory tract infection, headache, cough, oropharyngeal pain, constipation and dry mouth as common adverse events (frequency 1 in 10 to 1 in 100 people).

Patient factors	Resource implications
<ul style="list-style-type: none">• Umeclidinium/vilanterol is available as a dry powder multi-dose inhaler, which may be more convenient for some people than using 2 separate inhalers (LAMA plus LABA as single component inhalers).• Once daily dosing.• Individual patient assessment is needed when choosing an inhaler device.	<ul style="list-style-type: none">• The cost of Anoro Ellipta is £32.50 for 30 days' supply.• The cost of 2 separate inhalers (currently available LAMA plus LABA as single component inhalers) ranges from approximately £39.38 to £64.13 for 30 days' supply (depending on the LAMA and LABA used and device).

Introduction and current guidance

The NICE guideline on [chronic obstructive pulmonary disease \(COPD\)](#) states that COPD is characterised by airflow obstruction that is usually progressive and not fully reversible; it is predominantly caused by smoking. The guideline makes several recommendations about inhaled treatments for managing stable COPD, which are relevant to the likely place in therapy of umeclidinium/vilanterol (Anoro Ellipta: a long-acting muscarinic antagonist [LAMA] and long-acting beta₂ agonist [LABA] combination inhaler). See the [NICE guideline](#) or the NICE pathway on [COPD](#) for full details.

[Full text of Introduction and current guidance.](#)

Product overview

Anoro Ellipta is a multi-dose, dry powder combination inhaler containing a LAMA and a LABA. It is licensed as a maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD. The recommended dose is 1 inhalation once a day. Each delivered dose (the dose that leaves the mouthpiece of the inhaler) contains 65 micrograms of umeclidinium bromide, which is equivalent to 55 micrograms of umeclidinium, and 22 micrograms of vilanterol (as trifenate) (Anoro Ellipta [summary of product characteristics](#)).

[Full text of Product overview.](#)

Evidence review

- This evidence summary is based on the best available published evidence. This is 3 RCTs: 2 RCTs reported in the same paper ([Decramer et al. 2014](#)) and ([Maleki-Yazdi et al. 2014](#)). The 2 RCTs reported in Decramer et al. 2014 compared 2 different doses of umeclidinium/vilanterol with tiotropium alone and either umeclidinium alone or vilanterol alone over 24 weeks. Maleki-Yazdi et al. 2014 compared umeclidinium/vilanterol with tiotropium over 24 weeks. A fourth 24-week RCT is also briefly discussed ([Donohue et al. 2013](#)). All of these RCTs have disease-orientated FEV₁ primary outcomes.
- Decramer et al. 2014: study 1 found that there was a statistically significant improvement in trough FEV₁ of 0.090 litres (95% confidence interval [CI] 0.039 to 0.142; p=0.0006) with umeclidinium/vilanterol 62.5/25 micrograms (equivalent to a delivered dose of umeclidinium 55 micrograms plus vilanterol 22 micrograms) compared with both vilanterol 25 micrograms and tiotropium 18 micrograms (equivalent to a delivered dose of 10 micrograms). However, the clinical significance of this difference is unclear. In study 2 there was no statistically significant difference between umeclidinium/vilanterol 125/25 micrograms and umeclidinium 125 micrograms for the primary outcome. A step-down statistical testing procedure was used in this study. The results of all further statistical analyses (which included umeclidinium/vilanterol 62.5/25 micrograms) are described, but are not strictly inferential.
- Maleki-Yazdi et al. 2014 found that there was a statistically significant improvement in trough FEV₁ of 0.112 litres (95% CI 0.081 to 0.144; p<0.001) with umeclidinium/vilanterol 62.5/25 micrograms compared with tiotropium 18 micrograms.
- Decramer et al. 2014 and Maleki-Yazdi et al. 2014 reported patient-orientated additional outcomes such as time to first on-treatment exacerbation, [St George's Respiratory Questionnaire](#) (SGRQ) score, rescue salbutamol use and the [transition dyspnoea](#) (TDI) score. However, the studies were not powered to detect treatment differences in these endpoints. In Decramer et al. 2014 there was no statistically significant difference between umeclidinium/vilanterol 62.5/25 micrograms and tiotropium, umeclidinium or vilanterol monotherapy for time to first on-treatment exacerbation or TDI score. Study 1 of Decramer et al. 2014 and Maleki-Yazdi et al. 2014 both found a statistically significant reduction from baseline in the mean number of salbutamol puffs per day with umeclidinium/vilanterol compared with tiotropium. However, the clinical significance of these reductions (0.7 and 0.5 puffs per day) is unclear. In Maleki-Yazdi et al. 2014 there was a statistically significant improvement from baseline in the SGRQ total score of -2.10 points with umeclidinium/vilanterol compared with tiotropium. The clinical significance of this is unclear.

- Donohue et al. 2013 found that there were statistically significant improvements in trough FEV₁ on day 169 with umeclidinium/vilanterol 62.5/25 micrograms of 0.052 litres (95% CI 0.017 to 0.087; p≤0.01) compared with umeclidinium 62.5 micrograms and 0.095 litres (95% CI 0.060 to 0.130; p≤0.001) compared with vilanterol 25 micrograms.
- In Donohue et al. 2013, TDI score was included as an efficacy outcome and the study was powered to detect a 1 unit difference between treatments. There was a statistically significant improvement in TDI score at day 168 with umeclidinium/vilanterol 62.5/25 micrograms compared with placebo (1.2 units; 95% CI 0.7 to 1.7; p<0.001). There was no statistically significant difference for TDI score with umeclidinium/vilanterol compared with umeclidinium monotherapy (0.3 units; 95% CI -0.2 to 0.7) or vilanterol monotherapy (0.4 units; 95% CI -1.0 to 0.8).
- Umeclidinium/vilanterol has been compared with its individual components and the LAMA, tiotropium. There are no published studies which compare umeclidinium/vilanterol with currently available LAMA and LABA treatment given concomitantly.
- The [European public assessment report for umeclidinium/vilanterol](#) concluded that the overall safety profile was in line with the safety profile of other LAMAs and LABAs. However, it did highlight that long-term safety data is limited. A long-term 52-week safety study ([Donohue et al. 2014](#)) has been published. However this study evaluates umeclidinium/vilanterol 125/25 micrograms and does not include the licensed umeclidinium/vilanterol dose.

[Full text of Evidence review.](#)

Context

Umeclidinium/vilanterol is the first LAMA/LABA combination inhaler available in the UK for the treatment of COPD. Indacaterol/glycopyrronium (Ultibro Breezhaler 85/43 micrograms) was the first combination inhaler containing a LABA and a LAMA to receive a European marketing authorisation for COPD (see the evidence summary on [chronic obstructive pulmonary disease: indacaterol/glycopyrronium](#)). However, Ultibro Breezhaler was not available in the UK at the time umeclidinium/vilanterol was launched in June 2014. The manufacturer does not currently have a date for the UK launch of Ultibro Breezhaler (Novartis: personal communication September 2014).

[Full text of Context.](#)

Estimated impact for the NHS

The NICE guideline on [COPD](#) recommends that the choice of drug treatment should take into account the person's symptomatic response and preference, and the drug's potential to reduce exacerbations, side effects and costs. The use of dual therapy with a LAMA and LABA may be considered if an inhaled corticosteroid (ICS; as part of combination therapy with a LABA) is declined or not tolerated. NICE developed these recommendations in 2010, which predates the publication of the evidence for the newer LABAs and LAMAs such as vilanterol, indacaterol, olodaterol, glycopyrronium and umeclidinium. The umeclidinium/vilanterol combination inhaler is less expensive than the combined cost of other single-component LAMA or LABA inhalers and may be more convenient for people. However, compared with established drugs such as formoterol, salmeterol and tiotropium, the comparative efficacy and long-term safety of umeclidinium/vilanterol is unclear, particularly in terms of important patient-orientated outcomes such as reducing exacerbations, incidence of pneumonia and overall mortality.

[Full text of Estimated impact for the NHS.](#)

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.**

Full evidence summary

Introduction and current guidance

The NICE guideline on [chronic obstructive pulmonary disease \(COPD\)](#) states that COPD is characterised by airflow obstruction that is usually progressive and not fully reversible; it is predominantly caused by smoking. About 900,000 people in the UK have diagnosed COPD, and an estimated 2 million people have COPD that remains undiagnosed. COPD produces symptoms, disability and impaired quality of life, which may respond to pharmacological and other therapies that have limited or no impact on the airflow obstruction. Exacerbations often occur, during which there is a rapid and sustained worsening of symptoms beyond normal day-to-day variations.

The guideline includes the following key recommendations for stable COPD that are relevant to this evidence summary and the likely place in therapy of umeclidinium/vilanterol (Anoro Ellipta: a

long-acting muscarinic antagonist [LAMA] and long-acting beta₂ agonist [LABA] combination inhaler).

- 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 needed, offer the following as maintenance therapy:
 - if forced expired volume in 1 second (FEV₁) is 50% predicted or more: either a LABA or a LAMA
 - if FEV₁ is less than 50% predicted: either a LABA with an inhaled corticosteroid (ICS) in a combination inhaler, or a LAMA. Consider a LAMA in addition to a LABA where an ICS is declined or not tolerated
- In people with stable COPD and an FEV₁ of 50% predicted or more who remain breathless or have exacerbations despite maintenance therapy with a LABA:
 - consider a LABA with an ICS in a combination inhaler
 - consider a LAMA in addition to a LABA where an ICS is declined or not tolerated.
- Offer a LAMA in addition to a LABA with an ICS to people with COPD who remain breathless or have exacerbations despite taking a LABA with an ICS, irrespective of their FEV₁.
- Consider a LABA with an ICS in a combination inhaler in addition to a LAMA for people with stable COPD who remain breathless or have exacerbations despite maintenance therapy with a LAMA, irrespective of their FEV₁.
- 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.

The full NICE guideline on [COPD](#) includes details on what it considers the minimum clinically important difference for a number of outcome measures used in COPD clinical studies to be. These values are appropriate for comparisons of active treatment with placebo. However, it is unclear if they are appropriate as a benchmark for clinical significance for comparisons between a combination of 2 bronchodilators (LAMA and LABA) with 1 bronchodilator (either a LAMA or a LABA).

Outcome measure	Minimum clinically important difference
Relative risk reduction for mortality	15%
Relative risk reduction for exacerbations	20%
Relative risk reduction for hospitalisation	20%
Change in St George's Respiratory Questionnaire score	-4 points
Change in FEV ₁	0.100 litres
Change in transition dyspnoea index score	1 unit

Product overview

Drug action

Anoro Ellipta is a multi-dose, dry powder combination inhaler containing umeclidinium bromide (a long-acting muscarinic antagonist [LAMA]) and vilanterol (a long-acting beta₂ agonist [LABA]) (Anoro Ellipta [summary of product characteristics](#)).

Licensed therapeutic indication

Anoro Ellipta is licensed as a maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD (Anoro Ellipta [summary of product characteristics](#)). Anoro Ellipta was launched in the UK in June 2014.

Course and cost

The recommended dose is 1 inhalation once a day. Each delivered dose (the dose that leaves the mouthpiece of the inhaler) contains 65 micrograms umeclidinium bromide which is equivalent to 55 micrograms of umeclidinium and 22 micrograms of vilanterol (as trifenate) (Anoro Ellipta [summary of product characteristics](#)).

Anoro Ellipta is available as a 30-dose inhaler, the cost of which is £32.50 (1 month of treatment; excluding VAT; costs taken from [MIMS](#), September 2014). Based on this, the cost per patient per year is £390.

Evidence review

The clinical efficacy of umeclidinium/vilanterol administered once daily was evaluated in 8 phase III clinical studies in 6,835 adults with a clinical diagnosis of COPD; 5,618 people from five 6-month studies (2 placebo-controlled and 3 active [tiotropium]-comparator controlled), 655 people from two 3-month exercise endurance/lung function studies and 562 people from a 12-month supportive study (Anoro Ellipta [summary of product characteristics](#)).

This evidence summary is based on the best available published evidence. This is 3 randomised controlled trials (RCTs); 2 RCTs reported in the same paper ([Decramer et al. 2014](#)) and [Maleki-Yazdi et al. 2014](#). The 2 RCTs reported in Decramer et al. 2014 compared the safety and efficacy of 2 different doses of umeclidinium/vilanterol with tiotropium and either umeclidinium alone or vilanterol alone over 24 weeks. Maleki-Yazdi et al. 2014 compared umeclidinium/vilanterol with tiotropium over 24 weeks. A fourth 24-week RCT which compared umeclidinium/vilanterol with placebo, umeclidinium alone or vilanterol alone is also briefly discussed ([Donohue et al. 2013](#)).

A long-term 52 week safety study ([Donohue et al. 2014](#)) has been published. However this study evaluates umeclidinium/vilanterol 125/25 micrograms and does not include the licensed umeclidinium/vilanterol dose. It is therefore not included in this evidence summary.

[Decramer et al. 2014](#)

- Design: two 24-week, multicentre, randomised, blinded, parallel-group, double-dummy studies. Study 1 was conducted in 91 centres in 9 countries and study 2 was conducted in 95 centres in 10 countries. The method of allocation described suggests that this was concealed.
- Population: for both studies participants were aged 40 years and over (mean age 62.9 years in study 1 and 64.6 years in study 2) and had moderate to very severe COPD; as defined by the [American Thoracic Society and the European Respiratory Society](#). Participants were current or former smokers with a smoking history of at least 10 pack-years. They had a post-salbutamol FEV₁ of 70% or less predicted normal (mean FEV₁ around 47% in both studies), an FEV₁ to FVC (forced vital capacity) ratio of less than 0.7 and a score of 2 or higher on the modified [Medical Research Council dyspnoea scale](#). Exclusion criteria included hospital admission due to COPD or pneumonia within the previous 12 weeks or a diagnosis of asthma or other known respiratory disorder. Study 1 included 846 randomised participants and study 2 included 872 randomised participants.

- **Intervention and comparison:** In study 1 participants were randomised to umeclidinium/vilanterol 62.5/25 micrograms (equivalent to a delivered dose of umeclidinium 55 micrograms plus vilanterol 22 micrograms), umeclidinium/vilanterol 125/25 micrograms (equivalent to a delivered dose of umeclidinium 113 micrograms plus vilanterol 22 micrograms), vilanterol 25 micrograms (equivalent to a delivered dose of vilanterol 22 micrograms) or tiotropium 18 micrograms (equivalent to a delivered dose of 10 micrograms). In study 2 participants were randomised to umeclidinium/vilanterol 62.5/25 micrograms, umeclidinium/vilanterol 125/25 micrograms, umeclidinium 125 micrograms or tiotropium 18 micrograms. All doses were taken once a day. Umeclidinium and vilanterol were delivered via the dry powder Ellipta inhaler and tiotropium was delivered via the HandiHaler dry powder inhaler. The studies used a double-dummy design where participants were given 2 inhalers. Use of inhaled salbutamol for symptom relief was allowed throughout the study as were inhaled corticosteroids at a stable dose of up to 1000 micrograms per day fluticasone propionate or equivalent.
- **Outcomes:** the primary outcome for both studies was the trough FEV₁ (the mean of FEV₁ values obtained at 23 hours and 24 hours after the previous days dosing) on day 169. The study was powered to detect a 100 ml difference between treatments for trough FEV₁. Additional efficacy outcomes included time to first COPD exacerbation, [St George's Respiratory Questionnaire](#) (SGRQ) score (a measure of health-related quality of life), rescue salbutamol use (percentage of rescue free days and mean puffs per day) and [transition dyspnoea index](#) (TDI) focal score (a measure of dyspnoea). The primary analysis was based on the intention-to-treat (ITT) population split into several levels pre-specified by the authors to avoid spurious statistically significant findings arising through chance, given the number of possible comparisons.

The 2 studies in [Decramer et al. 2014](#) included a comparator arm investigating umeclidinium/vilanterol 125/25 micrograms. However, results are presented here only for the umeclidinium/vilanterol 62.5/25 micrograms arm because that is the dose and strength that has been licensed.

Table 1 Summary of [Decramer et al. 2014](#) study 1

	Umeclidinium/ vilanterol 62.5/25 micrograms once daily	Tiotropium 18 micrograms once daily	Vilanterol 25 micrograms once daily	Analysis
Randomised	n=212	n=209	n=209	

Efficacy (ITT population) ^{a,b}	n=212	n=208	n=209	
Primary outcome: trough FEV ₁ LS mean change from baseline on day 169 (litres) [SE]	0.211 (0.018)	0.121 (0.019)	0.121 (0.019)	Statistically significant increase in trough FEV ₁ for umeclidinium/vilanterol versus tiotropium or vilanterol alone: treatment difference 0.090 (95% CI 0.039 to 0.142; p=0.0006)
Selected additional efficacy outcomes:				
Time to first on-treatment exacerbation		Umeclidinium/vilanterol versus tiotropium HR 1.2 (95% CI 0.5 to 2.6; p=0.71)	Umeclidinium/vilanterol versus vilanterol HR 0.7 (95% CI 0.4 to 1.5; p=0.42)	No statistically significant difference for umeclidinium/vilanterol versus tiotropium or vilanterol alone.
Rescue salbutamol use (mean puffs per day) LS mean change from baseline (SE)	-2.0 (0.2)	-1.4 (0.2)	-1.8 (0.2)	Statistically significant reduction versus tiotropium: -0.7 (95% CI -1.2 to -0.1; p=0.0220) No statistically significant difference versus vilanterol: -0.3 (95% CI -0.8 to 0.3; p=0.39).
LS mean TDI focal score on day 168 (SE) ^c	2.3 (0.2)	2.4 (0.2)	2.1 (0.2)	No statistically significant difference versus tiotropium (p=0.72) or vilanterol (p=0.49)

LS mean change in SGRQ total score from baseline on day 168 (SE) ^d	-6.87 (1.02)	-7.62 (1.05)	-8.29 (1.06)	No statistical analysis presented
Safety	n=212	n=208	n=209	
Participants reporting 'on treatment' adverse events	51% (108/212)	39% (82/208)	47% (99/209)	No statistical analysis presented
Participants reporting 'on treatment' serious adverse events	3% (7/212)	6% (13/208)	7% (15/209)	No statistical analysis presented
Adverse events that led to withdrawal from study	5% (10/212)	4% (9/208)	5% (10/209)	No statistical analysis presented
<p>Abbreviations: CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; LS, least-squares; TDI, transition dyspnoea index; SE, standard error; SGRQ, St George's Respiratory Questionnaire</p> <p>^a 5 participants in the umeclidinium/vilanterol 62.5/25 microgram group, 5 participants in the tiotropium group and 4 participants in the vilanterol group were excluded from the efficacy analysis because of deviations from good clinical practice at the study site.</p> <p>^b ITT population – all randomly assigned participants who had received at least 1 dose of study drug during the treatment period.</p> <p>^c TDI: transition dyspnoea index – a measure of dyspnoea which ranges from -9 to +9. The lower the score, the more deterioration in severity of dyspnoea.</p> <p>^d SGRQ: St George's Respiratory Questionnaire – a measure of health-related quality of life. Scores range from 0 to 100 with higher scores indicating more limitations.</p>				

Table 2 Summary of [Decramer et al. 2014 study 2](#)

	Umeclidinium/ vilanterol 62.5/ 25 micrograms once daily	Tiotropium 18 micrograms once daily	Umeclidinium 125 micrograms once daily	Analysis
Randomised	n=218	n=215	n=222	
Efficacy (ITT population) ^a	n=217	n=215	n=222	
Primary outcome: trough FEV ₁ LS mean change from baseline on day 169 (litres) [SE]	0.208 (0.018)	0.149 (0.018)	0.186 (0.018)	Treatment difference versus tiotropium 0.060 (95% CI 0.010 to 0.109; p=0.0182 ^b) Treatment difference versus umeclidinium 0.022 (95% CI -0.027 to 0.072; p=0.38)
Selected additional efficacy outcomes:				
Time to first on-treatment exacerbation		Umeclidinium/ vilanterol versus tiotropium HR 1.9 (95% CI 1.0 to 3.6; p=0.06)	Umeclidinium/ vilanterol versus umeclidium HR 1.0 (95% CI 0.6 to 1.8; p=0.95)	No statistically significant difference for umeclidinium/vilanterol versus tiotropium or umeclidinium alone
Rescue salbutamol use (mean puffs per day) LS mean change from baseline (SE)	-2.7 (0.2)	-2.1 (0.2)	-2.1 (0.2)	No statistically significant difference for umeclidinium/vilanterol versus tiotropium -0.6 (95% CI -1.2 to 0.0; p=0.07) or umeclidinium alone -0.6 (95% CI -1.2 to 0.0; p=0.06)

LS mean TDI focal score on day 168 (SE) ^c	2.3 (0.3)	2.1 (0.2)	1.9 (0.2)	No statistically significant difference for umeclidinium/vilanterol versus tiotropium (p=0.55) or umeclidinium alone (p=0.25)
LS mean change in SGRQ total score from baseline (SE) ^d	-9.95 (0.98)	-9.78 (0.95)	-8.40 (0.97)	No statistical analysis presented
Safety	n=217	n=215	n=222	
Patients reporting 'on treatment' adverse events	59% (127/217)	59% (126/215)	59% (131/222)	No statistical analysis presented
Patients reporting 'on treatment' serious adverse events	10% (22/217)	4% (9/215)	7% (15/222)	No statistical analysis presented
Adverse events that led to withdrawal from study	9% (20/217)	5% (11/215)	8% (17/222)	No statistical analysis presented

Abbreviations: CI, confidence interval; ITT, intention-to-treat; LS, least-squares; TDI, transition dyspnoea index; SE, standard error; SGRQ, St George's Respiratory Questionnaire

^a ITT population – all randomly assigned participants who had received at least 1 dose of study drug during the treatment period.

^b p value nominal only because of restrictions of the predefined statistical testing hierarchy.

^c TDI: transition dyspnoea index – a measure of dyspnoea which ranges from –9 to +9. The lower the score, the more deterioration in severity of dyspnoea.

^d SGRQ: St George's Respiratory Questionnaire – a measure of health-related quality of life. Scores range from 0 to 100 with higher scores indicating more limitations.

Maleki-Yazdi et al. 2014

- Design: 24-week, multicentre, randomised, blinded, parallel-group, double-dummy study. The study was conducted in 71 centres in 8 countries. The method of allocation described suggests that this was concealed.
- Population: 905 participants aged 40 years and over (mean age 62.3 years) with moderate to very severe COPD; as defined by the American Thoracic Society and the European Respiratory Society. Participants were current or former smokers with a smoking history of at least 10 pack-years. They had a post-salbutamol FEV₁ of 70% or less predicted normal (mean FEV₁ around 46%), an FEV₁ to FVC (forced vital capacity) ratio of less than 0.7 and a score of 2 or higher on the modified Medical Research Council dyspnoea scale. Exclusion criteria included hospital admission due to COPD or pneumonia within the previous 12 weeks or a diagnosis of asthma or other known respiratory disorder.
- Intervention and comparison: participants were randomised to umeclidinium/vilanterol 62.5/25 micrograms (equivalent to a delivered dose of umeclidinium 55 micrograms plus vilanterol 22 micrograms) or tiotropium 18 micrograms (equivalent to a delivered dose of 10 micrograms). All doses were taken once a day. Umeclidinium/vilanterol was delivered via the dry powder Ellipta inhaler and tiotropium was delivered via the HandiHaler dry powder inhaler. The studies used a double-dummy design where participants were given 2 inhalers. Use of inhaled salbutamol for symptom relief was allowed throughout the study as were inhaled corticosteroids at a stable dose of up to 1000 micrograms per day fluticasone propionate or equivalent.
- Outcomes: the primary outcome was the trough FEV₁ (the mean of FEV₁ values obtained at 23 hours and 24 hours after the previous days dosing) on day 169. The study was powered to detect a 0.060 litre difference between treatments for trough FEV₁. Additional efficacy

outcomes included change from baseline in St George's Respiratory Questionnaire (SGRQ) score (a measure of health-related quality of life), time to first COPD exacerbation and rescue salbutamol use (mean puffs per day).

Table 3 Summary of [Maleki-Yazdi et al. 2014](#)

	Umeclidinium/ vilanterol 62.5/ 25 micrograms once daily	Tiotropium 18 micrograms once daily	Analysis
Randomised	n=454	n=451	
Efficacy (ITT population) ^a	n=454	n=451	
Primary outcome: trough FEV ₁ LS mean change from baseline on day 169 (litres) [SE]	0.205 (0.0114)	0.093 (0.0115)	Statistically significant increase in trough FEV ₁ for umeclidinium/ vilanterol versus tiotropium: 0.112 (95% CI 0.081 to 0.144; p<0.001)
Selected additional efficacy outcomes:			
LS mean change in SGRQ total score from baseline (SE) ^b	-7.27 (0.538)	-5.17 (0.548)	Statistically significant improvement with umeclidinium/ vilanterol versus tiotropium: -2.10 (95% CI -3.61 to -0.59; p=0.006)
Rescue salbutamol use (mean puffs per day) LS mean change from baseline (SE)	-1.3 (0.09)	-0.8 (0.09)	Statistically significant reduction with umeclidinium/vilanterol versus tiotropium: -0.5 (95% CI -0.7 to -0.2; p<0.001)
Safety	n=454	n=451	
Patients reporting 'on treatment' adverse events	44% (202/454)	42% (190/ 451)	No statistical analysis presented

Patients reporting 'on treatment' serious adverse events	4% (16/454)	4% (17/451)	No statistical analysis presented
Adverse events that led to withdrawal from study	4% (18/454)	3% (14/451)	No statistical analysis presented
Cardiovascular adverse events	2% (9/454)	2% (7/451)	No statistical analysis presented
Pneumonia and LRTI adverse events	1% (4/454)	1% (6/451)	No statistical analysis presented
<p>Abbreviations: CI, confidence interval; ITT, intention-to-treat; LRTI, lower respiratory tract infection; LS, least-squares; SE, standard error; SGRQ, St George's Respiratory Questionnaire</p> <p>^a ITT population – all randomly assigned participants who had received at least 1 dose of study drug during the treatment period.</p> <p>^b SGRQ: St George's Respiratory Questionnaire – a measure of health-related quality of life. Scores range from 0 to 100 with higher scores indicating more limitations.</p>			

Clinical effectiveness

[Decramer et al. 2014](#) reported 2 RCTs which compared umeclidinium/vilanterol 62.5/25 micrograms once daily with tiotropium 18 micrograms once daily and either vilanterol 25 micrograms or umeclidinium 125 micrograms once daily over 24 weeks in people with COPD. Both studies also included a comparator arm investigating umeclidinium/vilanterol 125/25 micrograms. However, only the results for the umeclidinium/vilanterol 62.5/25 micrograms arm are discussed here because that is the dose and strength that has been licensed.

In both studies, for all comparators, trough FEV₁ (the primary outcome) increased from baseline with a mean increase greater than the improvement that the full NICE guideline on [COPD](#) considers to be clinically important (0.100 litres or more). However, differences between the treatment arms were small and were less than the 0.100 litres considered to be clinically important (see table 1). The [European public assessment report for umeclidinium/vilanterol](#) states that a minimum clinically important difference of 0.100 litres is for comparisons with placebo and it may not be appropriate for comparisons between a combination of 2 bronchodilators (LAMA and LABA) with 1 bronchodilator (either a LAMA or a LABA).

The statistical analysis of the 2 studies reported in [Decramer et al. 2014](#) used a hierarchical design such that only if all comparisons reached statistical significance in hierarchical order would subsequent analyses be conducted. Study 1 found that there was a statistically significant improvement from baseline in trough FEV₁ of 0.090 litres with umeclidinium/vilanterol 62.5/25 micrograms compared with both vilanterol 25 micrograms and tiotropium 18 micrograms. In study 2 there was no statistically significant difference between umeclidinium/vilanterol 125/25 micrograms and umeclidinium 125 micrograms for the primary outcome. Therefore the results of all further statistical analyses (which included umeclidinium/vilanterol 62.5/25 micrograms) are described, but are not strictly inferential (see table 2).

Additional patient-orientated outcomes were reported in [Decramer et al. 2014](#), but the studies were not powered to detect a difference in these endpoints between treatment groups. Patient-orientated outcomes included time to first on-treatment exacerbation, St George's Respiratory Questionnaire (SGRQ) score, rescue salbutamol use and the transition dyspnoea index score (TDI). In both studies there was no statistically significant difference between umeclidinium/vilanterol 62.5/25 micrograms and tiotropium, umeclidinium or vilanterol monotherapy for time to first on-treatment exacerbation or TDI score. There was no statistically significant difference between umeclidinium/vilanterol 62.5/25 micrograms and umeclidinium or vilanterol monotherapy for rescue salbutamol use, and in study 2 there was no statistically significant difference between umeclidinium/vilanterol 62.5/25 micrograms and tiotropium for rescue salbutamol use. There was a statistically significant difference between these 2 groups for this outcome in study 1. However, the clinical significance of the difference (a reduction of 0.7 in the mean number of salbutamol puffs per day with umeclidinium/vilanterol) is unclear. Also, treatment comparisons for additional analyses such as rescue salbutamol use were not controlled for multiplicity.

In both studies there were significant increases in SGRQ scores from baseline for all groups including umeclidinium/vilanterol. No statistical analysis was presented for differences between treatment arms for change in SGRQ score. However, in both studies the difference between the groups for the mean change in SGRQ score was less than the improvement that the full NICE guideline on [COPD](#) considers to be clinically important (-4 points). This value is appropriate for comparisons of active treatment with placebo. However, it is unclear if it is appropriate as a benchmark for clinical significance for comparisons between a combination of 2 bronchodilators (LAMA and LABA) with 1 bronchodilator (either a LAMA or a LABA).

In [Maleki-Yazdi et al. 2014](#) there was a statistically significant improvement from baseline in trough FEV₁ of 0.112 litres with umeclidinium/vilanterol 62.5/25 micrograms once daily compared with tiotropium 18 micrograms once daily after 24 weeks treatment. This study also included patient-orientated additional outcomes but the study was not powered to detect a difference in these

endpoints between treatment groups. Patient-orientated outcomes included SGRQ score, rescue salbutamol use and time to first on-treatment COPD exacerbation. There was a statistically significant improvement from baseline in the SGRQ total score of -2.10 points with umeclidinium/vilanterol compared with tiotropium. The clinical significance of this is unclear for the reasons previously discussed in this evidence summary. There was also a statistically significant reduction from baseline in the mean number of salbutamol puffs per day with umeclidinium/vilanterol compared with tiotropium. However, the clinical significance of this reduction (0.5 puffs per day) is unclear. The percentage of people in each group reporting an on-treatment COPD exacerbation was small (4% with umeclidinium/vilanterol and 6% with tiotropium), but analysis of time to first on-treatment COPD exacerbation just favoured umeclidinium/vilanterol (hazard ratio 0.5; 95% CI 0.3 to 1.0; $p=0.044$).

Donohue et al. 2013 was a 24-week RCT which randomised 1532 participants 3:3:3:2 to umeclidinium/vilanterol 62.5/25 micrograms once daily ($n=413$), umeclidinium 62.5 micrograms once daily ($n=418$), vilanterol 25 micrograms once daily ($n=421$) or placebo ($n=280$). Participants were aged 40 years and over (mean age 63 years) with moderate to severe COPD. Concomitant use of inhaled salbutamol was allowed as rescue medication, as were inhaled corticosteroids at a stable dose of up to 1000 micrograms per day fluticasone propionate or equivalent. The primary efficacy outcome was trough FEV₁ on day 169. TDI score was included as an efficacy outcome and the study was powered to detect a 1 unit difference between treatments in TDI score. Additional efficacy outcomes included the time to first COPD exacerbation.

Compared with placebo there was a statistically significant improvement in trough FEV₁ on day 169 with umeclidinium/vilanterol 62.5/25 micrograms (0.167 litres; 95% CI 0.128 to 0.207; $p<0.001$). There was also a statistically significant improvement in TDI score with umeclidinium/vilanterol 62.5/25 micrograms compared with placebo (1.2 units; 95% CI 0.7 to 1.7; $p<0.001$). Compared with both umeclidinium and vilanterol monotherapy, there were statistically significant improvements in trough FEV₁ on day 169 with umeclidinium/vilanterol of 0.052 litres (95% CI 0.017 to 0.087; $p\leq 0.01$) and 0.095 litres (95% CI 0.060 to 0.130; $p\leq 0.001$) respectively. There was no statistically significant difference for TDI score at day 168 with umeclidinium/vilanterol compared with umeclidinium (0.3 units; 95% CI -0.2 to 0.7) or vilanterol (0.4 units; 95% CI -1.0 to 0.8) monotherapy. The study also found a statistically significantly lower risk for time to first COPD exacerbation with umeclidinium/vilanterol 62.5/25 micrograms compared with placebo (hazard ratio, 0.5; 95% CI 0.3 to 0.8; $p\leq 0.01$). However, it was not designed or powered to evaluate treatment effects on COPD exacerbations.

Safety and tolerability

The summary of product characteristics (SPC:[Anoro Ellipta](#)) lists urinary tract infection, sinusitis, nasopharyngitis, pharyngitis, upper respiratory tract infection, headache, cough, oropharyngeal pain, constipation and dry mouth as common (between 1 in 10 and 1 in 100) adverse reactions.

The SPC states that cardiovascular effects, such as cardiac arrhythmias, atrial fibrillation and tachycardia, may be seen after the administration of muscarinic receptor antagonists and sympathomimetics, including umeclidinium/vilanterol. People with clinically significant uncontrolled cardiovascular disease were excluded from clinical studies. Therefore, the SPC states that umeclidinium/vilanterol should be used with caution in people with severe cardiovascular disease. In addition, it states that consistent with its antimuscarinic activity, umeclidinium/vilanterol should be used with caution in people with urinary retention or with narrow-angle glaucoma.

In [Decramer et al. 2014](#) for both studies results were presented for 'on-treatment' adverse events, serious 'on-treatment' adverse events and adverse events that led to discontinuation of the study drug or withdrawal from the study (see table 1 and table 2 for more information). The authors state that the incidence of adverse events was similar across treatments. However, no statistical analysis was presented. No notable differences for blood pressure, heart rate or QT interval were seen in either study and no treatment-related changes in ECG or clinical laboratory parameters were recorded.

In [Maleki-Yazdi et al. 2014](#) results were also presented for 'on-treatment' adverse events, serious 'on-treatment' adverse events and adverse events that led to discontinuation of the study drug. Results were similar between the 2 treatment groups; however no statistical analysis was presented. The incidence of any cardiovascular adverse event or pneumonia and lower respiratory tract adverse events were also similar between the 2 treatment groups; however no statistical analysis was presented (see table 3 for more information). Seven deaths occurred during the study, 2 in the umeclidinium/vilanterol group (cardiac failure and death from unknown cause) and 5 in the tiotropium group (sudden death, pancreatic carcinoma, respiratory failure, pulmonary embolism and acute cardiac failure). None of the deaths were considered to be related to the study drugs.

The [European public assessment report for umeclidinium/vilanterol](#) concluded that the overall safety profile was in line with the safety profile of other LAMAs and LABAs. However, it did highlight that long-term safety data is limited. A long-term 52-week safety study ([Donohue et al. 2014](#)) has been published. However this study evaluates umeclidinium/vilanterol 125/25 micrograms and does not include the licensed umeclidinium/vilanterol dose.

Evidence strengths and limitations

Umeclidinium/vilanterol has been compared with its individual components and the LAMA, tiotropium. Vilanterol is not currently available as monotherapy. Umeclidinium ([Incruse](#)) was launched in the UK in October 2014. There are no published studies which compare umeclidinium/vilanterol with currently available LAMA and LABA treatment given concomitantly. It is therefore unclear how umeclidinium/vilanterol would compare to combined treatment with a currently available LAMA and LABA.

The NICE guideline on [COPD](#) recommends that the use of dual therapy with a LAMA and a LABA may be considered if an inhaled corticosteroid (ICS: as part of combination therapy with a LABA) is declined or not tolerated. In [Decramer et al. 2014](#), [Maleki-Yazdi et al. 2014](#) and [Donohue et al. 2013](#) participants were allowed to have concomitant treatment with an ICS. Pre-treatment use varied across the allocated groups by between 40% and 56%.

In Decramer et al 2014 the studies were powered to detect a 0.100 litre difference between treatments for trough FEV₁. However, in both studies the difference in trough FEV₁ between umeclidinium/vilanterol and tiotropium, vilanterol or umeclidinium monotherapy was less than 0.100 litres. The full NICE guideline on [COPD](#) considers a minimum clinically important difference in FEV₁ to be 0.100 litres. The [European public assessment report for umeclidinium/vilanterol](#) commented that the improvements in trough FEV₁ with umeclidinium/vilanterol 62.5/25 micrograms compared with tiotropium and the individual components were variable and did not show a consistent clinically relevant change. However, it stated that a minimum clinically important difference of 0.100 litres is for comparisons with placebo and it may not necessarily be appropriate as a benchmark for clinical significance for comparisons between a combination of 2 bronchodilators (LAMA and LABA) with 1 bronchodilator (either a LAMA or a LABA).

The NICE guideline on COPD recommends that the choice of drug treatment should take into account the person's symptomatic response and preference, and the drug's potential to reduce exacerbations, side effects and costs. Decramer et al. 2014 and Maleki-Yazedi et al. 2014 both had disease-orientated FEV₁ primary and secondary outcomes. Patient-orientated additional outcomes were measured in both studies, but they were not designed or powered to evaluate these outcomes. Donohue et al. 2013 did include a patient-orientated outcome (TDI score) which was powered to detect differences between treatment groups. However, in this study umeclidinium/vilanterol was only compared with its individual components and placebo.

For both studies in Decramer et al. 2014 a hierarchical design was used to avoid spurious statistically significant findings arising through chance, given the number of possible comparisons.

If a statistical test in the predefined hierarchy had a non-significant result, the results of all further statistical analyses would not be strictly inferential. In study 2 there was no statistically significant difference between umeclidinium/vilanterol 125/25 micrograms and umeclidinium 125 micrograms for the primary outcome, therefore statistical analysis of further comparisons which included umeclidinium/vilanterol 62.5/25 micrograms are presented for descriptive purposes only. Treatment comparisons for additional analyses such as rescue salbutamol use were not controlled for multiplicity.

There are limited published long-term efficacy and safety data for the licensed dose. Decramer et al. 2014, Maleki-Yazdi et al. 2014 and Donohue et al. 2013 were conducted over 24 weeks only.

Context

Alternative treatments

NICE recommendations for using inhaled treatments for chronic obstructive pulmonary disease (COPD) are outlined in the [introduction](#) to this evidence summary.

Umeclidinium/vilanterol is the first long-acting muscarinic antagonist/ long-acting beta₂ agonist (LAMA/LABA) combination inhaler available in the UK for the treatment of COPD. Indacaterol/ glycopyrronium (Ultibro Breezhaler 85/43 micrograms) was the first combination inhaler containing a LABA and a LAMA to receive a European marketing authorisation for COPD (see the evidence summary on [chronic obstructive pulmonary disease: indacaterol/glycopyrronium](#)). However, Ultibro Breezhaler was not available in the UK at the time umeclidinium/vilanterol was launched in June 2014. The manufacturer does not currently have a date for the UK launch of Ultibro Breezhaler (Novartis: personal communication September 2014).

There are also 4 combined inhaled corticosteroid (ICS)/LABA inhalers that are currently licensed for treating COPD:

- beclometasone/formoterol metered dose inhaler ([Fostair 100/6 micrograms: see the evidence summary on Chronic obstructive pulmonary disease – beclometasone/formoterol](#))
- budesonide/formoterol dry powder inhaler ([Symbicort Turbohaler 200/6 micrograms and Symbicort Turbohaler 400/12 micrograms](#))
- fluticasone furoate/vilanterol dry powder inhaler ([Relvar Ellipta 92/22 micrograms: see the evidence summary on chronic obstructive pulmonary disease – fluticasone furoate plus vilanterol](#))

- fluticasone propionate/salmeterol dry powder inhaler (Seretide Accuhaler 500/50 micrograms).

Four single-component LABAs are currently licensed for use in COPD in the UK, formoterol, indacaterol, olodaterol and salmeterol. An evidence summary on the use of olodaterol for the treatment of COPD is in development with an anticipated publication date of February 2015. Single-component LAMAs licensed for use in COPD are aclidinium, glycopyrronium, tiotropium and umeclidinium. Umeclidinium (Incruse) was launched in the UK in October 2014. An evidence summary on the use of umeclidinium for the treatment of COPD is in development with an anticipated publication date of January 2015.

Costs of alternative treatments

Drug	Usual dosage ^{a,b}	30-day cost excluding VAT
Single-component LABAs		
Formoterol fumarate 12 micrograms (Formoterol Easyhaler)	1 puff twice daily	£11.88 ^{c,d}
Indacaterol maleate 150 and 300 micrograms (Onbrez Breezhaler)	1 puff daily	£29.26 ^c
Olodaterol 2.5 micrograms (Striverdi Respimat)	2 puffs daily	£26.35 ^e
Salmeterol xinafoate 50 micrograms (Serevent Accuhaler)	1 puff twice daily	£29.26 ^{c,d}
Single-component LAMAs		
Aclidinium bromide 322 micrograms (Eklira Genuair)	1 puff twice daily	£28.60 ^e
Glycopyrronium bromide 50 micrograms (Seebri Breezhaler)	1 puff daily	£27.50 ^e
Tiotropium bromide 18 micrograms, dry powder (Spiriva Handihaler)	1 puff daily	£34.87 ^c
Tiotropium bromide 2.5 micrograms, aerosol (Spiriva Respimat)	2 puffs daily	£33.50 ^e
Combination LAMA/LABA inhalers		

Umeclidinium/vilanterol 55/22 micrograms (Anoro Ellipta)	1 puff daily	£32.50 ^e
Combination ICS/LABA inhalers		
Beclometasone/formoterol 100/6 micrograms (Fostair)	2 puffs twice daily	£29.32 ^c
Budesonide/formoterol 200/6 micrograms (Symbicort Turbohaler)	2 puffs twice daily	£38.00 ^c
Budesonide/formoterol 400/12 micrograms (Symbicort Turbohaler)	1 puff twice daily	£38.00 ^c
Fluticasone furoate/vilanterol 92/22 micrograms (Relvar Ellipta)	1 puff daily	£27.80 ^e
Fluticasone propionate/salmeterol 500/50 micrograms (Seretide Accuhaler)	1 puff twice daily	£40.92 ^c
<p>Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta₂ agonist; LAMA, long-acting muscarinic antagonist.</p> <p>^a Doses taken from the relevant summary of product characteristics.</p> <p>^b The doses shown do not represent the full range that can be used and they do not imply therapeutic equivalence.</p> <p>^c Costs taken from the Drug Tariff (October 2014). All costs include the inhaler device.</p> <p>^d Lowest cost dry powder formulations selected; other brands and formulations are available.</p> <p>^e Costs taken from MIMS (October 2014). All costs include the inhaler device.</p>		

Estimated impact for the NHS

Likely place in therapy

Umeclidinium/vilanterol has been compared with its individual components as monotherapy and the long-acting muscarinic antagonist (LAMA), tiotropium. There are no published studies which compare umeclidinium/vilanterol with currently available long-acting beta₂ agonist (LABA) and LAMA treatment given concomitantly.

[Maleki-Yazedi et al. 2014](#) showed a statistically significant improvement from baseline in trough FEV₁ of 0.112 litres with umeclidinium/vilanterol 62.5/25 micrograms compared with tiotropium 18 micrograms. There was also a statistically significant improvement from baseline in trough FEV₁

with umeclidinium/vilanterol 62.5/25 micrograms compared with tiotropium 18 micrograms in 1 of the studies reported in [Decramer et al. 2014](#). However, this was less than the improvement that the full NICE guideline on [COPD](#) considers to be clinically important. For the second study reported in [Decramer et al. 2014](#) statistical analysis for umeclidinium/vilanterol 62.5/25 micrograms is not strictly inferential due to the hierarchical design of the study.

There is limited evidence on patient-orientated outcomes such as shortness of breath, quality of life outcomes or exacerbation rates. [Decramer et al. 2014](#) and [Maleki-Yazedi et al. 2014](#) both had disease-orientated FEV₁ primary and secondary outcomes. Additional patient-orientated outcomes were measured in both studies, but they were not designed or powered to evaluate these outcomes. In [Donohue et al. 2013](#), transition dyspnoea index (TDI) score was included as an efficacy outcome and the study was powered to detect a 1 unit difference between treatments. However, in this study umeclidinium/vilanterol was only compared with its individual components and placebo. There was a statistically significant improvement in TDI score at day 168 with umeclidinium/vilanterol 62.5/25 micrograms compared with placebo. However, there was no statistically significant difference for TDI score with umeclidinium/vilanterol 62.5/25 micrograms compared with umeclidinium or vilanterol monotherapy.

The concomitant use of inhaled corticosteroids (ICS) as an option for people in these studies varied at pre-treatment by between 40% and 56% in the allocated groups. The NICE guideline on [COPD](#) recommends that the choice of drug treatment should take into account the person's symptomatic response and preference, and the drug's potential to reduce exacerbations, side effects and costs. The use of dual therapy with a LAMA and LABA may be considered if an ICS (as combination therapy with a LABA) is declined or not tolerated. NICE developed these recommendations in 2010, which predates the publication of the evidence for the newer LABAs and LAMAs such as vilanterol, indacaterol, glycopyrronium and umeclidinium.

The umeclidinium/vilanterol combination inhaler is less expensive than the combined cost of other single-component LAMA or LABA inhalers and may be more convenient for people. However, compared with established drugs such as formoterol, salmeterol and tiotropium, the comparative efficacy and long-term safety of umeclidinium/vilanterol is unclear, particularly in terms of reducing exacerbations.

Local decision makers will need to take these factors into account when considering the likely place in therapy of umeclidinium/vilanterol for COPD.

Estimated usage

Using data from the quality and outcomes framework the manufacturer estimates that 819,524 people in England have been diagnosed with COPD. They estimate that 28.84% of the total COPD population (which is approximately 236,350 people) may be eligible for Anoro Ellipta (Glaxo Smith Kline: personal communication June 2014).

Relevance to NICE guidance programmes

Umeclidinium/vilanterol was not considered appropriate for a NICE technology appraisal and is not currently planned into any other NICE work programme.

In 2010, NICE published a guideline on [chronic obstructive pulmonary disease](#), which has been incorporated into a [NICE pathway](#). A [review decision](#) was made on this guideline in July 2014 and it was decided that this guideline should not be updated at this time.

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Development of this evidence summary

The [integrated process statement](#) sets out the process NICE uses to select topics for the evidence summaries: new medicines and how the summaries are developed, quality assured and approved for publication.

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Declarations of interest

No relevant interests declared.

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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