Commissioning Support

Fluticasone furoate 92mcg, vilanterol trifenatate 22mcg, umeclidinium bromide 65mcg

(Trelegy Ellipta®▼)

For maintenance treatment of chronic obstructive pulmonary disease (COPD)

Commissioning guidance:

Commissioners may wish to bear the following in mind when considering the commissioning of Trelegy Ellipta:

- The need for accurate diagnosis and identification of the disease severity as moderate to severe.
- The need for accurate recording of the patient's diagnosis and exacerbation history through use of a standard form, such as the COPD Assessment Test.[1]
- Local guidance advises consideration of the patient's eligibility for pulmonary rehabilitation, as well as other measures, such as smoking cessation and flu vaccination as part of the management of COPD.[2]
- In patients who need the triple combination of ICS/LABA/LAMA (inhaled corticosteroid/long-acting beta agonist/long acting muscarinic antagonist), there may be benefit in terms of increased patient convenience and compliance with the use of a single inhaler instead of two.
- There is a lower 30-day acquisition cost associated with the use of the triple inhaler compared with the use of two inhalers to deliver ICS/LABA + LAMA.

Strength of the evidence for efficacy

A large phase III double blind randomised controlled trial (RCT: IMPACT) found that triple ICS/LABA/LAMA treatment via the Trelegy Ellipta inhaler was more effective than dual ICS/LABA (Relvar) or LAMA/LABA (Anoro) in lowering the annual rate of exacerbations in people with COPD who had experienced at least one exacerbation. There were also significantly greater improvements in lung function (trough forced expiratory volume in one second; FEV_1) and quality of life (St George's Respiratory Questionnaire; SGRQ) with the triple therapy *vs*. dual therapies. A second double-blind, double-dummy RCT showed that Trelegy Ellipta showed greater improvements in lung function and quality of life compared with twice daily ICS/LABA therapy with 400 mcg budesonide/12 mcg formoterol (Symbicort Turbohaler). Finally, a phase III, double-blind RCT found that that triple therapy via the Trelegy Ellipta inhaler was non-inferior to the same active ingredients delivered via two separate inhalers for the outcome of improvement in lung function over 24 weeks. Improvement in quality of life (SGRQ) was also demonstrated.

MTRAC considered Trelegy Ellipta because it was a newly licensed product that primary care prescribers may be asked to prescribe.

Description of technology

Trelegy Ellipta (dry powder inhaler [DPI] containing ICS: fluticasone furoate 92 mcg; LABA: vilanterol trifenatate 22 mcg; LAMA: umeclidinium bromide 65 mcg [delivered doses per inhalation]) is licensed as a maintenance treatment in adult patients with moderate to severe COPD who are not adequately treated by a combination of an inhaled corticosteroid and a LABA.[3] The recommended dose is one inhalation, once daily.

See the Summary of Product Characteristics (SPC) for full details of this product.[3]

Background

COPD is a common inflammatory disease characterised by persistent respiratory symptoms and pulmonary airflow obstruction that is usually progressive and not fully reversible.[4] It is a common cause of long-term disability and death that presents a major burden to healthcare services.

There are estimated to be over 3 million people with COPD in the UK.[5] Quality and outcomes framework (QOF) data for 2016/17 show that the mean prevalence of diagnosed COPD in the West Midlands (NHS England region) is 1.86% (74,366 patients).[6] Between April 2010 and March 2011, COPD was the primary diagnosis in 31,795 emergency hospital admissions in the West Midlands.[7]

Current guidance advises that triple therapy with an ICS/LABA + LAMA is recommended for use in people with moderate to severe COPD who have continued breathlessness and exacerbations despite treatment with an ICS/LABA combination or LAMA (GOLD category D: high risk of exacerbations, more symptoms).[2,4,8]

Clinical evidence for efficacy and safety

Three published RCTs evaluated Trelegy Ellipta for the treatment of moderate to very severe COPD in people with a history of exacerbations.[9-11]

The IMPACT trial (n = 10,335; duration 52 weeks)[11], compared Trelegy Ellipta (umeclidinium bromide 62.5 mcg [UMEC]; fluticasone furoate 92 mcg [FF]; vilanterol trifenatate 22 mcg [VI]) with dual inhalers containing ICS/LABA (Relvar: FF/ VI) or LAMA/LABA

NICE accredited
www.nice.org.uk/accreditation

NICE has accredited the process used by the Midlands Therapeutics Review and Advisory Committee to produce Commissioning support summaries. Accreditation is valid for 5 years from 7 March 2017. More information on accreditation can be viewed at www.evidence.nhs.uk

For full details of our accreditation visit: www.nice.org.uk/accreditation

(Anoro:UMEC/VI). The primary outcome was the annual rate of exacerbations with triple therapy compared with either Anoro or Relvar. Selected secondary outcomes were the change from baseline in lung function (trough FEV_1; pre-bronchodilator FEV_1) and quality of life (SGRQ). The trial found a significantly lower rate of moderate or severe exacerbations with the Trelegy Ellipta inhaler *vs.* the Relvar and Anoro Ellipta inhalers (rate 0.91 per year *vs.* 1.07 and 1.21 for Relvar and Anoro, respectively [p < 0.001]). The trial also showed statistically significantly greater improvements in lung function and quality of life for Trelegy *vs.* Relvar or Anoro.[11]

In a trial reported by Bremer et al[9], Trelegy Ellipta was compared with the same combination of components delivered via two Ellipta inhalers. The first was an ICS/LABA inhaler containing fluticasone furoate and vilanterol, plus a second separate LAMA inhaler delivering umeclidinium *(whilst not explicitly stated in the paper, these are assumed to be the Relvar 92/22 and Incruse Ellipta inhalers)*. The 1,055 participants enrolled in the trial were aged over 40, with a smoking history of at least 10 pack-years, and a history of exacerbations in the year before trial entry. The primary outcome was change in lung function (trough FEV_1) at Week 24. Secondary outcomes included measures of breathlessness (Transition Dyspnoea Index [TDI]) and quality of life (SGRQ).

Results showed that there were no significant differences between the treatment groups for any of the primary or secondary outcomes measured. The mean change in trough FEV_1 was 0.113 L in the Trelegy Ellipta group compared with 0.095 L in the group using two Ellipta inhalers; the difference was 0.018 L (95% Confidence Interval [CI] -0.013 to 0.050); the value of the lower limit of the CI meeting the criterion for non-inferiority (>-0.05 L). In both treatment groups, roughly the same number (about 51%) of participants showed a response to treatment on the SGRQ scale, and in both groups, 56% of participants showed a clinically significant improvement in breathlessness (TDI focal score improvement >1). Moderate to severe exacerbations were reported for 24% of participants in the Trelegy Ellipta group and 27% of participants in the group using two inhalers.[9]

The FULFIL trial (n = 1,810)[10] compared Trelegy Ellipta with twice-daily ICS/LABA dual combination inhaler (budesonide 400 mcg plus formoterol 12 mcg; Symbicort Turbohaler). Participants enrolled in the trial had symptoms of exacerbations and breathlessness relating to GOLD group D and had suffered at least two moderate or one severe exacerbation in the year before the trial. The primary outcomes in the trial were measures of lung function (change from baseline in trough FEV_1) and quality of life (change from baseline in SGRQ total score) at Week 24.

There were significantly greater improvements in trough FEV_1 in the Trelegy Ellipta group compared with the Symbicort group (mean treatment difference 0.17L; 95% CI 0.15 to 0.19; p < 0.001).[10] There were also significantly greater improvements in the SGRQ total score for Trelegy Ellipta *vs*. Symbicort (-6.6 units *vs*. -4.3 units; p < 0.001) but not after the extension phase at 52 weeks. Incidence rates of moderate to severe exacerbations over 24 weeks' treatment were lower with Trelegy Ellipta *vs*. Symbicort (10% *vs*. 14%; *absolute risk reduction 4%; number needed to treat 25 over 24 weeks [authors calculation]*). Comparison of mean annualised rates indicated this to be a statistically significant reduction (35% reduction in annualised rates; p = 0.002).[10]

Adverse events

The first trial[9] reported viral upper respiratory tract infection (10% [Trelegy] and 11% [two inhaler group]), headache (6% in both groups) and worsening of COPD (4% to 6%) amongst the most frequent adverse events. The incidences of pneumonia (3% and 4%) and cardiovascular events (6% and 5%) were similar between groups. [9] In the FULFIL[10] trial, the incidence of treatment-emergent adverse events was 39% in the Trelegy Ellipta group and 38% in the Symbicort group. The most common adverse events were nasopharyngitis (7% and 5% for the Trelegy and Symbicort groups) and headache (5% and 6%). Worsening of COPD was one of the most common adverse events in the Symbicort group. The most common serious adverse events were COPD exacerbation (1.3% and 2.3%) and pneumonia (1% and 0.3%).

Considerations for cost impact

The current prices of the new triple therapy combined inhalers are shown below (yearly cost, excluding VAT; Source MIMS Online, August 2018):

- Trimbow (2 inhalations, twice daily; pMDI*) £541.42
- Trelegy Ellipta (1 inhalation, once daily; DPI) £541.42

**pressurised metered dose inhaler*

References

1. COPD Assessment Test. GlaxoSmithKline Services Unlimited 2016
2. Turner A. Diagnosis and management of stable COPD. Pan Birmingham Respiratory Clinical Network 2017
3. GlaxoSmithKline UK. Trelegy. EMC 2017
4. Global Initiative for Chronic Obstructive Lung Disease 2018
5. An Outcomes Strategy for COPD and Asthma: NHS Companion Document. Department of Health 2012
6. QOF 2016/17 results. NHS Digital 2017
7. Hospital episode statistics data. HESonline 2012
8. Chronic obstructive pulmonary disease in over 16s: diagnosis and management (CG101). NICE 2010
9. Bremner PR et al. *Respir Res* 2018; 19(1):19.
10. Lipson DA et al. *Am J Respir Crit Care Med* 2017; 196(4):438-446.
11. Lipson DA N et al. Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD. *NEJM* 2018; 378 (18);1671-80

WARNING: This sheet should be read in conjunction with the Summaries of Product Characteristics
This guidance is based upon the published information available in English at the time the drug was considered. It remains open to review in the event of significant new evidence emerging.

Keele University Centre for Medicines Optimisation