Bedfordshire and Luton Joint Prescribing Committee (JPC)

18th September 2019
Review September 2021

Bulletin 280: Fluticasone/vilanterol 92/22 micrograms inhalation powder (Relvar® Ellipta®) for the treatment of COPD

JPC Recommendation:

- The committee agreed to add Fluticasone/vilanterol (Relvar®Ellipta®) powder for inhalation to the formulary within it's licensed indication as a 1st line choice ICS / LABA option for the treatment of COPD.

Bedfordshire CCG
Luton CCG

New Medicine Review

Choice of combination Inhaled corticosteroid (ICS) and Long Acting Beta Agonist (LABA) inhaler for Chronic Obstructive Pulmonary Disease (COPD)

Medicine	Fluticasone/vilanterol 92/22 micrograms inhalation powder (Relvar Ellipta®)
Document status	Final , approved September 2019
Date of last revision	August 2019
Proposed Sector of prescribing	Primary and secondary care
Introduction Summary Key points Evidence level	Fluticasone furoate is a once-daily inhaled corticosteroid (ICS) and vilanterol is a once-daily inhaled long-acting beta2 agonist (LABA). A combination multi-dose dry powder inhalation device (the Ellipta® device) containing fluticasone furoate 100 micrograms and vilanterol 25 micrograms (delivered doses of 92 micrograms of fluticasone furoate and 22 micrograms of vilanterol) has been licensed and launched for the symptomatic treatment of COPD in adults. The JPC previously considered Relvar Ellipta® in 2013 prelaunch and again in 2014, following marketing authorisation being granted. There are currently 4 ICS/LABA combinations licensed for the maintenance treatment of patients with chronic obstructive pulmonary disease. Currently the formulary and COPD guidelines include formoterol + budesonide (Symbicort® Turbohaler 400/12 or MDI 200/6 or DuoResp® Spiromax®) beclomethasone + formoterol (Fostair® cfc-free inhaler MDI +/- spacer) but not fluticasone furoate/vilanterol (Relvar® Ellipta®) or fluticasone propionate + salmeterol (Seretide® Accuhaler®) Clinical experience from Dr Bagmane at Bedford Hospital suggests once daily preparations are better at supporting patients that struggle to comply with twice daily.
The intervention Mechanism of action	Relvar®▼ Ellipta® is a combination inhaler containing 2 active ingredients not previously available: fluticasone furoate (an inhaled corticosteroid [ICS]) and vilanterol (a long-acting beta2 agonist [LABA]). These are administered using the multi-dose, dry powder Ellipta® inhalation device.
Licensed indication	Relvar Ellipta is indicated for the symptomatic treatment of adults with COPD with a FEV1<70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.
Formulation/Available Products	1. Beclomethasone + formoterol (Fostair®) 100/6 MDI +/- spacer. Two puffs twice daily.

2. Beclomethasone + formoterol (Fostair® NEXThaler®) 100/6. Two inhalations twice daily.

3. Formoterol + Budesonide (DuoResp Spiromax®) 160/4.5 micrograms and 320/9 micrograms inhalation powder. 160 / 4.5 strength - Two inhalations twice daily, 320 / 9 strength-One inhalation twice daily.

4. Formoterol + Budesonide (Symbicort® Turbohaler®) 400/12 micrograms inhalation powder. One inhalation twice daily.

5. Formoterol + Budesonide (Symbicort®) MDI 200/6 micrograms per actuation. One inhalation twice daily

	6. Fluticasone + vilanterol (Relvar® Ellipta®) 92 micrograms/22 micrograms inhalation powder, pre-dispensed. 
Usual dosage	One inhalation of Relvar Ellipta 92/22 micrograms once daily.
Treatment alternatives/ place in therapy	The Bedfordshire and Luton COPD and ACO Guidelines recommend offering a ICS/LABA if the patients symptoms persist despite using a salbutamol (or an alternative SABA) and if the MRC is 3 or above and the CAT is 10 or above.
Future alternatives	
National guidance	NICE guidance (NG115) on Chronic Obstructive Pulmonary Disease recommends the use of ICS/LABAs for the management of COPD in patients who have asthmatic features/features suggesting steroid responsiveness. BTS GOLD guidelines (2019) recommends in some patients, initial therapy with LABA/ICS may be the first choice; this treatment has the greatest likelihood of reducing exacerbations in patients with blood eosinophil counts ≥300 cells/μl. LABA/ICS may also be first choice in COPD patients with a history of asthma Neither guidance makes a recommendation about which LAMA/LABA should be chosen but suggest that treatment should be individualised
Local Guidance	The Bedfordshire and Luton COPD and ACO Guidelines recommend offering a ICS/LABA combination inhaler if the patients symptoms persist despite using a salbutamol (or an alternative SABA) and if the MRC is 3 and above, and the CAT is 10 or above. Or in patients experiencing persistent breathlessness or exacerbations on LAMA inhaler. All ICS/LABA inhalers on the formulary currently are joint in their formulary position.
Evidence for use	Since the JPC last reviewed the inclusion of fluticasone/vilanterol on the formulary the following studies have been published. • Vestbo et al. (2016) evaluated the effectiveness and safety of fluticasone/vilanterol compared with existing maintenance therapy (usual care). In the usual care group the prescribers could freely modify COPD maintenance treatment according to local clinical practice. In patients with COPD and a history of exacerbations, a once-daily treatment regimen of fluticasone/vilanterol was associated with a lower rate of exacerbations than usual care, without a greater risk of SAEs. • In the SUMMIT(2016) study, Vestbo et all assessed whether fluticasone/vilanterol 92/22mcg, fluticasone, and vilanterol could improve survival compared with placebo in patients with moderate COPD and heightened cardiovascular risk. In patients with moderate COPD and heightened cardiovascular risk, treatment with fluticasone/vilanterol did not affect mortality or cardiovascular

outcomes but is associated with fewer exacerbations of COPD and is well tolerated. Inhaled therapy improved lung function and fluticasone, alone or in combination with vilanterol, was associated with a reduction in the rate of decline in FEV1 compared to placebo.

Previous review for the JPC reported the following evidence:
This evidence review is based on the 4 randomised controlled trials (RCTs) that provide the best published evidence for fluticasone furoate/vilanterol for treating chronic obstructive pulmonary disease (COPD) and that have been published in full. Dransfield et al. (2013) [3] published results from two 52-week randomised, double-blind, parallel group studies that investigated whether fluticasone furoate/vilanterol in combination (3 different doses of fluticasone furoate) would prevent more exacerbations compared with vilanterol alone.
A second RCT included in this evidence summary (Kerwin et al. 2013) [4] compared 2 strengths of fluticasone furoate/vilanterol with the same strengths of the individual components and placebo in patients with COPD. The 2 co-primary outcomes were the weighted mean FEV_1 (forced expired volume in 1 second; 0 to 4 hours post-dose) on day 168, and the change from baseline in trough FEV_1 (23–24 hours post-dose) on day 169. An additional study (Martinez et al. 2013) [5] had the same design as that by Kerwin et al. (2013) [4] but for methodological reasons, statistical analysis of the results for fluticasone furoate/vilanterol 100/25 micrograms could not be performed.
A further relevant phase III trial has been completed, (Agusti et al 2014) [6]. This trial assessed the 24-hour spirometry effect (FEV_1) of fluticasone furoate/vilanterol 100/25 micrograms once daily compared with fluticasone propionate/salmeterol 500/50 micrograms (Seretide 500® Accuhaler) twice daily over a 12-week treatment period in people with COPD. It was designed as a superiority trial but as statistical significance of the primary endpoint was not met; statistical significance could not be inferred for comparisons of secondary endpoints.

Dransfield et al. (2013) [3]

- Design: 2 simultaneous, replicate, 52-week, randomised, double-blind, parallel group studies. Each had a 4-week open-label run-in period using combination fluticasone propionate/salmeterol 250/50 micrograms twice daily. The method of allocation described suggests that this was concealed.
- Population: 1622 adults in study 1 and 1633 adults in study 2. Study 1 involved 167 sites in 15 countries and study 2 involved 183 sites in 15 countries. Participants were 40 years or older (mean 64 years) with COPD (post-bronchodilator FEV_1 70% predicted or less, mean range 44.3% to 46.4%, and FEV_1/FVC [forced vital capacity] ratio 0.7 or less), a history of at least 1 COPD exacerbation in the previous year that needed systemic or oral corticosteroids, antibiotics or admission to hospital, and a smoking history of 10 or more pack-years.
- Intervention and comparison: participants were randomised in approximately equal numbers to 4 treatments, taken once daily using the Ellipta inhaler:
    - fluticasone furoate 50 micrograms (emitted dose 44 micrograms) plus vilanterol 25 micrograms (emitted dose 22 micrograms)

- fluticasone furoate 100 micrograms (emitted dose 92 micrograms) plus vilanterol 25 micrograms (emitted dose 22 micrograms)
- fluticasone furoate 200 micrograms (emitted dose 184 micrograms) plus vilanterol 25 micrograms (emitted dose 22 micrograms)
- vilanterol 25 micrograms (emitted dose 22 micrograms).

- Outcome: the primary efficacy end point was the yearly rate of moderate and severe COPD exacerbations. Moderate exacerbations were defined as worsening symptoms of COPD needing treatment with oral corticosteroids and/or antibiotics. Severe exacerbations were defined as those that needed hospital admission. Secondary and additional end points included the time to first moderate or severe exacerbation, yearly rate of severe exacerbations, the number of night-time awakenings due to symptoms, and dyspnoea score. Specific safety end points included haematological and clinical measurements, incidence of bone fractures and clinically diagnosed pneumonia. The 2 studies were analysed separately and in a predefined pooled analysis, based on the intention-to-treat population. Results of this pooled analysis are summarised in table 2.

Table 2 Summary of the pooled analysis, Dransfield et al. (2013) [3]

	Fluticasone furoate/vilanterol once daily (micrograms)			**Vilanterol 25 micrograms once daily**
	50/25	**100/25**	**200/25**	
Efficacy (ITT population)	n=820	n=806	n=811	n=818
Primary outcome				
Moderate and severe exacerbations; LS mean yearly rate	0.93	0.81	0.85	1.11
LS mean yearly RR for moderate and severe exacerbations (95% CI) compared with vilanterol alone	0.8 (0.7 to 1.0), p=0.014	0.7 (0.6 to 0.8), p<0.0001	0.8 (0.7 to 0.9), p=0.0003	–
Selected secondary and additional outcomes				

Time to first moderate or severe exacerbation: HR (95% CI) compared with vilanterol alone	0.9 (0.8 to 1.0), p=0.114	0.8 (0.7 to 0.9), p=0.0002	0.8 (0.7 to 0.9), p=0.0001	–
Severe exacerbation LS mean yearly rate	0.08	0.09	0.08	0.10
LS mean yearly RR for severe exacerbations (95% CI) compared with vilanterol alone	0.8 (0.6 to 1.2), p=0.313	0.9 (0.6 to 1.4), p=0.695	0.8 (0.5 to 1.2), p=0.280	–
Night-time awakenings, LS mean difference (95% CI) from vilanterol alone	−0.06 (−0.10 to −0.01), p=0.011	−0.08 (−0.12 to −0.03), p=0.001	−0.07 (−0.12 to −0.03), p=0.002	–
Dyspnoea score[a]: LS mean difference (95% CI) from vilanterol alone	−0.08 (−0.12 to −0.03), p=0.0006	−0.09 (−0.014 to −0.05), p<0.0001	−0.11 (−0.16 to −0.07), p<0.0001	–
Abbreviations: CI, confidence interval; HR, hazard ratio; ITT, Intention-to-treat; LS, least squares; RR, rate ratio. [a] Dyspnoea was scored on a scale of −2 to +2, with −2 indicating 'much less than usual' and +2 indicating 'much more than usual'. [b] No statistical analysis of safety outcomes was presented.				

Kerwin et al. (2013) [4]

- Design: 24-week double-blind, placebo-controlled RCT. The method of allocation described suggests that this was concealed.
- Population: 1030 adults in 9 countries aged at 40 years or older (mean 63 years) with COPD (post bronchodilator FEV_1 70%

predicted or less, mean range 46.9–49.9%, and FEV_1/FVC ratio 0.7 or less), a smoking history of at least 10 pack-years, and a score of at least 2 on the Modified Medical Research Council Dyspnoea Scale. No previous history of COPD exacerbations was needed but about a quarter of participants had had at least 1 moderate exacerbation of COPD (needing treatment with oral corticosteroids and/or antibiotics but not hospital admission) and about 7% had had at least 1 severe exacerbation (needing hospital admission) in the year before trial entry.

- Intervention and comparison: participants were randomised in approximately equal numbers to 5 treatments, taken once daily in the morning using a dry powder inhaler:
  - fluticasone furoate 50 micrograms (emitted dose 44 micrograms) plus vilanterol 25 micrograms (emitted dose 22 micrograms)
  - fluticasone furoate 100 micrograms (emitted dose 92 micrograms) plus vilanterol 25 micrograms (emitted dose 22 micrograms)
  - fluticasone furoate 100 micrograms (emitted dose 92 micrograms)
  - vilanterol 25 micrograms (emitted dose 22 micrograms)
  - placebo.
- Outcomes: there were 2 co-primary outcomes: weighted mean FEV_1 (0–4 hours post-dose) on day 168, and the change from baseline in trough FEV_1 (23–24 hours post-dose) on day 169.The primary analysis was based on the intention-to-treat population split into 2 levels pre-specified by the authors to avoid spurious statistically significant findings arising through chance, given the number of possible comparisons:
  - The level 1 analysis consisted of 6 key comparisons of the co-primary end points for fluticasone furoate/vilanterol 100/25 micrograms and vilanterol 25 micrograms. These are summarised in the discussion of the evidence for clinical effectiveness.
  - The authors specified that only if all comparisons reached statistical significance at level 1 would they move on to level 2 analyses, which included comparison with fluticasone furoate/vilanterol 50/25 micrograms. The level 1 analysis did not meet the pre-defined criteria and so no formal statistical testing was performed at level 2.
- Secondary and additional outcomes included changes in dyspnoea score, night-time awakenings and other symptom-related end points but the statistical hierarchy used in the analysis meant that no statistical significance can be inferred from the results for these outcomes.

Agusti et al (2014)[6]

- Design – 12 week randomised, multicentre (62 centres in Europe and Asia), double-blind, double-dummy, parallel-group, comparative efficacy/safety study. Patients entered a 2-week, placebo run-in period.
- Intervention and comparison: participants were randomised in equal numbers to receive in a double blind manner Fluticasone

furoate/vilanterol (FF/VI)100/25 micrograms daily via the Ellipta dry powder inhaler that emits a dose of 92 micrograms Fluticasone furoate and 22 micrograms vilanterol or Fluticasone propionate/salmeterol (FP/SAL) 500/50 micrograms twice daily via Accuhaler device. Patients receiving FF/VI also took a placebo Accuhaler once in the morning and once in the evening and patients receiving FP/SAL took a placebo once in the morning using the Ellipta dry powder inhaler.

- Outcome: the primary efficacy endpoint was the 24 hour effect of FF/VI on lung function after 12 weeks of treatment (day 84), as compared with FP/SAL. This was assessed through the change from baseline in weighted mean (wm) FEV_1. Secondary efficacy endpoints were time to 100mL increase from baseline from 0-4 h on day 1, change from baseline in trough FEV_1 on day 85, health status, *post-hoc* analysis of the difference in lung function 0-4 h, 0-12 hand 12-24 h post-dose on day 84. Safety and tolerability were assessed by the incidence of adverse events (AEs) and severe AEs (SAEs) and AEs of special interest. The trial was designed as a superiority study based on the extrapolation of previous $wmFEV_1$ results with salmeterol and vilanterol monotherapy. A treatment difference of 60mL with a standard deviation (SD) of 190mL between FF/VI and FP/SAL was assumed. Although an improvement from baseline in 0-24 hour $wmFEV_1$ was observed in both arms of the trial (fluticasone furoate/vilanterol {mean +/- SD = 130 +/-22mL} and fluticasone propionate/salmeterol {mean +/- SD = 108 +/- 221mL), the difference in improvement between the two arms (22mL) (primary endpoint) was not statistically significant (p=0.282) and therefore superiority of fluticasone furoate/vilanterol over fluticasone propionate/salmeterol was not proven. As statistical significance could not be achieved for the primary endpoint, statistical significance could not be inferred for comparisons of secondary endpoints.

Clinical effectiveness

Discussion of the evidence for clinical effectiveness focuses on fluticasone furoate/vilanterol 100/25 micrograms because that is the dose and strength that has been submitted for licensing. In their predefined pooled analysis, Dransfield et al. (2013) [3] found that the mean yearly rate for moderate and severe exacerbations for fluticasone furoate/vilanterol 100/25 micrograms was 0.81 compared with 1.11 for vilanterol 25 micrograms alone. The yearly rate ratio was 0.7 (95% confidence interval [CI] 0.6 to 0.8), a reduction of 30% in relative terms. This was similar in people with a history of frequent exacerbations; defined as at least 2 moderate or severe exacerbations in the previous year (yearly rate ratio 0.7, 95% CI 0.6 to 0.9, p=0.0005). The full NICE guideline on COPD [1]considered a relative reduction in the risk of exacerbations of 20% or more to be clinically important. This dose of fluticasone furoate/vilanterol also increased the time to first moderate or severe exacerbation compared with vilanterol 25 micrograms alone (hazard ratio 0.8, 95% CI 0.7 to 0.9, p=0.0002). However, it was not shown to reduce the mean yearly rate of severe exacerbations (those needing admission to hospital) compared with vilanterol 25 micrograms alone (rate ratio 0.9, 95% CI 0.6 to 1.4, p=0.695).

	Compared with vilanterol 25 micrograms alone, fluticasone furoate/vilanterol 100/25 micrograms also produced statistically significant improvements in night-time awakenings (mean difference −0.08, 95% CI −0.12 to −0.03, p=0.0012) and dyspnoea (mean difference −0.09, 95% CI −0.014 to −0.05, p<0.0001, on a scale of −2 to +2, with −2 indicating 'much less than usual' and +2 indicating 'much more than usual'). Kerwin et al. (2013) [4] found that fluticasone furoate/vilanterol 100/25 micrograms was statistically significantly superior to placebo in improving post-dose weighted mean FEV_1 (173 ml, 95% CI 123 to 224 ml, p<0.001) and trough FEV_1 (115 ml, 95% CI 60 to 169 ml, p<0.001) after 24 weeks' treatment. However, there was no statistically significant difference in trough FEV_1 between fluticasone furoate/vilanterol 100/25 micrograms and vilanterol 25 micrograms (48 ml, 95% CI -6.0 to 102ml, p=0.082). A further study by Martinez et al. (2013) [5] was of a similar design to that by Kerwin et al. (2013) and was intended to provide multiple statistical comparisons between fluticasone furoate/vilanterol 200/25 micrograms and fluticasone furoate/vilanterol 100/25 micrograms compared with their individual components and placebo. The authors used a similar hierarchy of statistical analysis to Kerwin et al. (2013) [4], which involved analysis of comparisons of fluticasone furoate/vilanterol 200/25 micrograms in the first stage. Pre-specified criteria were not met so the second stage, which would have included comparisons of fluticasone furoate/vilanterol 100/25 micrograms, was not conducted. A short-term study by Agusti et al (2014)[6] assessed the 24-hour spirometry effect (FEV_1) of fluticasone furoate/vilanterol 100/25 micrograms once daily compared with fluticasone propionate/salmeterol 500/50 micrograms (Seretide 500 Accuhaler) twice daily over a 12-week treatment period in people with COPD. It was designed as a superiority trial but statistical significance of the primary endpoint was not met.
Safety*	The most commonly reported adverse reactions with fluticasone furoate and vilanterol were headache and nasopharyngitis. Other common side effects include oropharyngeal pain, abdominal pain, pneumonia and pyrexia. With the exception of pneumonia and fractures, the safety profile was similar in patients with asthma and COPD. During clinical studies, pneumonia and fractures were more frequently commonly observed in patients with COPD. Paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. Cardiovascular effects, such as cardiac arrhythmias e.g. supraventricular tachycardia and extrasystoles may be seen with sympathomimetic medicinal products including Relvar Ellipta. In a placebo-controlled study in subjects with moderate COPD and a history of, or an increased risk of cardiovascular disease, there was no increase in the risk of cardiovascular events in patients receiving fluticasone furoate/vilanterol compared with placebo (see section 5.1). However, fluticasone furoate/vilanterol should be used with caution in patients with severe cardiovascular disease or heart rhythm abnormalities, thyrotoxicosis, uncorrected hypokalaemia or patients predisposed to low levels of serum potassium.

	Safety concerns raised when the Joint Prescribing committee previously reviewed the Relvar Ellipta include: • Inhaler was predominatntly blue in colour which may lead to it being confused for a reliever inhaler • Product had a 6 week shelf life once opened • Packaging made reference to Relvar and Ellipta in a way that was thought to be confusing to the patient • Micrograms stated as both mcg and μg which introduces the potential for confusion
Costs **Tariff status** **Activity costs**	

Drug & Dosage	**30 day cost/per patient**	**Annual Cost per patient**
Relvar® Ellipta® 92/22	£22.00	£264
Fostair® 100/6 MDI	£29.32	£351.84
Fostair® NEXThaler® 100/6	£29.32	£351.84
DuoResp Spiromax® 160/4.5 micrograms and 320/9 micrograms inhalation powder	£29.97	£359.64
Symbicort® Turbohaler® 400/12 micrograms inhalation powder	£28.00	£336
Symbicort® MDI 200/6 micrograms per actuation	£28.00	£336

N.B. Doses are for general comparison and do not imply therapeutic equivalence

Cost effectiveness (if available)	Information taken from SMC submission in 2014 The company submitted a cost-minimisation analysis of fluticasone furoate/vilanterol for the symptomatic treatment of adults with COPD with a FEV1 <70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy. The comparators included fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate (which have both been accepted for use by SMC in COPD (FEV1 <50% predicted normal). The time horizon for the analysis was five years. The data to support comparable efficacy were based on Bayesian mixed treatment comparisons assessing the probability of non-inferiority of fluticasone furoate/vilanterol compared with fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate. A 12-week study directly compared fluticasone furoate/vilanterol with fluticasone propionate/salmeterol, however the purpose of this study was to demonstrate superiority and the primary superiority endpoint was not met. There were no direct clinical data versus budesonide/formoterol fumarate dihydrate. Only drug costs were included in the analysis. Costs were presented over one to five years. The results showed that the cost of fluticasone furoate/vilanterol is £338 in year one and £1,645 over a five years time horizon compared with a cost in year one of £498 for fluticasone propionate/salmeterol and £2,422 over a five years time horizon and compared with a cost of £462 in year one for budesonide/formoterol

	fumarate dihydrate and £2,249 over a five years time horizon. Fluticasone furoate/vilanterol is therefore associated with cost savings of £160 and £124 in year one compared with fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate, respectively, and £777 and £604 over a five years time horizon compared with fluticasone propionate/salmeterol and budesonide/formoterol fumarate dihydrate, respectively. Fluticasone furoate/vilanterol would therefore be the preferred treatment on cost-minimisation grounds. The economic case has been demonstrated for patients with an FEV1 <50% predicted normal. However, as the comparators are not in routine use for COPD patients with FEV1 50 % to <70% predicted normal, the case has not been demonstrated in the group of patients with less severe disease.
Potential number of patients in Bedfordshire and Luton **Impact per 100,000 population** **Affordability considerations**	COPD prevalence is estimated at 2-4% but the diagnosed prevalence is about 1.5% (1,500 per 100,000) which increases to 10% in men aged over 75. (14) An average GP practice of 6,600 patients is likely to have about 100 patients on its COPD disease register. This equates to approximately 6,100 and 3,000 patients with COPD in Bedfordshire and Luton respectively.
Decisions from other bodies **Comments sought from –**	SMC have approved fluticasone/vilanterol for treatment in patients with severe COPD (FEV_1 <50% predicted normal). AWMSG have approved fluticasone/vilanterol for treatment in patients with COPD with a FEV1 <70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy. Milton Keynes Formulary has approved fluticasone/vilanterol for prescribing, Cambridgeshire and Peterborough formulary have it listed as non-formulary.
Evidence strengths and limitations	

PAC New Drug Template – Adapted from East Anglia Medicines Information, NHS Suffolk, NHS Cambridgeshire and NHS Derby templates

**Consult Summary of Prescribing Characteristics for full prescribing detail.*

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.

Appendix 1- Search Strategy

BTS GOLD strategy for chronic obstructive pulmonary disease. December 2018, accessed via www.guidelines.org.uk

Drug Tariff, NHSBSA, August 2019 accessed via www.nhsbsa.nhs.uk

NICE Guidelines (NG115) Chronic obstructive pulmonary disease in over 16s: diagnosis and management. Updated July 2019, accessed via www.nice.org.uk

Relvar Ellipta (fluticaseon furoate 92micrograms/vilanterol 22micrograms) Summary of Product Characteristics. Accessed via www.medicines.org.uk on 23rd August 2019.

Scottish Medicines Consortium. Fluticasone furoate/vilanterol (Relvar) detailed advice, April 2014. Accessed via www.scottishmedicines.org.uk

Vestbo J et al. Salford Lung Study: Effectiveness of fluticasone furoate/vilanterol (FF/VI) versus usual standard of care in patients with COPD. N Engl J Med. 2016 Sep 29;375(13):1253-60

Vestbo, J., et al., Comparison of FF/VI and VI versus placebo on survival rates of COPD patients with heightened cardiovascular risk (SUMMIT). Lancet. 2016 Apr 30;387(10030):1817-26.

Treatment assessed (Month and year): Choice of combination Inhaled Corticosteroid (ICS) and Long Acting Beta Agonist (LABA) inhaler for Chronic Obstructive Pulmonary Disease (COPD)
JPC Recommendation To be agreed at the September 2019 JPC meeting
1) Clinical Effectiveness The evidence base shows that all the ICS/LABA inhalers are effective bronchodilators which produce clinically significant improvements in lung function (FEV1).
2) Cost Effectiveness The Scottish Medicines Consortium has provided health economic analysis in their reports on fluticasone/vilanterol. The economic case has been demonstrated for patients with an FEV1 <50% predicted normal. However, as the comparators were not in routine use at the time of the report for COPD patients with FEV1 50 % to <70% predicted normal, the case has not been demonstrated in the group of patients with less severe disease.
3) Equity & Equality Impact Assessment* No impact envisioned
4) Needs of the community COPD prevalence locally is increasing and underdiagnosed.
5) Need for healthcare (incorporates patient choice and exceptional need) 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.
6) Policy drivers NICE Clinical Guideline NG115 on COPD Bedfordshire and Luton COPD and ACO Guidelines
7) Disinvestment Potential for disinvestment in ICS/LABA inhalers not recommended for use by the JPC.

The JPC agreed the following sections within the PCT Ethical and Commissioning Framework were not relevant to JPC discussions: Health Outcomes, Access, and Affordability.

***Equality Impact Assessment for BCCG only**

Where the implementation of the decision of the Bedfordshire and Luton Joint Prescribing Committee (JPC) may impact on one or more equality group differently to others, BCCG will require an equality impact assessment to be completed. The guidance on this can be found in the attached document. Please summarise the equality impact in the in the Equity & Equality Impact Assessment box above.

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Protected Characteristics (under the Equality Act):-

Age; Disability; Gender reassignment; Marriage & Civil Partnership (in employment only); Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual orientation; carers; other identified groups.

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

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** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*