Bedfordshire and Luton Joint Prescribing Committee (JPC)

18th September 2019
Review September 2021

Bulletin 282: Fluticasone furoate/ Vilanterol (Relvar®Ellipta®) for the treatment of Asthma (select group of patients)

JPC Recommendation:

- The Committee agreed to add Fluticasone furoate/ Vilanterol (Revlar®Ellipta®) to the formulary within it's licensed indication as:-
  - an option for the treatment of asthma in young people who have 'difficult to control' asthma and who are under the care of a Specialist outreach team and tertiary centre.

Bedfordshire CCG
Luton CCG

New Medicine Review

Choice of combination Inhaled corticosteroid (ICS) and Long Acting Beta Agonist (LABA) inhaler for Asthma

Medicine	Fluticasone furoate/ vilanterol 92/22 micrograms and 184/22 micrograms inhalation powder (Relvar Ellipta®)
Document status	Final
Date of last revision	August 2019 , Approved Sept 2019
Proposed Sector of prescribing	Primary and secondary care
Introduction **Summary Key points** **Evidence level**	Fluticasone furoate / vilanterol combination dry powder inhaler (Relvar®▼ Ellipta®) is a once daily inhaler containing fluticasone furoate (inhaled steroid) and vilanterol (long - acting beta2 agonist.) It is licensed for use for the treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long in -acting beta2-agonist and inhaled corticosteroid) is appropriate, that is patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting beta2-agonists, and those already adequately controlled on both inhaled corticosteroid and long-acting beta 2-agonist. 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: 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. Two strengths are available fluticasone furoate / vilanterol 92/22 and 184/22 microgram.
Licensed indication	Relvar Ellipta is indicated for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta2-agonist and inhaled corticosteroid) is appropriate: - patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting beta2-agonists. - patients already adequately controlled on both inhaled corticosteroid and long-acting beta2-agonist.
Formulation/Available Products	1. Beclomethasone + formoterol (Fostair®) 100/6 MDI +/- spacer. Twice daily.

	 2. Beclomethasone + formoterol (Fostair® NEXThaler®) 100/6. Twice daily.  3. Formoterol + Budesonide (DuoResp Spiromax®) 160/4.5 micrograms and 320/9 micrograms inhalation powder. Twice daily  4. Formoterol + Budesonide (Symbicort® Turbohaler®) 400/12 micrograms inhalation powder. Twice daily.  5. Fluticasone + vilanterol (Relvar® Ellipta®) 92 micrograms/22 micrograms inhalation powder, pre-dispensed. 
Usual dosage	The summary of product characteristics states a starting dose of Relvar Ellipta 92/22 mcg should be considered for adults and adolescents 12 years and over who require a low to mid dose of ICS in combination with a LABA. Relvar Ellipta 184/22 mcg should be considered for adults and adolescents 12 years and over who require a high dose of inhaled corticosteroid in combination with a LABA.

	<table><tr><td></td><td>Low dose</td><td>Moderate dose</td><td>High dose</td></tr><tr><td colspan="4">Fluticasone furoate + vilanterol</td></tr><tr><td>Dry powder inhaler</td><td colspan="2">92/22 microgram inhaler</td><td>184/22 microgram inhaler</td></tr><tr><td>Relvar® Ellipta®)</td><td>1 puff once a day</td><td>1 puff once a day</td><td>1 puff once a day</td></tr></table>
Treatment alternatives/ place in therapy	The BTS SIGN guideline comments that it is difficult to establish the exact equipotent dose of fluticasone furoate but positions Relvar as shown in the table below. <table><tr><td></td><td colspan="2">Low dose</td><td>Moderate dose</td><td>High dose</td></tr><tr><td colspan="5">Fluticasone furoate + vilanterol</td></tr><tr><td>Dry powder inhaler</td><td colspan="3">92/22 microgram inhaler</td><td>184/22 microgram inhaler</td></tr><tr><td>Relvar® Ellipta®)</td><td>n/a</td><td>1 puff once a day</td><td>1 puff once a day</td><td>1 puff once a day</td></tr></table> GINA 2019: Fluticasone furoate at 92 mcg contained within Relvar Ellipta 92/22 mcg is specified as a low dose ICS in the ‘Global Strategy for Asthma Management and Prevention’ GINA 2019. Fluticasone furoate at 184 mcg contained within Relvar 184/22 mcg is positioned as a high dose ICS/LABA. NICE Asthma Guidance 2017: NICE positions Relvar 92/22 mcg as a mid-dose ICS/LABA, and Relvar 184/22 mcg as a high dose ICS/LABA in their ICS dosing table, however subsequently clarify that this positioning is a guide to similar clinical effectiveness: “Dosages in the tables are not strict dose equivalences but are a guide to similar clinical effectiveness. Prescribers should also take into account the possibility of adverse effects from ICS, which may differ between ICS and according to dosage”.
Future alternatives	
National guidance	NICE guidance (NG80) on Asthma recommends the use of ICS/LABAs for the management of asthma in both adults and children as part of the pharmacological management. BTS SIGN guidelines (2019) recommends the first choice as add-on therapy to inhaled corticosteroids in adults is an inhaled long-acting β2 agonist, which should be considered before increasing the dose of inhaled corticosteroid. 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 Asthma Guidelines for adults (aged 17 years and over) recommends the use of ICS/LABA inhalers as part of the ICS dose

	escalation and dose de-escalation pathway. The Bedfordshire and Luton Paediatric Wheeze and Asthma Guidelines recommends the use of ICS/LABA inhalers as part of the pharmacological treatment pathway for children aged 5-16 years. All ICS/LABA inhalers on the formulary currently are joint in their formulary position for the treatment of asthma.
Evidence for use	Since the JPC last reviewed fluticasone/vilanterol for asthma the following evidence has been published: The Salford Lung Study (SLS) in asthma was a 52-week open-label effectiveness study (n=4,233) comparing Relvar Ellipta with usual care (90% of patients screened were randomised for inclusion whereas a typical efficacy randomised clinical trial includes <5% of patients). Eligible patients ≥18years had to be taking regular maintenance inhaler therapy with corticosteroids (ICS) alone or in combination with a long acting β-agonist (LABA). Prior to randomisation patients treatment was optimised by their GP (36% of patients were prescribed ICS and 64% of patients were prescribed ICS/LABA). Relvar Ellipta was shown to be superior to usual care with other ICS/LABAs in helping 25% more patients (70% vs. 56% - an absolute difference of 14%) improve asthma control in everyday clinical practice (OR 1.95, 95% CI 1.60, 2.38) in pre-specified sub-group analysis. The most commonly used ICS/LABAs were Seretide (fluticasone propionate/salmeterol) 30%, Symbicort (budesonide/formoterol) 15% and Fostair (beclometasone/formoterol) 12%. There has been a total of 2,083,923 patient years of exposure. This data has been assessed and has led to the removal of the black triangle (June 2018) through agreement with the regulatory bodies who appraised the entirety of the safety data. The pharmacological properties of fluticasone furoate help to explain why Relvar demonstrated superior asthma control vs other ICS/LABAs, with similar risk of serious adverse event (SAE) in everyday clinical practice. The risk/benefit of Relvar has now been evaluated in a robust 52-week RCT that included 4,233 patient's representatives of those seen in everyday clinical practice. Eligible patients were on either ICS or ICS/LABA maintenance treatment prior to randomisation. The safety profiles were comparable between the treatment arms (SAE incidence 13% for fluticasone furoate/vilanterol and usual care). This supports Relvars favourable efficacy: safety profile in a real-world setting. Summary of evidence previously considered by JPC, taken from SMC submission 2014: The British Thoracic Society (BTS)/Scottish Intercollegiate Guidelines Network (SIGN) guidance recommends, at step 3 of their treatment algorithm, adding an inhaled LABA in adult patients taking ICS at doses of 200 to 800 micrograms beclometasone dipropionate/day who are not adequately controlled on ICS alone.1 Combination inhalers are recommended to guarantee that the LABA is taken with the ICS and to improve inhaler adherence. There are a number of comparator ICS/LABA combination inhalers available which are licensed for the regular treatment of asthma where use of a

	combination product (LABA and ICS) is appropriate, in patients not adequately controlled with ICS and 'as needed' inhaled SABA or in patients already adequately controlled on both ICS and LABA. However the European Medicines Agency (EMA) did not consider there were data for fluticasone furoate/vilanterol in patients already adequately controlled on both ICS and LABA.3 As a result only the “step-up” indication was approved by the EMA. The exact equivalence of fluticasone furoate to other ICS is not known. The British National Formulary (February 2014) notes that fluticasone furoate 92 micrograms once daily is approximately equivalent to fluticasone propionate 250 micrograms twice daily.7 This implies that the fluticasone dose in the fluticasone furoate/vilanterol 92/22 micrograms formulation approximates to a medium dose of ICS. Therefore the use of a low dose ICS (plus LABA) would not be possible with fluticasone furoate/vilanterol. Furthermore, as fluticasone furoate (and vilanterol) are not licensed individually for the treatment of asthma, patients will require a change to their ICS when commenced on fluticasone furoate/vilanterol. One 24-week study compared fluticasone furoate/vilanterol 92/22 micrograms with fluticasone propionate/salmeterol 250/50 micrograms twice daily and no significant difference between treatments was shown for change from baseline in 0 to 24 hour serial wm FEV1 at 24 weeks. This study was not designed to test non-inferiority. Furthermore, in another study no significant difference was demonstrated in the co-primary endpoints for fluticasone furoate/vilanterol 92/22 micrograms versus fluticasone furoate 92 micrograms after 12 weeks treatment. However, in a 24-week study fluticasone furoate/vilanterol 184/22 micrograms was significantly superior to fluticasone furoate 184 micrograms and to fluticasone propionate 500 micrograms twice daily. In addition, the exacerbation study demonstrated superiority of fluticasone furoate/vilanterol 92/22 micrograms versus fluticasone furoate 92 micrograms for the probability for one or more asthma exacerbations by week 52. While the 12-week study (HZA106827) may be considered to be shorter than recommended by in EMA guidance (which notes that chronic treatment of asthma studies should be of at least 6 months) 11, overall the EMA, in its European Public Assessment Report for Relvar Ellipta, considered the study durations were acceptable3. All studies (except the comparative study of fluticasone furoate/vilanterol versus fluticasone propionate/salmeterol and the safety study) recruited patients who were receiving ICS ±LABA. The proportion of patients on ICS plus LABA was approximately 40% in study HZA106827, 75% in study HZA106829 and 51% for study HZA106837.5,8,9 However, the licensed indication is for patients not adequately controlled with ICS and 'as needed' inhaled SABA.10 Therefore, patients receiving ICS plus LABA who were recruited to these studies would not be eligible for fluticasone furoate/vilanterol in clinical practice. All studies did include a four-week run-in period prior to randomisation in which patients received ICS (plus when required SABA). There are limited direct comparative data and none comparing fluticasone furoate/vilanterol 184/22 micrograms with ICS/LABA combination inhalers. Consequently, Bayesian hierarchical mixed treatment comparisons (MTC) were conducted to compare (when data permitted): - Fluticasone furoate/vilanterol (daily dose 92/22 micrograms) with medium dose ICS/LABA; fluticasone propionate/salmeterol,

	budesonide/formoterol fumarate dihydrate, beclomethasone/ formoterol fumarate dihydrate and fluticasone propionate/ formoterol fumarate dihydrate. - Fluticasone furoate/vilanterol (daily dose 184/22 micrograms) with high dose ICS/LABA; fluticasone propionate/salmeterol, budesonide/formoterol fumarate dihydrate and fluticasone propionate/ formoterol fumarate dihydrate. The MTC included studies of patients on an ICS or ICS/LABA at screening and analysed four outcomes: mean change from baseline in peak expiratory flow (PEF), FEV1 (both primary outcomes), mean rate of moderate and severe exacerbations and mean change from baseline in AQLQ total score. The results of the MTC indicated that fluticasone furoate/vilanterol 92/22 micrograms and 184/22 micrograms had a high probability of non-inferiority versus other ICS/LABA combinations for PEF, FEV1 and AQLQ outcomes. The evidence for non-inferiority for the exacerbation rate outcome was not robust due to high study-to-study variability. Another limitation of the MTC was heterogeneity in outcomes in common control arms between the studies. However, overall the MTC was considered to be acceptable. Fluticasone furoate/vilanterol delivered by the Ellipta® device is the first ICS/LABA combination inhaler to be licensed only for once daily use in the treatment of asthma. A once daily dosing regimen of ICS/LABA combination inhaler may be preferred by patients and provide benefits in terms of treatment compliance over a twice daily dosing regimen which may be required for the comparators. However, the double-dummy design of the comparative study of once daily fluticasone furoate/vilanterol versus twice daily fluticasone propionate/salmeterol means that this, as well as inhaler device preference, was not assessed. Clinical experts consulted by SMC considered that the place in therapy of fluticasone furoate/vilanterol would be as an alternative to existing ICS/LABA combination inhalers where once daily administration is preferred. It was noted that, once in-use, the shelf life of the fluticasone furoate/vilanterol inhaler is relatively short at just six weeks. The EMA considered the most frequent adverse events (headache, nasopharyngitis and upper respiratory tract infections) observed with fluticasone furoate/vilanterol in the treatment of asthma (and COPD) were similar to those reported for other approved ICS/LABA combination products. However the risk of pneumonia was not considered to be fully characterised and the company are to undertake studies in asthma and COPD to investigate the risk of pneumonia with fluticasone furoate/vilanterol compared with other ICS/LABA combination products.
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. Taken from NICE Evidence Summary (2014:

- Systemic effects may occur with any ICS; particularly at high doses prescribed for long periods. Because fluticasone furoate is a new ICS more information about its effect on cortisol suppression relative to other inhaled corticosteroids is needed.
- Cardiovascular events, particularly tachycardia, are known risks associated with LABAs. The summary of product characteristics states that fluticasone furoate/vilanterol should be used with caution in people with severe cardiovascular disease.

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

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 92/22 and 184/22 micrograms for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta2-agonist (LABA) and inhaled corticosteroid) is appropriate in patients not adequately controlled with inhaled corticosteroids (ICS) and 'as needed' inhaled short acting beta2-agonists (SABA). The comparators included fluticasone propionate/salmeterol (Seretide Accuhaler®, Seretide Evohaler®), budesonide/formoterol fumarate (Symbicort®), fluticasone propionate/formoterol fumarate (Flutiform®) and beclometasone dipropionate/formoterol fumarate (Fostair®). SMC clinical experts confirmed the comparators to be appropriate and indicated fluticasone propionate/salmeterol to be the treatment most likely to be displaced by fluticasone furoate/vilanterol. The time horizon was five years and the perspective was NHS Scotland.

	The data to support comparable efficacy were based on Bayesian mixed treatment comparisons (MTCs) assessing the probability of non-inferiority of fluticasone furoate/vilanterol compared with each of the comparator ICS/LABAs. A 24 week study directly compared fluticasone furoate/vilanterol with fluticasone propionate/salmeterol; however, the purpose of this was to demonstrate superiority and the primary superiority endpoint was not met. Only drug costs were included in the analysis. Costs were presented over one to five years with a weighted cost provided for low/medium dose comparator ICS/LABAs. The results estimate the introduction of fluticasone furoate/vilanterol 184/22 micrograms will lead to cost savings of £25-£452 per year (£117-£2,111 over 5 years) when compared to alternative high-dose ICS/LABA preparations. For the comparison of fluticasone furoate/vilanterol (92/22 micrograms) to low/medium dose ICS/LABA comparators, the results of the analysis estimate cost savings when compared to fluticasone propionate/salmeterol (Accuhaler® & Evohaler®) and budesonide/formoterol. However, compared with low/medium doses of fluticasone propionate/formoterol fumarate and beclometasone dipropionate/formoterol fumarate, fluticasone furoate/vilanterol 92/22 micrograms is associated with incremental costs of £31 and £18, respectively in year 1 and £147 and £84, respectively in year 5. It is worth noting that these are the comparators with the lowest current market share. When the costs are weighted by the proportions of patients receiving low/medium and high dose ICS/LABA (i.e. the relative use of ICS/LABA comparator treatments in clinical practice), results of the analysis estimate cost savings from introducing fluticasone furoate/vilanterol 92/22 micrograms and 184/22 micrograms versus fluticasone propionate/salmeterol (Accuhaler® & Evohaler®) and budesonide/formoterol.fumarate However, compared with fluticasone propionate/formoterol fumarate and beclometasone dipropionate/formoterol fumarate, fluticasone furoate/vilanterol is associated with incremental costs of £22 and £61, respectively in year one (£105 and £284 in year five). As noted above, these are the comparators with the lowest current market share. The main concerns with the analysis were: • There are limited direct comparative data and none comparing fluticasone furoate/vilanterol 184/22 micrograms with other ICS/LABA combination inhalers. • Lack of data to compare fluticasone furoate/vilanterol with all ICS/LABA comparators across all four outcome measures; the evidence networks in the MTC did not allow for all comparator doses to be compared with fluticasone furoate/vilanterol, across all four included outcome measures • Uncertainty around the appropriateness of the comparator doses, such that dose equivalence has not been demonstrated. Despite these concerns, the economic case has been demonstrated.
Potential number of patients in	Taken from previous Relvar JPC review (2014): Annually (ePACT April 14 to March 15) Bedfordshire CCG spend £4 million and Luton CCG spend £1.6 million on the ICS/LABA combination products.

Bedfordshire and Luton **Impact per 100,000 population** **Affordability considerations**	Not all of this spend will be for asthma. As some of these products are also licensed for COPD a significant proportion of this spend will also be for COPD. Extract from NICE Evidence Summary (ESNM 34) Estimated usage The manufacturers of Relvar®▼Ellipta® (GlaxoSmithKline) estimate that there are currently 935,000 people with asthma who are prescribed ICS monotherapy (plus as-needed short-acting beta 2 agonists). They estimate that 40% of these people have poorly controlled asthma. Therefore, approximately 374,000 people may be eligible for combined ICS/LABA treatment. Local Potential Usage Figures Extrapolating from the above quoted GSK figures, and assuming this is based on the population of England (approx. 53 million), then potential numbers of patients who could fit the licensing criteria for the use of fluticasone furoate/ vilanterol would be in the region of: Bedfordshire (population 440,000) ~ 3,100 patients Luton CCG (population 210,000) ~ 1,480 patients There are significant savings to be made by choosing cost effective products for asthma as a first line choice and also as a switch option as well as reviewing the use of high dose inhaled corticosteroids in light of the safety concerns and stepping down treatment.
Decisions from other bodies **Comments sought from –**	SMC and AWMSG have approved fluticasone/vilanterol for regular treatment of asthma in adults and adolescents aged 12 years and older. 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

AWMSG, fluticasone furoate/vilanterol (as trifenatate) (Relvar® Ellipta®) final appraisal recommendation, 2014. Accessed via www.awmsg.org

BTS SIGN 158: British guideline on the management of asthma. July 2019. Accessed via www.brit-thoracic.org.uk

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

Gina Report: Global Strategy for Asthma Management and Prevention (2019). Accessed via www.ginasthma.org/gina-reports

NICE Guidelines (NG80) Asthma: diagnosis, monitoring and chronic asthma management. Published November 2017, accessed via www.nice.org.uk

NICE Evidence Summary (ESNM34) Asthma: fluticasone furoate/vilanterol (Relvar Ellipta) combination inhaler. Published March 2014, 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 Ellipta) detailed advice. June 2014, accessed via www.scottishmedicines.org.uk

Woodcock et al., Effectiveness of fluticasone furoate plus vilanterol on asthma control in clinical practice: an open-label, parallel group, randomised controlled trial (Salford Lung Study in Asthma). Lancet. 2017 Nov 18;390(10109):2247-2255

Treatment assessed (September 2019):
Choice of combination Inhaled Corticosteroid (ICS) and Long Acting Beta Agonist (LABA) inhaler for Asthma

JPC Recommendation

- The Committee agreed to add Fluticasone / Vilanterol (Revlar®Ellipta®) to the formulary within its licensed indication for the following -
  - as an option for the treatment of asthma in young people who have 'difficult to control asthma and who are under the care of a Specialist outreach team and tertiary centre.

1) Clinical Effectiveness
The evidence base shows that all the ICS/LABA inhalers are effective bronchodilators which produce clinically significant improvements in asthma control.

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 patient. However, in was noted there was uncertainty around the appropriateness of the comparator doses, such that dose equivalence has not been demonstrated.

3) Equity & Equality Impact Assessment*
No impact envisioned

4) Needs of the community
Asthma prevalence (both GP treated and symptoms untreated) is estimated to be 16% in women and 13% in men (Health Survey England, 2001).

QoF 2012 prevalence across England showed that prevalence of GP treated asthma was estimated at 5.9% on average.
In Bedfordshire the prevalence is slightly higher than national average at 6.4% (27,877 patients approximately) and in Luton it is slightly lower at 5.4% (11,562 patients approximately)
(data from NHS information Centre Disease prevalence QoF for 2011-12)

Prescribing rates suggest that a large proportion of asthma patients are being over treated on High dose inhaled corticosteroids and there is a need to address this.

5) Need for healthcare (incorporates patient choice and exceptional need)
The choice of treatment for a person with asthma 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 asthma

6) Policy drivers
NICE Clinical Guideline NG80 on Asthma
Bedfordshire and Luton Asthma Guidelines
BTS SIGN Guidelines on the Management of Asthma

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

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** 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*