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Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Revinty Ellipta

Fluticasone furoate / Vilanterol

Procedure no: EMEA/H/C/002745/P46/010

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Abbreviations

A&E	Accident & Emergency
AE	Adverse event
AEC	Absolute Eosinophil Count
APC	Admitted patient care
BDP/FOR	Beclometasone dipropionate/formoterol fumarate
BUD/FOR	Budesonide/formoterol
BMI	Body mass index
CCI	Charlson comorbidity index
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
COVID	Coronavirus
CPRD	Clinical Practice Research Datalink
EHR	Electronic Health Record
ERS	European Respiratory Society
FF/VI	Fluticasone furoate/vilanterol
FP/SAL	Fluticasone/salmeterol
GINA	Global Initiative for asthma
GP	General practice/ practitioner
GSK	GlaxoSmithKline
HCRU	Health care resoGurce utilisation
HES	Hospital Episode Statistics
HRA	Health Research Authority
ICD-10	International Classification of Diseases version 10
ICS	Inhaled corticosteroid
IMD	Index of Multiple Deprivation
IPTW	Inverse probability of treatment weighting
LABA	Long-acting beta-agonist
LAMA	Long-acting muscarinic antagonist
LM	Leukotriene modifier
LTRA	Leukotriene receptor antagonist
MART	Maintenance And Reliever Therapy
MITT	Multiple inhaler triple therapy
MRC	Medical Research Council
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OCS	Oral corticosteroid
OP	Outpatient
PS	Propensity score
QoL	Quality of life
SABA	Short-acting beta-agonist
SAMA	Short-acting muscarinic antagonist
SAP	Statistical analysis plan
SD	Standard deviation
SES	Socioeconomic status
SMD	Standard mean difference
UK	United Kingdom
WHO	World Health Organisation

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1. Introduction

On 1st October 2024, the MAH submitted a completed paediatric study (study Nº 221678) for Relvar Ellipta and its duplicate Revinty Ellipta (fluticasona furoate/vilanterol [as trifenatate]), in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

On 13th November 2013, Relvar Ellipta (Fluticasone furoate/Vilanterol [as trifenatate] Inhalation Powder [FF/VI]) was approved by the European Commission (EC) for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination product (long-acting beta2-agonist and inhaled corticosteroid) is appropriate, as well as for the symptomatic treatment of adults with chronic obstructive pulmonary disease (COPD).

In accordance with Article 46 of the regulation (EC) No 1901/2006 GSK hereby submits to the EMA the final study report for the study 221678 which involved patient characteristics and treatment patterns in patients with asthma newly initiating either FF/VI and ICS/LABA combinations including BUD/FOR or BDP/FOR in UK clinical practice. The presented study is not part of the agreed paediatric investigation plan (PIP), therefore it is not considered part of a clinical development program.

2.2. Information on the pharmaceutical formulation used in the study<ies>

Fluticasone furoate/Vilanterol (as trifenatate) Inhalation Powder (FF/VI) is authorised in the European Union (EU) as a pre-dispensed multi dose dry powder inhaler in strengths of 100/25 micrograms and 200/25 micrograms. Both strengths of this inhalation powder for oral inhalation are approved in the paediatric population (adolescents aged 12 years and older) for use as a once-daily (OD) treatment of asthma. Each single inhalation provides a delivered dose (the dose leaving the mouthpiece) of 92 micrograms of FF and 22 micrograms of VI, or 184 micrograms of FF and 22 micrograms of VI respectively.

Further forms of ICS/LABA therapies considered in the present study include budesonide/formoterol (BUD/FOR) [Symbicort®] and beclometasone dipropionate/formoterol fumarate (BDP/FOR) [Fostair®].

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for the non-interventional study number 221678 (EFFERENT) titled "Patient characteristics and treatment patterns in patients with asthma newly initiating ICS/LABA combinations in UK clinical practice".

2.3.2. Clinical study

Non-interventional study number 221678 (EFFERENT) titled "Patient characteristics and treatment patterns in patients with asthma newly initiating ICS/LABA combinations in UK clinical practice".

Description

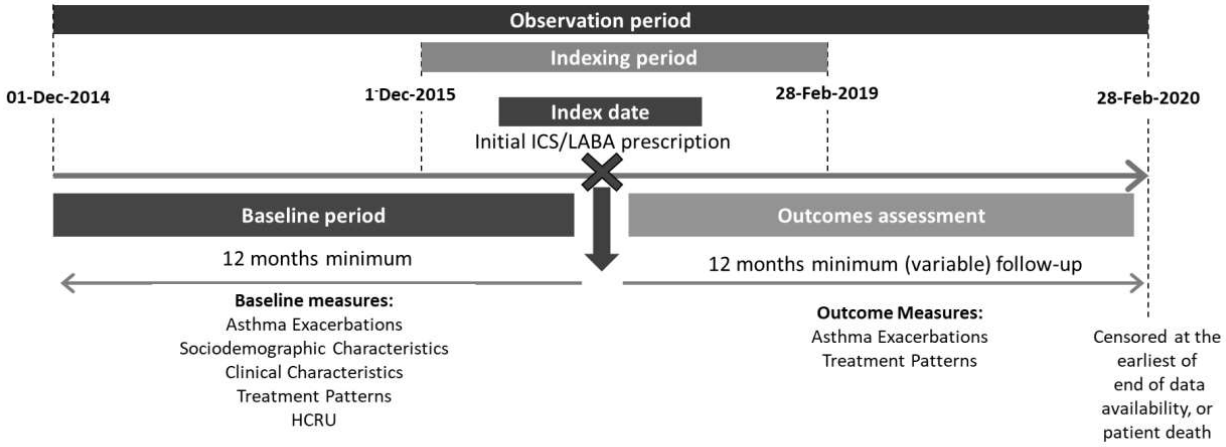
A new-user retrospective cohort study design was employed using linked primary care electronic health record (EHR) data, through the Clinical Practice Research Datalink (CPRD) Aurum, and secondary care administrative data through the Hospital Episode Statistics (HES) Admitted Patient Care (APC), Outpatient (OP), and Accident and Emergency (A&E) datasets.

The proposed study was conducted using CPRD Aurum, which is a longitudinal, representative anonymised EHR database of primary care interactions in England. This was linked to the HES-APC, HES OP and HES-A&E datasets. HES linkage enabled the identification of severe (hospitalised) asthma exacerbation events that would otherwise not be reliably captured in CPRD Aurum.

The index date was defined as the first/earliest prescription date of a single device FF/VI, BUD/FOR or BDP/FOR inhaler within the indexing period of 1st December 2015 and 28th February 2019, where no fixed-dose ICS/LABA prescriptions were observed in the prior 12 months. The index period start date of 1st December 2015 ensured that the study population consists of patients identified only when all products of interest were available in the UK (from November 2013), with a two-year period to allow all products of interest to be introduced to care. The index period end date of 28th February 2019 ensures 12 months of follow-up can be observed for patients prior to the impact of the COVID-19 pandemic on the UK healthcare service, as this study does not aim to assess this impact.

Sociodemographic characteristics, clinical characteristics treatment patterns and healthcare resource utilisation (HCRU) was described over a minimum of 12 months prior to the index date. The variable follow up period spanned from the index date to a minimum of 12 months. Throughout the follow-up period asthma exacerbations and treatment patterns were captured.

Figure 1 - Study schematic



Methods

Study participants

Adult and adolescent patients with asthma aged 12+ newly initiating FF/VI or BUD/FOR or patients with asthma aged 18+ newly initiating BDP/FOR, within the indexing period were included in the study. The setting was patients with asthma receiving care in a primary care setting in England.

The following inclusion criteria were applied for all patients included in the study:

1. At least one prescription of either FF/VI, BUD/FOR or BDP/FOR inhaler within the indexing period. The first/earliest such prescription within the indexing period defined the index date.

2. At least one diagnosis of asthma defined according to a validated algorithm at any time in the patient history prior to and including the index date.

3. ≥ 12 years of age at index date for patients initiating FF/VI or BUD/FOR or ≥18 years of age at index for patients initiating BDP/FOR.

4. Continuously registered with a general practice (GP) for a minimum of 12 months prior to and a minimum of 12 months following the index date.

5. Patient record eligible for linkage to HES and Index of Multiple Deprivation (IMD).

Patients meeting any of the following exclusion criteria were excluded from the study:

1. More than one fixed-dose ICS/LABA therapy prescribed on the index date

2. One or more prescriptions for any fixed-dose ICS/LABA therapy within the baseline period.

3. One or more prescription of ICS and one or more prescription of LABA within the baseline period.

4. One or more prescription(s) of ICS/LAMA/LABA single inhaler triple therapy within the baseline period.

5. At least one diagnostic code for COPD at any time in the observation period.

6. At least one diagnostic code of any medical conditions incompatible with an asthma diagnosis at any time in the patient's medical history, i.e:

    i. Conditions that are related to lung or bronchial developmental anomalies and degenerative processes such as bronchiolitis obliterans, cystic fibrosis, pulmonary fibrosis (not pulmonary hypertension), pulmonary resection.

ii. Other significant respiratory disorders other than asthma that can interfere with clinical asthma diagnosis or substantially change the natural history of the disease including chronic obstructive pulmonary diseases and acute respiratory failure.

7. One or more prescription of a biologic therapy within the baseline or follow up period.

Treatments

The present retrospective study is focused in the following ICS/LABA combinations in UK clinical practice:

1. Fluticasone furoate/vilanterol (Relvar® Ellipta™)
2. Budesonide/formoterol (Symbicort®)
3. Beclometasone dipropionate /formoterol fumarate (Fostair®)

Objective(s)

Primary Objective:
To describe the characteristics of patients with asthma in England within the year prior to newly initiating ICS/LABA, separately for patients receiving FF/VI, BUD/FOR or BDP/FOR.

Secondary Objective:

1. To describe the characteristics (as per primary objective) of patients with asthma in England in the year prior to newly initiating ICS/LABA, separately for patients receiving FF/VI, BUD/FOR or BDP/FOR, stratified by age group and SABA use in prior six months.

2. To describe seasonal trends in rate of moderate to-severe asthma exacerbations in patients with asthma in England (including moderate and severe exacerbations reported separately) across a variable follow-up (minimum 12 months) after initiating FF/VI, BUD/FOR or BDP/FOR therapy, stratified by GINA treatment step at index and SABA use in prior six months.

3. To describe treatment patterns following initiation of FF/VI, BUD/FOR or BDP/FOR in asthma patients in England, stratified by SABA use in prior six months, including: - Respiratory treatment classes prescribed at 3, 6, 9, 12, 18, 24 and 36 months following initiation of the index therapy - Change in ICS dosage (escalation, de-escalation, or maintained dose) at 3-, 6-, 9- and 12 months following initiation of the index therapy.

Exploratory objective:
1. To describe the suitability of CPRD-HES for future research using treatment groups of patients with asthma initiating FF/VI, BUD/FOR or BDP/FOR, balanced using a propensity score (PS) matching model.

Outcomes/endpoints

Pre-index outcomes:

Asthma exacerbations: Frequency of asthma exacerbations in the 12-month baseline period was described as a continuous variable, as a binary variable (Y/N), and categorized into the following groups: 0, 1, 2+. Asthma exacerbations were categorized as follows:

- Severe exacerbation: Hospitalization, A&E visit, or Aurum exacerbation code with a term suggestive of a severe event (e.g. "severe", "life-threatening").
- Moderate exacerbation: OCS prescription or Aurum exacerbation code with a term which is not suggestive of a severe event.

Where multiple events within 7 days were observed, the most severe event determined the severity of the exacerbation (i.e. moderate or severe). A sensitivity analysis was conducted whereby a 14 day period was used to determine where subsequent events are independent exacerbations.

Treatment patterns: The ICS dosage for ICS/LABA index therapy and baseline (pre-index) ICS dosage was reported as well as the baseline respiratory therapies 3- , 6-, 9- and 12-month periods prior to index. Respiratory therapy switches were reported where a patient was considered to have a switch where any other controller medication was prescribed more than 7 days after the last component of a treatment regimen to be prescribed.

HCRU / direct medical costs: Where applicable, the following elements of HCRU / costs were be assessed: primary care (GP) consultations, outpatient attendances, hospitalisations and emergency visits. All-cause and asthma-related HCRU were calculated and reported.

Sociodemographic characteristics: index year, age, sex, region, ethnicity and socioeconomic status.

Clinical characteristics: BMI, GINA treatment step, smoking status, Medical Research Council (MRC) Dyspnoea Scale score, Charlson Comorbidity Index (CCI), eosinophil levels and time since initial asthma diagnosis.

Post-index outcomes:

Asthma exacerbations: Rate of overall, moderate, and severe asthma-related exacerbations were reported for each calendar month (Jan-Dec) in the variable (minimum 12-month) follow up period.

Treatment use/patterns: Post-index respiratory medication in the 3, 6, 9, 12, 18, 24 and 36 months after index was reported for count of unique treatment classes prescribed, proportion of patients on different classes of controller medications (both non-mutually exclusive and mutually exclusive groups) and change in ICS dosage.

Stratification definitions:

Age at index (for FF/VI and BUD/FOR cohorts only): 12-17 years; ≥18 years.

Index ICS/LABA therapy: ICS/LABA prescribed on index date: FF/VI; BUD/FOR;BDB/FOR

Gina Step: Treatment Step as defined by 2019 GINA [14]. Patients were classified into Step 1-5 according to treatment received prior to index. For treatment received at index, patients were classified into Step 3, Step 4 or Step 5; due to the indexing criteria for this study, no patients were classified into Steps 1 (as-needed low dose ICS-formoterol) and 2 (Daily low dose inhaled ICS or as-needed low dose ICS-formoterol). The study used the same operational definition of the GINA Steps as has been used in another GSK study using UK primary care prescribing data (GSK study: 214485); the specifics of this definition was detailed in full within the SAP. Any patients whose treatment use at index was not classifiable into a GINA Step were considered.

SABA prescription prior to index: One or more prescription for a SABA inhaler in the 6 months prior to and including the index date. A 6-month period was sufficient to observe SABA refills where SABA use is regular.

Maintenance asthma therapy immediately prior to index: The most recent respiratory treatment regimen (by class) prescribed in the three months prior to index. Details of how regimens were defined is provided in the SAP. The following categories were used: ICS, LABA, LAMA, LABA/LAMA, ICS and rescue medication (i.e. SABA, SAMA, SABA/SAMA or OCS), LABA and rescue medication, LAMA and rescue medication, LABA/LAMA and rescue medication, other (LM, Mast cell stabilizer, Methylxanthine).

Sample size

This was a descriptive study, whereby formal sample size calculations were not carried out as sample is fixed by the duration of the study period and available data. All patients who met the eligibility criteria were included in the study cohort. However, although formal sample size calculations were not carried

out, the Applicant has conducted sample size estimations with stepwise attrition to inform the feasibility of the study.

Randomisation and blinding (masking)

N/A

Statistical Methods

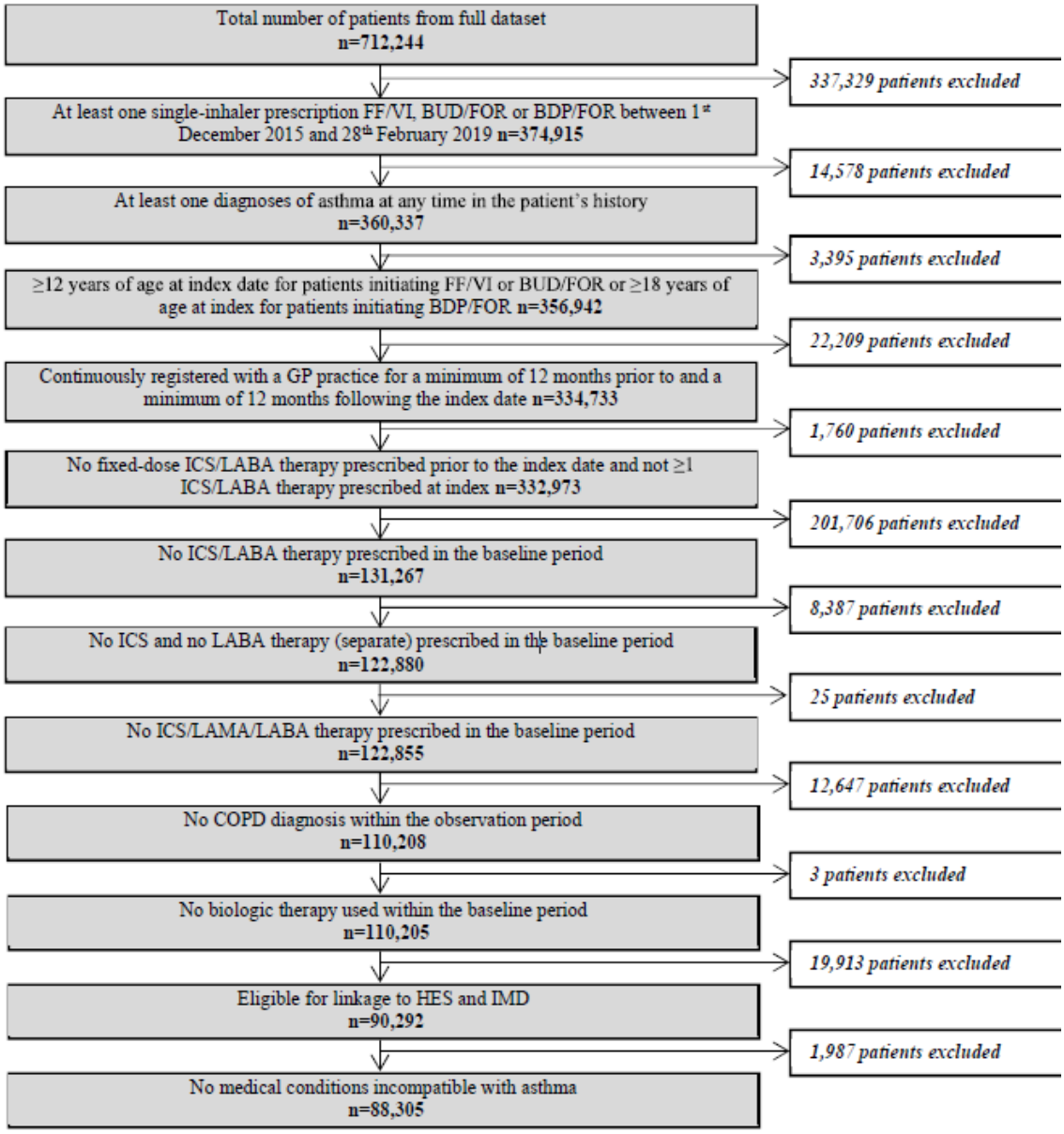
All analyses were conducted using Stata 17 software, or the latest available version (StataCorp, College Station, TX). For descriptive analyses, counts, means, medians, standard deviation (SD), 25th and 75th percentile, minimum and maximum values were reported for numeric variables, whilst relative frequencies and proportions/ percentages were reported for categorical variables. Rates were calculated by dividing frequency of events by person time at-risk. Additionally, a sensitivity analysis was conducted for the observation of asthma exacerbations as outlined in primary objective.

Results

Participant flow/recruitment/number analysed

A total of 88,305 patients met the eligibility criteria and were included in the study cohort (Figure 2 **- Patient attrition**). Patients were indexed on their first prescription of ICS/LABA (BDP/FOR, BUD/FOR or FF/VI) in the index period. 54,384 patients were indexed on a BDP/FOR prescription, 29,288 patients were indexed on a BUD/FOR prescription, and 4,633 patients were indexed on an FF/VI prescription. All patients who met the eligibility (88,305 patients) were included in the primary analyses and sensitivity analysis.

Figure 2 - Patient attrition



<u>Primary objective</u>: characteristics of patients with asthma in England in the year prior to newly initiating ICS/LABA, separately for patients receiving FF/VI, BUD/FOR or BDP/FOR.:

- <u>Asthma exacerbations</u>: In the 12 months prior to index, the percentage of patients who experienced at least one moderate-to-severe exacerbation was 16.3%, 11.8% and 15.1% for patients indexed on BDP/FOR, BUD/FOR and FF/VI, respectively. For patients indexed on BDP/FOR, BUD/FOR and FF/VI, the mean number of moderate exacerbations per patient was 0.22, 0.16 and 0.21, respectively. A very low proportion of patients who were included in the study experienced a severe exacerbation in the 12 months prior to index (1.1%).

- Treatment patterns: Across all three treatment groups, patients were most commonly prescribed SABA (72.0%), ICS (58.2%) and/or OCS (25.5%). Of these, SABA was prescribed the most with 79.1%, 57.9% and 78.2% of patients prescribed it at 12 months prior to index, for patients indexed on BDP/FOR, BUD/FOR and FF/VI, respectively.

- HCRU: Over half of the study cohort had at least one asthma-related primary care consultation in the 12 months prior to index (60.2%). The mean number of asthma-related consultations per patient in the 12 months prior to index was 1.49, 1.03 and 1.43 for patients indexed on BDP/FOR, BUD/FOR and FF/VI, respectively.

- Baseline demographics and clinical characteristics were presented in detail in Table 5 and Table 6 of the clinical study report (CSR).

Secondary Objective-1): ***characteristics of patients with asthma in England in the year prior to newly initiating ICS/LABA, stratified by age groups and SABA use in prior six months.***

- Asthma exacerbations: In each treatment group, the proportion of patients with a moderate-to-severe exacerbation in the baseline was higher among those who has received a SABA prescription in the 6 months prior to index. The mean number of exacerbation for adult patient indexed on FF/VI was 0.11 and 0.26 for no SABA and at least on SABA prescription in the 6 months prior to index. Minimal difference in the mean number of exacerbations per patient was seen between the different age groups. [CSR Table 11 and Table 12].

- Treatment patterns: Patients who were 18 years or older at index were observed to be prescribed a numerically higher dose of ICS than patients between the age of 12 and 17 years. For patients indexed on FF/VI and with a SABA prescription in the 6 months prior to index, 8.5% of patients aged 12 to 17 years and 17.8% of patients ages 18 years or older were indexed on a high dose of ICS. [CSR Table 13].

  The mean number of baseline respiratory treatment classes was observed to be higher for patients aged 12 to 17 years than patients aged 18 years or older, regardless of SABA use in the 6 months prior to index. A similar trend was observed in the proportion of patients with an ICS prescription in the 12 months prior to index. For the patients indexed on FF/VI with a SABA prescription in the 6 months prior to index, 85.4% of those aged 12 to 17 years and 70.8% of those aged 18 years or older had at least one prescription of ICS in the 12 months prior to index. [CSR Table 14]

- HCRU: The proportion of patients to experience an asthma-related consultation and the mean number of consultations was higher among those who had received a SABA prescription in the 6 months prior to index as well as those in the 18 years or older age groups. [CSR Table 15]

Secondary objective-2): ***seasonal trends in rate of moderate-to-severe asthma exacerbations in patients with asthma in England across a variable follow-up after initiating FF/VI, BUD/FOR or BDP/FOR therapy***

The rate of exacerbations stratified by receipt of a SABA prescription in the 6 months prior to index decreased throughout Q1 (January to March) and Q2 (April to June) and increased from August to December. When stratified by GINA step at baseline, the same seasonal trends were observed where the rates of exacerbations were low in Q2 and Q3 but higher in Q1 and Q4 with the highest number in January for all GINA steps, when not considering Steps 1 or 2.

Secondary objective- 3): ***treatment patterns following FF/VI, BUD/FOR or BDP/FOR initiation in asthma patients in England, stratified by SABA use in prior six months.***

The mean number of respiratory treatments prescribed in the 12 months post index was 2.35 (0.92) for the whole study cohort. Patients were most commonly prescribed SABA (none: 70.8%; any: 83.5%) and OCS (none: 23.0%; any: 28.7%). Of the patients with no SABA prescriptions in the 6 months prior to index, 9.1% were prescribed ICS in the 12 months post index, and 19.2% of those with any SABA prescriptions in the 6 months baseline.

Exploratory objective: **suitability of CPRD-HES for future research using treatment groups of patients with asthma initiating FF/VI, BUD/FOR or BDP/FOR, balanced using a propensity score (PS) matching model.**

Due to high levels of missingness MRC dyspnoea scale score and AEC were removed as covariates from the PS model. Additionally, the SAMA/SABA category (baseline therapy) was removed due to being a perfect predictor. Every covariate included in the model had a standard mean difference (SMD) value of less than 0.1 meaning that the treatment groups (FF/VI vs. BDP/FOR and FF/VI vs. BUD/FOR) were well matched.

Efficacy results

No efficacy results have been provided.

Safety results

The Applicant states that there was no potential to collect serious and non-serious AEs, pregnancy exposures, or incidents related to any GSK product during the conduct of this research, as the minimum criteria needed to report AEs, pregnancy exposures, and incidents are not present in the data source.

2.3.3. Discussion on clinical aspects

Fluticasone furoate/vilanterol inhalation powder (FF/VI) is currently approved by the European Commission for the regular treatment of asthma in adults and adolescents aged 12 years and older, where use of a combination product (long-acting beta2-agonist and inhaled corticosteroid) is appropriate (i.e. patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting beta-2-agonist) and patients already adequately controlled on both inhaled corticosteroid and long-acting beta-2- agonist.

This Article 46 procedure of Regulation (EC) No1901/2006, concerns the submission of the final study report for the study number 221678. The presented study is not part of the agreed paediatric investigation plan (PIP), therefore it is not considered part of a clinical development program and it can be considered only as an ancillary study.

The study 221678 presented by the Applicant is a retrospective observational study aimed to describe the characteristics of patients with asthma in England within the year prior to newly initiating ICS/LABA, separately for patients receiving FF/VI, BUD/FOR or BDP/FOR (primary objective), stratified by age group and SABA use in prior 6 months (secondary objective). Additionally, other secondary objectives were included in the study to describe seasonal trends in rate of moderate to severe asthma exacerbations and to describe treatment patterns following initiation of ICS/LABA therapy. An additional exploratory objective was included to describe the suitability of CPRD-HES for future

research using treatment groups of patients with asthma initiating ICS/LABA, balanced using a propensity score matching model.
A total of 88,305 patients met the eligibility criteria and were included in the study cohort (54,384 patients were indexed on a BDP/FOR prescription, 29,288 patients were indexed on a BUD/FOR prescription, and 4,633 patients were indexed on an FF/VI prescription). The clinical characteristics profile for the FF/VI and BDP/FOR treatment groups were broadly similar, whereas patients initiating BUD/FOR represent a distinct group with a lower proportion of current smokers, lower mean BMI, lower mean CCI, and were less likely to have moderate-severe exacerbations than each of the FF/VI and BDP/FOR treatment groups. Overall, the proportion of patients to experience either a moderate or severe exacerbation in baseline was low and SABA users were shown to be older, more likely deprived, more comorbid, more likely a current smoker, more likely obese, and more likely to exacerbate.

If taken into account the combination ICS/LABA subject to this P46 procedure (FF/VI) and the target population (ages 12-17), the only data provided in the study 221678 that would be applicable to the peadiatric population derives from the first secondary objective (characteristics of patients with asthma in England in the year prior to newly initiating ICS/LABA), which stratifies the data from the primary objective by age and SABA treatment. In this respect, the following data can be extracted from tables 12-15 of the study report, based on whether the patients were receiving treatment with SABA in the preceding 6 months or not, separately:

For the patients indexed on FF/VI (4,633), only 276 (6%) were 12-17 years old (n=63 no prior SABA treatment; n=213 with prior SABA treatment). The main age at index, the ratio of male to female and the mean BMI were similar for patients with no prior SABA treatment in the 6 months prior to index (15.22 years, 54% male, BMI 22.41 kg/m2) and with prior SABA treatment (14.98 years, 46.5% male, BMI 21.89 kg/m2).

For the 63 patients with no prior SABA prescription in the 6 months prior to index, 57 (90.5%) did not experienced moderate to severe exacerbations in the 12 months prior to index, 26 (12.2%) patients experienced 1 exacerbation, and 5 (2.3%) patients experienced two or more exacerbations. The majority of the 63 patients with no prior SABA prescription were on a low to medium dose of ICS (100 mcg) at index (54 patients), and only 9 were on a high dose (200 mcg). Regarding the baseline respiratory therapies in the 12 months prior to index, 27 (42.9%), 10 (15.9%) and 5 (7.9%) patients received ICS, OCS and LTRA respectively. Twenty six (41.3%) patients had any asthma-related consultations in the 12 months prior to index.

For the 213 patients with prior SABA prescription in the 6 months prior to index, 182 (85.4%) did not experienced moderate to severe exacerbations in the 12 months prior to index, 5 (7.9%) patients experienced 1 exacerbation, and 1 (1.6%) patients experienced two or more exacerbations. At index, 195 patients were on a low to medium dose of ICS (100 mcg), and 18 were on a high dose (200 mcg). Regarding the baseline respiratory therapies in the 12 months prior to index, 182 (85.4%), 47 (22.1%), 30 (14.1%) and 1 (0.5%) patients received ICS, OCS, LTRA and SAMA respectively. Furthermore, in the 12 months prior to index 157 (73.7%) patients had any asthma-related consultations. The study does not provide new efficacy or safety data, only descriptive data have been submitted.

It should be noted that the study was conducted in patients from a country outside the European Union (England), which has its own distinct characteristics in terms of population, climate, healthcare system and seasonal trends. As a result, extrapolating the findings from this observational study to the overall European population may be difficult and no conclusions can be made.

Furthermore, the limitations inherent to observational studies should be acknowledged, including the high potential for bias due to the study design. Additional limitations specifically related to this study

include factors related to patient management, data sources, potential misclassification, missing data, the restricted study duration and the limited applicability of the findings to current clinical practice.

In conclusion, the study 221678 has been submitted by the Applicant to comply with the requirements of Article 46 of the regulation 1901/2006. However, the study does not provide new PK, efficacy or safety data as it was designed solely as a descriptive study. Therefore, the benefit-risk balance of fluticasone furoate/vilanterol inhalation powder remains unchanged.

3. Rapporteur's overall conclusion and recommendation

☒ **Fulfilled:**

The study 221678 presented by the Applicant is a retrospective observational study aimed to describe patient characteristics and treatment patterns in patients with asthma newly initiating ICS/LABA combinations in UK clinical practice. Study 221678 does not provide new PK, efficacy or safety data as it was designed solely as a descriptive study. Therefore, the benefit-risk balance remaines unchanged and no regulatory actions are required.

4. Request for supplementary information

Not applicable.