Relvar Salford Lung Study in COPD (SLS COPD) Key results: Relvar Ellipta (92/22 mcg) ± LAMA reduces moderate/severe COPD exacerbations compared with usual care, and twice-daily ICS/LABA ± LAMA. More patients with COPD achieved improvement in their COPD-related health status with Relvar, compared with usual care

The Salford Lung Study in COPD (SLS COPD): study population

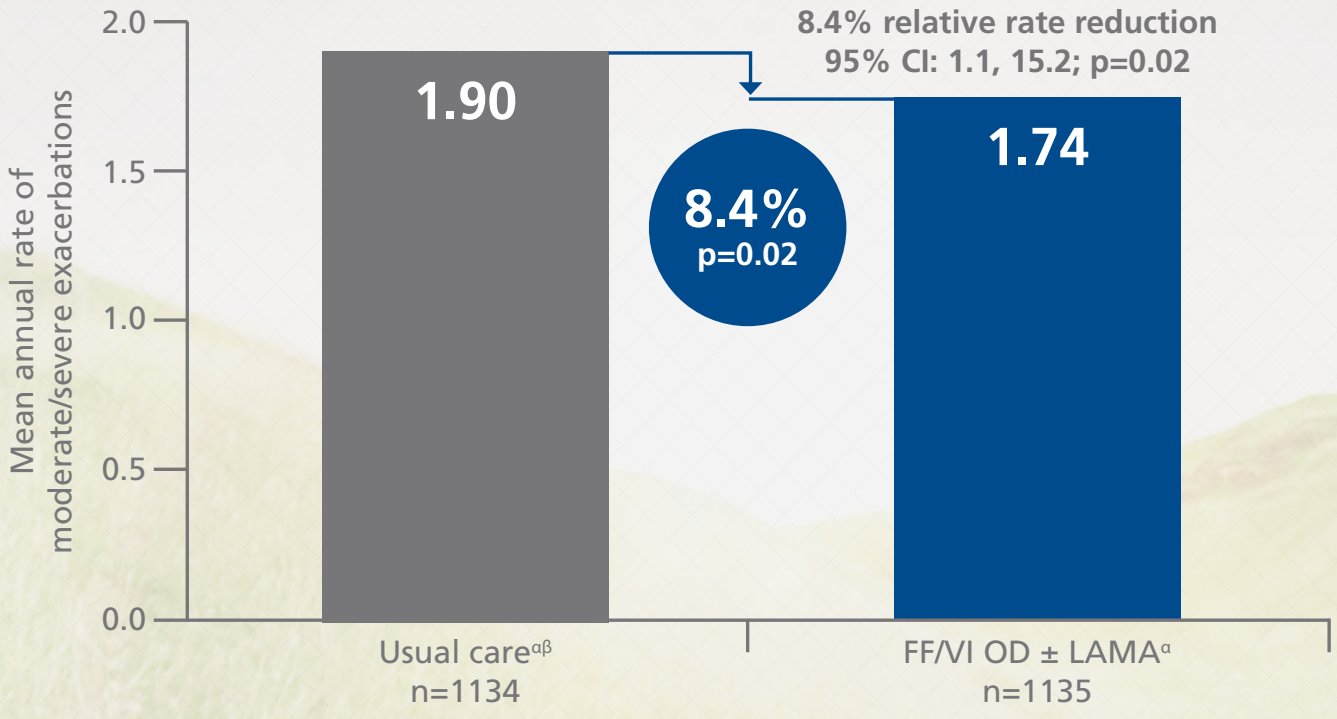
In SLS COPD, the intention-to-treat (ITT) population consisted of 2,799 randomised patients who received ≥1 prescription of study medication. The primary endpoint was the mean annual rate of moderate/severe COPD exacerbations in the primary effectiveness analysis (PEA) population (n=2,269). The PEA were a subset of the entire ITT population who had experienced ≥1 moderate/severe COPD exacerbation in the preceding year and were randomised to either initiation of Relvar Ellipta* 92/22mcg (fluticasone furoate/vilanterol [FF/VI] OD) or continuation on their usual care.[1]

A subset of 908 patients in the usual care** arm and 927 in the FF/VI OD* group were randomised to the ICS/LABA ± LAMA stratum and were on twice-daily ICS/LABA[†] treatment at baseline.[1]

The SLS COPD: key results

Primary comparison was Relvar Ellipta (n=1,135) vs. usual care (n=1,134).[2] In the PEA population, the rate of moderate/severe exacerbations was 1.74 exacerbations per year in the FF/VI group, compared with 1.90 per year in the usual care group, indicating an 8.4% (95% CI: 1.1, 15.2; p=0.02) lower rate in the FF/VI OD group.[1]**

Once-daily Relvar 92/22 mcg[α] can result in significantly fewer moderate/severe COPD exacerbations compared with usual care[1β]



This means that Relvar can help prevent **1** **moderate/severe COPD exacerbation for every** **7** patients treated over 12 months compared with usual care.[β] NNT=6.25 (CI: 3,47, 46.99)[1]

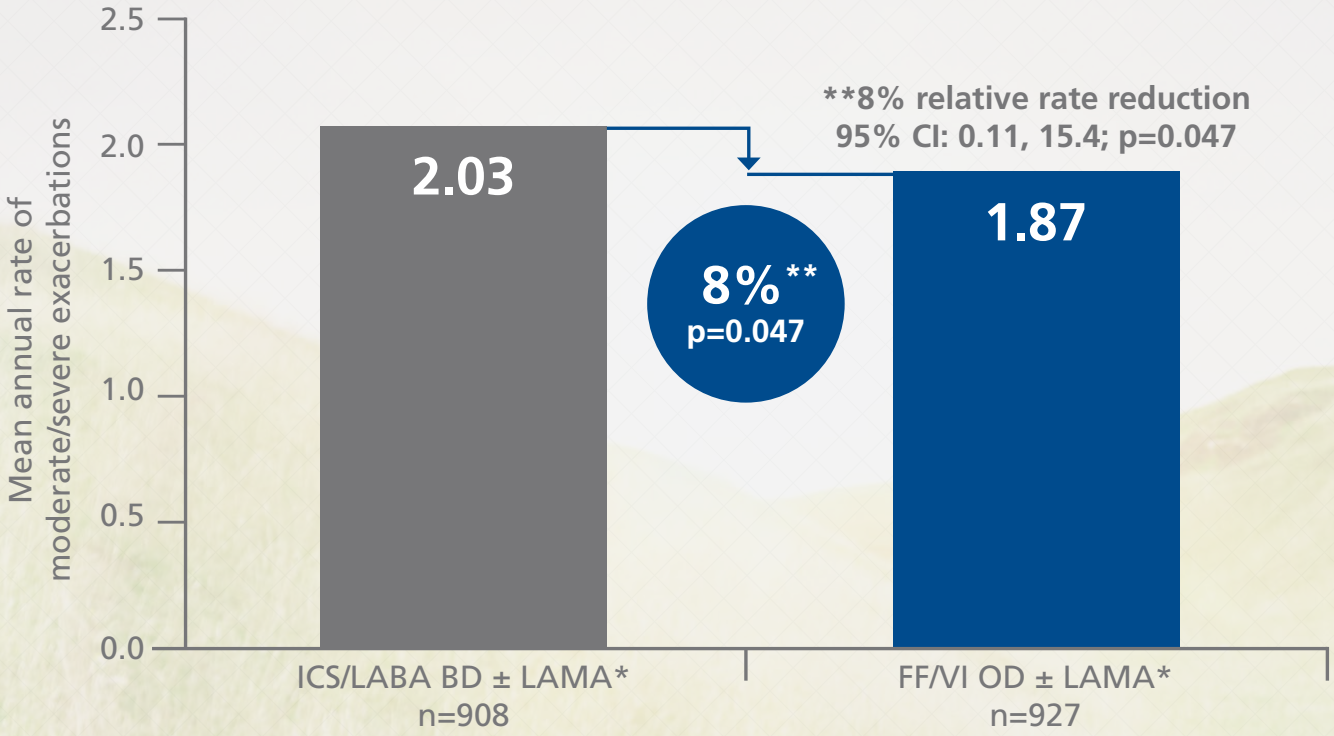
[α]Patients could receive a LAMA throughout the treatment period, in addition to their randomised treatment. The primary comparison was Relvar (n=1,135) vs. usual care (n=1,134).[2] The analysis was based on all ITT patients with ≥1 exacerbation in the year prior to randomisation.[1]

[β]Usual care was a physician-determined COPD maintenance treatment in accordance with usual clinical practice. The intention was to keep the treatment experience as close to normal as possible. Of all ITT patients with ≥1 exacerbation in the year prior to randomisation (n=2,269, i.e. 81% of the total number of patients included in the study), at baseline: 88% were on an ICS-containing regimen, 54% were on triple therapy (a combination of ICS/LABA/LAMA) and 12% were on a LABA and/or LAMA only.[1]

ICS/LABA=inhaled corticosteroid/long-acting β_2-adrenoceptor agonist; LAMA=long-acting muscarinic antagonist; NNT=number needed to treat; PEA=primary effectiveness analysis; ITT=intention-to-treat

In addition, once-daily Relvar (92/22 mcg) significantly reduced moderate/severe COPD exacerbations compared with twice-daily ICS/LABA (95% CI: 0.11, 15.4; p=0.047).[1*†]

Once-daily Relvar 92/22 mcg significantly reduced moderate/severe COPD exacerbations compared with twice-daily ICS/LABA[1α]



This means that Relvar can help prevent **1 moderate/severe COPD exacerbation for every 7** patients treated over 12 months compared with twice daily ICS/LABA[α]
NNT=6.25 (95% CI: 3.21, 447.83)[1]

[α]Patients could receive a LAMA throughout the treatment period in addition to their randomised treatment. Subset of patients randomised to an ICS/LABA ± LAMA strata and were taking an ICS/LABA at baseline.[1] Primary comparison was Relvar Ellipta (n=1,135) vs. usual care[β] (n=1,134).[2] This analysis was based on all ITT patients with ≥-1 moderate/severe exacerbation in the year prior to randomisation. In this primary effectiveness population, the rate of moderate/severe exacerbations was 1.74 exacerbations per year in the FF/VI group, compared with 1.90 per year in the usual care group, indicating an 8.4% (95% CI: 1.1, 15.2; p=0.02) lower rate in the FF/VI OD* group.[1] In common with other ICS-containing medicines, there is an increased risk of pneumonia in patients with COPD treated with Relvar.[3]

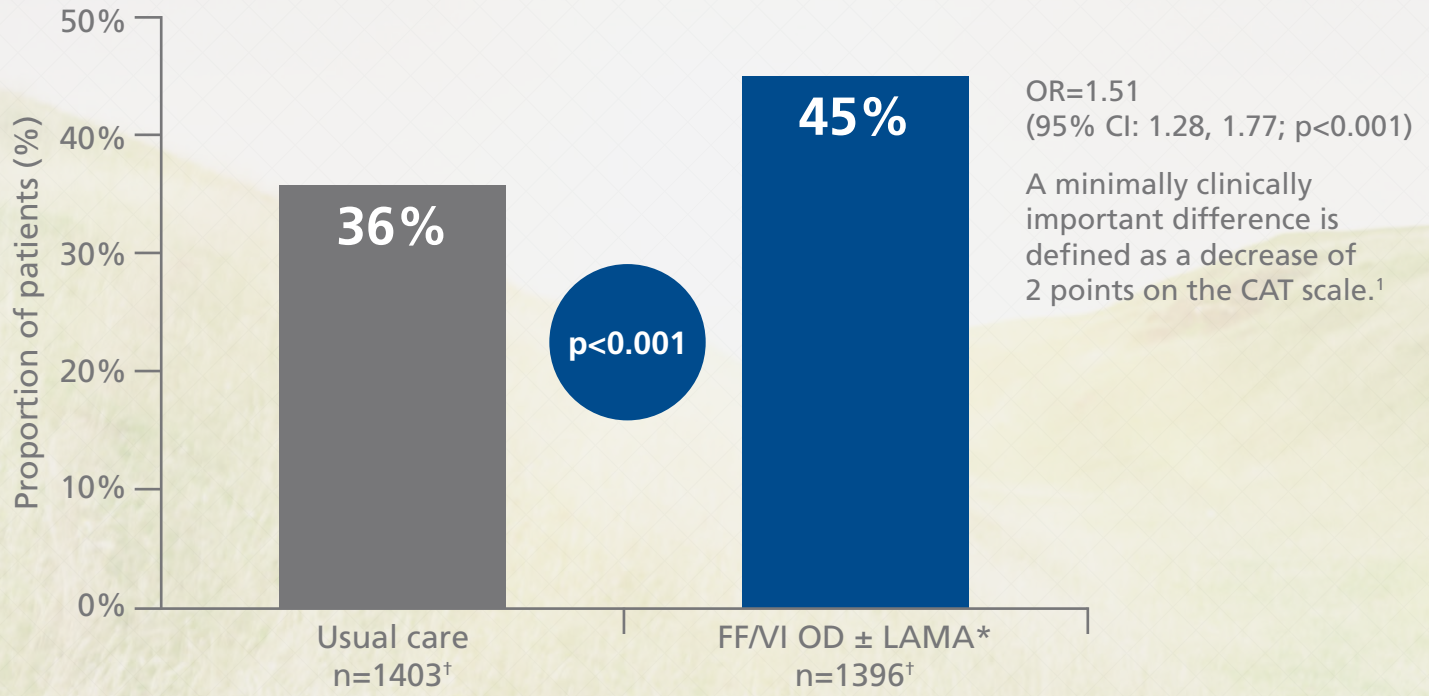
[β]Usual care was a physician-determined COPD maintenance treatment in accordance with usual clinical practice. The intention was to keep the treatment experience as close to normal as possible. Of all ITT patients with ≥1 exacerbation in the year prior to randomisation (n=2,269, i.e. 81% of the total number of patients included in the study), at baseline: 88% were on an ICS-containing regimen, 54% were on triple therapy (a combination of ICS/LABA+LAMA) and 12% were on a LABA and/or LAMA only.[1]

ICS/LABA=inhaled corticosteroid/long-acting β_2-adrenoceptor agonist; LAMA=long-acting muscarinic antagonist; NNT=numbers needed to treat.

SLS COPD: Results from other endpoints

In addition to the primary endpoint results, significantly more patients achieved an improvement in their COPD-related health status with Relvar 92/22 mcg*, compared with usual care,[1] as measured by the COPD Assessment Test (CAT).[‡]**

More patients achieve CAT[α] score improvement of ≥2 units with Relvar[β], compared with usual care[1δγ]



OR=1.51
(95% CI: 1.28, 1.77; p<0.001)

A minimally clinically important difference is defined as a decrease of 2 points on the CAT scale.[1]

[α]CAT: COPD Assessment Test (a questionnaire designed to measure the impact of COPD on a patient's wellbeing and daily life).[4] Quality of life was measured via the European Quality of Life-5 Dimensions questionnaire).[1]

[β]Patients could receive a LAMA throughout the treatment period in addition to their randomised treatment.[1]

[δ]Usual care was a physician-determined COPD maintenance treatment in accordance with usual clinical practice. The intention was to keep the treatment experience as close to normal as possible. Of all ITT patients with ≥1 moderate/severe COPD exacerbation in the year prior to randomisation (n=2,269, i.e. 81% of the total number of patients included in the study), at baseline: 88% were on an ICS-containing regimen as part of usual care, 54% were on triple therapy (a combination of ICS/LABA+LAMA) and 12% were on a LABA and/or LAMA only.[1]

[γ]Analysis based on patients who completed CAT questionnaire at baseline and at month 12 (i.e. usual care[†] n=1,325; FF/VI n=1,317).[1]

ICS/LABA=inhaled corticosteroid/long-acting β_2-adrenoceptor agonist; LAMA=long-acting muscarinic antagonist; NNT=numbers needed to treat; CAT=COPD Assessment Test

The SLS COPD: Additional effectiveness results

The study also showed:

- No significant difference between FF/VI 92/22 mcg and usual care** in reduction of the mean annual rate of severe exacerbations (0.09 and 0.08 exacerbations per year, respectively, p=0.52).[1]
- No significant difference between FF/VI 92/22 mcg and usual care** in the time to first moderate/severe exacerbation; hazard ratio: 0.93 (0.85, 1.02) and in the time to first severe exacerbation; hazard ratio: 1.27 (0.98, 1.66; p=0.08) in the entire study population.[1]
- No difference between FF/VI 92/22 mcg and usual care** in COPD-related contacts with primary care.[1]
- A 12.3% increase (95% CI: 5.4, 19.6) in the annual rate of all primary care contacts in the FF/VI 92/22 mcg group.[1]
- No difference between FF/VI 92/22 mcg and usual care** in the rate of secondary healthcare contacts.[1]

The SLS COPD: safety results

Overview of safety in a population of patients receiving Relvar 92/22 mcg compared to usual care** in everyday clinical practice[1]

- 29% of patients in the FF/VI 92/22 mcg group and 27% in the usual care** group experienced an on-treatment SAE
- There was no notable difference between treatment groups for any adverse event of specific interest (AESI)
- 45 patients in the FF/VI 92/22 mcg group and 30 patients in the usual care** group died during the study
- One patient death in each group was recorded as being related to the trial medication (pneumonia in 1 patient in the usual care** group, and pulmonary embolism/deep-vein thrombosis in patient in the FF/VI group)

Relvar 92/22 mcg is associated with a comparable incidence of on-treatment pneumonia compared to usual care[1a]

	Usual care[a] n=1403	FF/VI n=1396
Number (%) of subjects who had at least one SAE of pneumonia	**83** (6%)	**94** (7%)
Comparison of FF/VI vs. usual care[a] Incidence ratio 95% CI		**1.1** (0.9,1.5)

(ITT population: defined by the Pneumonia Special Interest Group)

The non-inferiority margin for the ratio of the proportions with pneumonia on FF/VI versus usual care is set at 2.

Non-inferiority is demonstrated if the upper limit of the two-sided 95% confidence interval for the incidence ratio FF/VI/usual care is less than 2.

ITT=intention-to-treat; SAE: serious adverse event; ICS/LABA=inhaled corticosteroid/long-acting β_2-adrenoceptor agonist; LAMA=long-acting muscarinic antagonist.

[a]Usual care was a physician-determined COPD maintenance treatment in accordance with usual clinical practice. The intention was to keep the treatment experience as close to normal as possible. Of all ITT patients with ≥1 COPD exacerbation in the year prior to randomisation (n=2,269, i.e. 81% of the total number of patients included in the study), at baseline: 88% were on an ICS-containing regimen as part of usual care, 54% were on triple therapy (a combination of ICS/LABA+LAMA) and 12% were on a LABA and/or LAMA only.[1]

In common with other ICS-containing medicines, there is an increased risk of pneumonia in patients with COPD treated with Relvar 92/22 mcg.[3]

What does it mean for you and your patients?

"The Salford Lung Study is going to benefit patients in a number of ways – not just by demonstrating that Relvar 92/22 mcg can bring real benefits (i.e. reducing the rate of moderate/severe COPD exacerbations and improving disease-related health status) but also in the immense mass of data we've got in this study that will help us understand just how patients with COPD, and their doctors, and their healthcare systems, behave."

— Dr David Leather, Medical VP – Global Respiratory Franchise, GSK, UK.

The data from the SLS COPD provides new and valuable insights into COPD treatments and outcomes, including how Relvar 92/22 mcg compares with other commonly-used COPD maintenance treatments and how it can benefit the patients that physicians see in their practice every day.[1]

The SLS COPD showed that Relvar 92/22 mcg can benefit the patients with COPD you see in your everyday clinical practice,[1] reducing their daily COPD burden, and has a comparable safety profile to other COPD treatments.[1] The only ICS/LABA that provides 24-hour continuous efficacy in a once-daily dose, Relvar is delivered through Ellipta™, a device associated with higher patient preference and fewer critical errors[§] compared with other inhalers.[6–10]

* Patients could receive a LAMA throughout the treatment period in addition to their randomised treatment. Subset of patients randomised to an ICS/LABA ± LAMA strata and were taking an ICS/LABA at baseline.[1]

** Usual care was a physician-determined COPD maintenance treatment in accordance with usual clinical practice. The intention was to keep the treatment experience as close to normal as possible. Of all ITT patients with ≥1 COPD exacerbation in the year prior to randomisation (n=2,269, i.e. 81% of the total number of patients included in the study), at baseline: 88% were on an ICS-containing regimen, 54% were on triple therapy (a combination of ICS/LABA+LAMA) and 12% were on a LABA and/or LAMA only.[1]

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‡ CAT: COPD Assessment test (a questionnaire designed to measure the impact of COPD on a patient's wellbeing and daily life).[4] Quality of life was measured via the European Quality of Life-5 Dimensions questionnaire).[1]

§ Critical errors defined as errors that are likely to result in no or minimal medication being inhaled.[10]

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RELVAR- Abbriviated PI

Therapeutic indications

Asthma

Relvar Ellipta 92/22 mcg and Relvar Ellipta 184/22 mcg 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 $beta_2$-agonist and inhaled corticosteroid) is appropriate:

- patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting $beta_2$-agonists.

COPD (Chronic Obstructive Pulmonary Disease)

Relvar Ellipta 92/22 mcg is indicated for the symptomatic treatment of adults with COPD with a FEV_1<70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.

Relvar Ellipta – Abbreviated PI

For full information see MOH approved prescribing information

Generic name of the drug and active ingredients

Relvar Ellipta 92/22 mcg: Each single inhalation provides a delivered dose (the dose leaving the mouthpiece) of 92 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifenatate). This corresponds to a pre-dispensed dose of 100 micrograms of fluticasone furoate and 25 micrograms vilanterol (as trifenatate).

Relvar Ellipta 184/22 mcg: Each single inhalation provides a delivered dose (the dose leaving the mouthpiece) of 184 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifenatate). This corresponds to a pre-dispensed dose of 200 micrograms of fluticasone furoate and 25 micrograms vilanterol (as trifenatate).

Excipients with known effect:

Each delivered dose contains approximately 25 mg of lactose (as monohydrate).

Dosage and method of administration

Asthma

Adults and adolescents aged 12 years and over

One inhalation of Relvar Ellipta 92/22 micrograms once daily or one inhalation of Relvar Ellipta 184/22 micrograms once daily.

COPD

Adults aged 18 years and over

One inhalation of Relvar Ellipta 92/22 micrograms once daily.

Contraindications. Hypersensitivity to the active substances or to any of the excipients

Special warnings and precautions for use

Deterioration of disease

Fluticasone furoate/vilanterol should not be used to treat acute asthma symptoms or an acute exacerbation in COPD.

Asthma-related adverse events and exacerbations may occur during treatment with fluticasone furoate/vilanterol. Patients should be asked to continue treatment but to seek medical advice if asthma symptoms remain uncontrolled or worsen after initiation of treatment with Relvar Ellipta.

Paradoxical bronchospasm

Relvar Ellipta should be discontinued immediately, the patient assessed and alternative therapy instituted if necessary.

Cardiovascular effects

fluticasone furoate/vilanterol should be used with caution in patients with severe cardiovascular disease or heart rhythm abnormalities, thyrotoxicosis, uncorrected hypokaleamia or patients pre disposed to low levels of serum potassium.

Patients with hepatic impairment

For patients with moderate to severe hepatic impairment, the 92/22 micrograms dose should be used and patients should be monitored for systemic corticosteroid-related adverse reactions

Systemic corticosteroid effects

Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, growth retardation in children and adolescents, cataract and glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

Hyperglycaemia

There have been reports of increases in blood glucose levels in diabetic patients and this should be considered when prescribing to patients with a history of diabetes mellitus.

Pneumonia in patients with COPD

An increase in the incidence of pneumonia, including pneumonia requiring hospitalisation, has been observed in patients with COPD receiving inhaled corticosteroids. There is some evidence of an increased risk of pneumonia with increasing steroid dose but this has not been demonstrated conclusively across all studies.

There is no conclusive clinical evidence for intra-class differences in the magnitude of the pneumonia risk among inhaled corticosteroid products.

Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations.

Risk factors for pneumonia in patients with COPD include current smoking, older age, low body mass index (BMI) and severe COPD.

Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. There is no additional benefit of the 184/22 micrograms dose compared to the 92/22 micrograms dose and there is a potential increased risk of systemic corticosteroid-related adverse reactions (see section 4.8).

Interaction with other medicinal products and other forms of interaction

Interaction with beta-blockers: Concurrent use of both non-selective and selective beta$_2$-adrenergic blockers should be avoided unless there are compelling reasons for their use.

Caution is advised when co-administering with strong CYP 3A4 inhibitors (e.g. ketoconazole, ritonavir) as there is potential for increased systemic exposure to both fluticasone furoate and vilanterol, and concomitant use should be avoided.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Women of chilbearing potential/Contraception in females

Pregnancy

There are no or limited data from the use of fluticasone furoate and vilanterol trifenatate in pregnant women.

Administration of fluticasone furoate/vilanterol to pregnant women should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

Breast-feeding

There is insufficient information on the excretion of fluticasone furoate or vilanterol trifenatate and/or metabolites in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue fluticasone furoate/vilanterol therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no fertility data in humans.

Undesirable effects

The most commonly reported adverse reactions with fluticasone furoate and vilanterol were headache and nasopharyngitis. Common adverse reaction: Candidiasis of mouth and throat, Bronchitis, Influenza, Oropharyngeal pain, Sinusitis, Pharyngitis, Rhinitis, Cough, Dysphonia, Abdominal pain, Arthralgia, Back pain, Pyrexia, Upper respiratory tract infection, pneumonia , fractures and muscle spasms.

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.

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