Relvar

25% more patients improve asthma control vs. other ICS/LABAs in everyday practice*[1,2]

Molecules selected for their long duration of action[3,4]

Relvar's ICS offers high airway protection with low systemic effect[5]

Easy-to-use Ellipta device[6]

For your asthma patients needing an ICS/LABA, will you prescribe Relvar to control and protect?

When stepping up from an ICS, Relvar (FF/VI 92/22 mcg) is indicated[7]

Relvar is well tolerated. The most common adverse events reported are headache and nasopharyngitis[7]

*The primary endpoint was the proportion of patients who achieved an improvement in ACT score from baseline of ≥3 or a total ACT score of ≥20, in patients in the PEA population initiated on Relvar vs. continuing on usual care at 24 weeks. The primary endpoint was met ($p<0.001$). Data presented are from a subset of patients prescribed ICS/LABA at baseline who were initiated on Relvar or continued on their ICS/LABA. Data showed a relative difference of 25% calculated based on the absolute number of patients showing an improvement treated with ICS/LABA (637) vs usual care (511), and an absolute difference of 14%[1]

In this study there was no significant difference in serious adverse events reported between Relvar and usual care. The most common serious adverse events of special interest were cardiovascular disease, asthma and bronchospasm, and pneumonia[1]

References

1. Woodcock A *et al. Lancet* **2017; 390:2247–2255. 2. Svedsater H** *et al. Salford Lung Study. Respir Med* **2018; 141:198–206. 3. Bardsley G** *et al. Respir Res* **2018;19:133. 4. Braithwaite I** *et al. Respir Med* **2016; 119:115–121. 5. GSK Data on File 22034; 2019. 6. Svedsater H** *et al. NPJ Prim Care Respir Med* **2014; 24:14019. 7. Relvar Ellipta approved PI by Israeli MoH.**

PM-IL-FFV-EDTL-200004
November 2020

RELVAR ELLIPTA
fluticasone furoate/vilanterol

RELVAR- abbreviated PI, NOV 18

For full information see MOH approved prescribing information

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 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.

COPD (Chronic Obstructive Pulmonary Disease): Relvar Ellipta 92/22 mcg 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.

QUALITATIVE AND QUANTITATIVE COMPOSITION:
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, for which a short-acting bronchodilator is required. 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 -** Paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with a short-acting inhaled bronchodilator. Relvar Ellipta should be discontinued immediately, the patient assessed and alternative therapy instituted if necessary. **Cardiovascular effects -** Cardiovascular effects, such as cardiac arrhythmias e.g. supraventricular tachycardia and extrasystoles may be seen with sympathomimetic medicinal products including Relvar Ellipta. uticasone 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. **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 -** Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. Fluticasone furoate/vilanterol should be administered with caution in patients with pulmonary tuberculosis or in patients with chronic or untreated infections. **Visual disturbance -** Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids. **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 eceiving inhaled corticosteroids. There is some evidence of an increased risk o f 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. **Pneumonia in patients with asthma -** The incidence of pneumonia in patients with asthma was common at the higher dose

Fertility, pregnancy and lactation: 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. There is insufficient information on the excretion of fluticasone furoate or vilanterol trifenatate and/or metabolites in human milk.
A risk to breastfed newborns/infants cannot be excluded.
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.

Adverse events:
Very common (≥1/10) : headache and nasopharyngitis. Common adverse reactions (≥1/100 to <1/10): 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.

Trade marks are owned by or licensed to the GSK group of companies.

GlaxoSmithKline. 25 Basel street, P.O. Box 3345, Petach-Tikva 4951038 Israel, Tel: 03-9297100.
Medical information service: il.medinfo@gsk.com
Adverse events reporting service: il.safety@gsk.com , Tel: 03-9297100

Avamys
Fluticasone furoate

Effective AR relief for moments that matters[1-8]

Effective reduction in all major symptoms associated with AR[1]

INCS are recommended as first-line by guidelines over combination therapy[2-5]

Delivered by a patient friendly, easy-to-use device with fine mist[6-8]

Avamys moments

The most common AEs were: epistaxis, nasal ulceration and headache.[4]
AE: Adverse Events; AR: Allergic Rhinitis; INCS: Intranasal Corticosteroid

Avamys
Fluticasone furoate
Designed for AR relief

References:

1. Vasar M, Houle PA, Douglass JA, *et al*. Fluticasone furoate nasal spray: effective monotherapy for symptoms of perennial allergic rhinitis in adults/adolescents. *Allergy Asthma Proc* 2008;29(3):313-321.
2. Villa E, Magnoni MS, Micheli D, Canonica GW. A review of the use of fluticasone furoate since its launch. *Expert Opin Pharmacother* 2011;12(13):2107-2117.
3. Baumann D, Bachert C, Högger P. Dissolution in nasal fluid, retention and anti-inflammatory activity of fluticasone furoate in human nasal tissue *ex vivo*. *Clin Exp Allergy* 2009;39(10):1540-1550.
4. Valotis A, Högger P. Human receptor kinetic and lung tissue retention of the enhanced-affinity of glucocorticoid fluticasone furoate. *Respir Res* 2007;8(1):54.
5. Salter M, Biggadike K, Matthews JL, *et al*. Pharmacological properties of the enhanced-affinity of glucocorticoid fluticasone furoate *in vitro* and *in vivo* model of respiratory inflammatory disease. *Am J Physiol Lung Cell Mol Physiol* 2007;293(3):L660-L667.
6. Rossios C, To Y, To M, et al. Long-acting fluticasone furoate has superior pharmacological profile to fluticasone propionate in human respiratory cells. *Eur J Pharmacol* 2011;670(1):244-251.
7. Scadding GK, Kariyawasam HH, Scadding G, *et al*. BSACI guidelines for the diagnosis and management of allergic and non-allergic rhinitis. *Clin Exp Allergy* 2017:47:856-889.
8. Fluticasone Furoate Global Data Sheet; version 11, 03 April 2018.
9. Brozek J, Bousquet J, Agache I, *et al*. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines 2016 revision. *J Allergy Clin Immunol* 2017;140:(4):950-958.

AVAMYS- Abbreviated PI DEC 2018

For full product information see MOH approved prescribing information

COMPOSITIO N- Each spray actuation delivers 27.5 micrograms of fluticasone furoate
THERAPEUTIC INDICATIONS - Treatment of the symptoms of seasonal and perennial allergic rhinitis in patients aged 2 years and older.
DOSAGE AND ADMINISTRATION - Adults and Adolescents Aged 12 Years and Older: The recommended starting dosage is 110 mcg once daily administered as 2 sprays (27.5 mcg/spray) in each nostril. When the maximum benefit has been achieved and symptoms have been controlled, reducing the dosage to 55 mcg (1 spray in each nostril) once daily may be effective in maintaining control of allergic rhinitis symptoms. Children Aged 2 to 11 Years: The recommended starting dosage in children is 55 mcg once daily administered as 1 spray (27.5 mcg/spray) in each nostril. Children not adequately responding to 55 mcg may use 110 mcg (2 sprays in each nostril) once daily. Once symptoms have been controlled, dosage reduction to 55 mcg once daily is recommended.
CONTRAINDICATIONS - patients with hypersensitivity to the active substance or to any of its excipients.
WARNINGS AND PRECAUTIONS - Epistaxis and Nasal Ulceration :In clinical trials of 2 to 52 weeks duration, epistaxis and nasal ulcerations were observed more frequently and some epistaxis events were more severe in patients treated with AVAMYS Nasal Spray than those who received placebo . Candida Infection- When such an infection develops, it may require treatment with appropriate local therapy and discontinuation of AVAMYS Nasal Spray. Therefore, patients using AVAMYS Nasal Spray over several months or longer should be examined periodically for evidence of Candida infection or other signs of adverse effects on the nasal mucosa. Nasal septal perforation: Post marketing cases of nasal septal perforation have been reported in patients following the intranasal application of AVAMYS Nasal Spray Impaired Wound Healing: Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal ulcers, nasal surgery, or nasal trauma should not use AVAMYS Nasal Spray until healing has occurred. Nasal and inhaled corticosteroids may result in the development of glaucoma and/or cataracts. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure (IOP), glaucoma, and/or cataracts. Hypersensitivity reactions, including anaphylaxis, angioedema, rash, and urticaria, may occur after administration of AVAMYS Nasal Spray. Discontinue AVAMYS Nasal Spray if such reactions occur. Persons who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals. If a patient is exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If a patient is exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. If chickenpox or measles develops, treatment with antiviral agents may be considered. Corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculous infections of the respiratory tract, untreated local or systemic fungal or bacterial infections, systemic viral or parasitic infections, or ocular herpes simplex because of the potential for worsening of these infections.When intranasal steroids are used at higher-than-recommended dosages or in susceptible individuals at recommended dosages, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, the dosage of AVAMYS Nasal Spray should be discontinued slowly, consistent with accepted procedures for discontinuing oral corticosteroid therapy. The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency. In addition, some patients may experience symptoms of corticosteroid withdrawal, e.g., joint and/or muscular pain, lassitude, depression. Patients previously treated for prolonged periods with systemic corticosteroids and transferred to topical corticosteroids should be carefully monitored for acute adrenal insufficiency in response to stress. In those patients who have asthma or other clinical conditions requiring long-term systemic corticosteroid treatment, rapid decreases in systemic corticosteroid dosages may cause a severe exacerbation of their symptoms. Coadministration with ritonavir is not recommended because of the risk of systemic effects secondary to increased exposure to fluticasone furoate. Use caution with the coadministration of AVAMYS Nasal Spray and other potent cytochrome P450 3A4 (CYP3A4) inhibitors, such as ketoconazole Effect on Growth: Corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. Monitor the growth routinely of pediatric patients receiving AVAMYS Nasal Spray. To minimize the systemic effects of intranasal corticosteroids, including AVAMYS Nasal Spray, titrate each patient's dose to the lowest dosage that effectively controls his/her symptoms
ADVERSE REACTIONS - Epistaxis, ulcerations, Candida albicans infection, impaired wound healing, and nasal septal perforation ,Cataracts and glaucoma, Immunosuppression Hypothalamic-pituitary-adrenal (HPA) axis effects, including growth reduction. Adults and Adolescents Aged 12 Years and Older: Adverse Reactions with >1%: Headache, epistaxis, Pharyngolaryngeal pain, nasal ulceration, back pain. Pediatric Patients Aged 2 to 11 Years: Adverse Reactions with >3%: Headache, Nasopharyngitis, Epistaxis, Pyrexia, Pharyngolaryngeal pain, Cough.
USE IN SPECIFIC POPULATIONS - Pregnancy Category C. AVAMYS Nasal Spray should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Hypoadrenalism may occur in infants born of mothers receiving corticosteroids during pregnancy. Such infants should be carefully monitored. Since there are no data from controlled trials on the use of intranasal fluticasone furoate by nursing mothers, caution should be exercised when AVAMYS Nasal Spray is administered to a nursing woman. The growth of pediatric patients receiving intranasal corticosteroids, including AVAMYS Nasal Spray, should be monitored routinely (e.g., via stadiometry). The potential growth effects of prolonged treatment should be weighed against the clinical benefits obtained and the risks/benefits of treatment alternatives. To minimize the systemic effects of intranasal corticosteroids, including AVAMYS Nasal Spray, each patient's dose should be titrated to the lowest dosage that effectively controls his/her symptoms. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. Use AVAMYS Nasal Spray with caution in patients with moderate or severe hepatic impairment. No dosage adjustment is required in patients with renal impairment
OVERDOSAGE - Chronic overdosage may result in signs/symptoms of hypercorticism. overdose is unlikely to require any therapy other than observation.

Trade marks are owned by or licensed to the GSK group of companies.

GlaxoSmithKline. 25 Basel street, P.O. Box 3345 Petach-Tikva 4951038 Israel, Tel: 03-9297100.
Medical information service: il.medinfo@gsk.com
Adverse events reporting service: il.safety@gsk.com , Tel: 03-9297100

PM-IL-FLP-BTHC-200001 November 2020