SERETIDE
salmeterol/fluticasone propionate

gsk

Seretide

significantly reduce hospitalization for COPD exacerbation

Annual admission rates were **17%** lower with Seretide than with placebo ($p \leq 0.03$)[1]

NNT
Number Needed to Treat

32

Treat 32 patients
to prevent 1 Admission/yr[1]

Abbreviated PI for Seretide[2,3]

Seretide *Accuhaler:* Moulded plastic device containing a foil strip with 28 or 60 regularly placed blisters each containing 50 micrograms of salmeterol as salmeterol xinafoate and 100, 250 or 500 micrograms of fluticasone propionate. **Seretide *Evohaler:*** Each single actuation of **Seretide** provides: Salmeterol xinafoate equivalent to 25 micrograms of salmeterol and 50, 125 or 250 micrograms of fluticasone propionate. **Indications: Asthma and Chronic Obstructive Pulmonary Disease (COPD). Dosage and Administration: Seretide** is for inhalation only. Patients should be made aware that **Seretide** must be used regularly for optimum benefit, even when asymptomatic. Patients should be regularly reassessed by a doctor, so that the strength of **Seretide** they are receiving remains optimal and is only changed on medical advice. **Asthma (Reversible Obstructive Airways Disease):** The dose should be titrated to the lowest dose at which effective control of symptoms is maintained. Where the control of symptoms is maintained with twice daily **Seretide**, titration to the lowest effective dose could include **Seretide** given once daily. If a patient is inadequately controlled on inhaled corticosteroid therapy alone, substitution with **Seretide** at a therapeutically equivalent corticosteroid dose may result in an improvement in asthma control. For patients whose asthma control is acceptable on inhaled corticosteroid therapy alone, substitution with **Seretide** may permit a reduction in corticosteroid dose while maintaining asthma control. **Recommended Doses**: **Adults and adolescents 12 years and older: Seretide *Accuhaler:*** One inhalation (50 micrograms salmeterol and 100, 250 or 500 micrograms fluticasone propionate) twice daily. **Seretide *Evohaler:*** Two inhalations (25 micrograms salmeterol and 50, 125 or 250 micrograms fluticasone propionate) twice daily. **Children 4 years and older: Seretide *Accuhaler:*** One inhalation (50 micrograms salmeterol and 100 micrograms fluticasone propionate) twice daily. **Seretide *Evohaler:*** Two inhalations (25 micrograms salmeterol and 50 micrograms fluticasone propionate) twice daily. There are no data available for use of **Seretide** in children aged under 4 years. **Chronic Obstructive Pulmonary Disease (COPD):** For adult patients the recommended dose is **Seretide *Accuhaler:*** One inhalation 50/250 micrograms to 50/500 micrograms salmeterol/fluticasone propionate twice daily. **Seretide *Evohaler:*** Two inhalations 25/125 micrograms to 25/250 micrograms salmeterol/fluticasone propionate twice daily. At a dose of 50/500 micrograms twice daily, **Seretide** has been shown to reduce all-cause mortality. **Special patient groups:** There is no need to adjust the dose in elderly patients or in those with renal or hepatic impairment. **Contraindications: Seretide** is contraindicated in patients with a history of hypersensitivity to any of the ingredients. **Warnings and Precautions: Seretide *Accuhaler/ Evohaler*** are not for relief of acute symptoms for which a fast and short-acting bronchodilator (e.g. salbutamol) is required. Patients should be advised to have their relief medication available at all times. Increasing use of short-acting bronchodilators to relieve symptoms indicates deterioration of control and patients should be reviewed by a physician. Sudden and progressive deterioration in control of asthma is potentially life-threatening and the patient should be reviewed by a physician. Consideration should be given to increasing corticosteroid therapy. Also, where the current dosage of **Seretide** has failed to give adequate control of Asthma, the patient should be reviewed by a physician. Treatment with **Seretide** should not be stopped abruptly in patients with asthma due to risk of exacerbation, therapy should be titrated-down under physician supervision. For patients with COPD cessation of therapy may be associated with symptomatic decompensation and should be supervised by a physician. There was an increased reporting of pneumonia in studies of patients with COPD receiving **Seretide** (see Adverse Reactions). Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of pneumonia and exacerbation frequently overlap. As with all inhaled medication containing corticosteroids, **Seretide** should be administered with caution in patients with active or quiescent pulmonary tuberculosis. **Seretide** should be administered with caution in patients with thyrotoxicosis. Cardiovascular effects, such as increases in systolic blood pressure and heart rate, may occasionally be seen with all sympathomimetic drugs, especially at higher than therapeutic doses. For this reason, **Seretide** should be used with caution in patients with pre-existing cardiovascular disease. A transient decrease in serum potassium may occur with all sympathomimetic drugs at higher therapeutic doses. Therefore, **Seretide** should be used with caution in patients predisposed to low levels of serum potassium. Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods; these effects are much less likely to occur than with oral corticosteroids (see Overdose). Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. It is important, therefore for Asthma patients, that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control is maintained. The possibility of impaired adrenal response should always be borne in mind in emergency and elective situations likely to produce stress and appropriate corticosteroid treatment considered (see Overdose). It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroid is regularly monitored. Because of the possibility of impaired adrenal response, patients transferring from oral steroid therapy to inhaled fluticasone propionate therapy should be treated with special care, and adrenocortical function regularly monitored. Following introduction of inhaled fluticasone propionate, withdrawal of systemic therapy should be gradual and patients encouraged to carry a steroid warning card indicating the possible need for additional therapy in times of stress. There have been very rare reports of increases in blood glucose levels (see Adverse Reactions) and this should be considered when prescribing to patients with a history of diabetes mellitus. During post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone propionate and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side-effects. It was observed in a drug interaction study that concomitant use of systemic ketoconazole increases exposure to *SEREVENT*. This may lead to prolongation in the QTc interval. Caution should be exercised when strong CYP3A4 inhibitors (e.g. ketoconazole) are co-administered with *SEREVENT*. As with other inhalation therapy paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with a fast and short-acting inhaled bronchodilator. Salmeterol-FP *Accuhaler* or Evohaler should be discontinued immediately, the patient assessed and alternative therapy instituted if necessary. The pharmacological side-effects of beta-2 agonist treatment, such as tremor, subjective palpitations and headache have been reported, but tend to be transient and to reduce with regular therapy. **Interactions:** Both non-selective and selective beta-blockers should be avoided unless there are compelling reasons for their use. Under normal circumstances, low plasma concentrations of fluticasone propionate are achieved after inhaled dosing, due to extensive first pass metabolism and high systemic clearance mediated by cytochrome P450 3A4 in the gut and liver. Hence, clinically significant drug interactions mediated by fluticasone propionate are unlikely. A drug interaction study in healthy subjects has shown that ritonavir (a highly potent cytochrome P450 3A4 inhibitor) can greatly increase fluticasone propionate plasma concentrations, resulting in markedly reduced serum cortisol concentrations. During postmarketing use, there have been reports of clinically significant drug interactions in patients receiving intranasal or inhaled fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone propionate and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side-effects. Studies have shown that other inhibitors of cytochrome P450 3A4 produce negligible (erythromycin) and minor (ketoconazole) increases in systemic exposure to fluticasone propionate without notable reductions in serum cortisol concentrations. Nevertheless, care is advised when co-administering potent cytochrome P450 3A4 inhibitors (e.g. ketoconazole) as there is potential for increased systemic exposure to fluticasone propionate. Co-administration of ketoconazole and *SEREVENT* resulted in a significant increase in plasma salmeterol exposure (1.4-fold Cmax and 15-fold AUC) and this may cause a prolongation of the QTc interval. **Pregnancy and Lactation:** Administration of drugs during pregnancy and lactation should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus or child. Administration during lactation should only be considered if the expected benefit to the mother is greater than any possible risk to the child. **Effects on Ability to Drive and Use Machines:** There have been no specific studies of the effect of **Seretide** on the above activities, but the pharmacology of both drugs does not indicate any effect. **Adverse Reactions:** All of the adverse reactions associated with the individual components, salmeterol xinafoate and fluticasone propionate, are listed below. There are no additional adverse reactions attributed to the combination product when compared to the adverse event profiles of the individual components. **Clinical trial data: Very common**: headache. **Common**: candidiasis of mouth and throat, pneumonia (in COPD patients), hoarseness/dysphonia, , muscle cramps, arthralgia. **Uncommon**: cutaneous hypersensitivity reactions, dyspnoea, cataract, hyperglycaemia, anxiety, sleep disorders, tremor, palpitations, tachycardia, atrial fibrillation, throat irritation, contusions. **Rare**: oesophageal candidiasis, anaphylactic reactions, glaucoma, behavioural changes, including hyperactivity and irritability (predominantly in children), cardiac arrhythmias including supraventricular tachycardia and extrasystoles, **Postmarketing data:** Rare: angioedema (mainly facial and oropharyngeal oedema) and bronchospasm, Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decreased bone mineral density, paradoxical bronchospasm. **Overdose:** The expected symptoms and signs of salmeterol overdosage are those typical of excessive beta 2-adrenergic stimulation including tremor, headache, tachycardia, increases in systolic blood pressure and hypokalaemia. There is no specific treatment for an overdose of salmeterol and fluticasone propionate. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary. Acute inhalation of fluticasone propionate doses in excess of those approved may lead to temporary suppression of the hypothalamic-pituitary-adrenal axis. This does not usually require emergency action as normal adrenal function typically recovers within a few days. If higher than approved doses of **Seretide** are continued over prolonged periods, significant adrenocortical suppression is possible. There have been very rare reports of acute adrenal crisis, mainly occurring in children exposed to higher than approved doses over prolonged periods (several months or years); observed features have included hypoglycaemia associated with decreased consciousness and/or convulsions. Situations which could potentially trigger acute adrenal crisis include exposure to trauma, surgery, infection or any rapid reduction in the dosage of the inhaled fluticasone propionate component. **List of Excipients (for Accuhaler):** Lactose (which contains milk protein), **(for Evohaler):** HFA134a. **Seretide EVOHALER**, **ACCUHALER** are trademarks of the GlaxoSmithKline group of companies. Version number: Abb Seretide Accuhaler IPI 21 TH 04/20 (P). Abb Seretide Evohaler IPI 19 TH 01/19. Full Prescribing Information is available on request. Please read the full prescribing information prior to administration, available from GlaxoSmithKline (Thailand), 12th Floor Wave Place, 55 Wireless Road, Lumpini, Patumwan, Bangkok 10330. **"GSK is committed to the effective collection and management of human safety information relating to our products and we encourage healthcare professionals to report adverse events to us at safety_th@gsk.com"**

References

1. Calverley PMA, *et al. N Engl J Med* 2007;356:775–789.
2. Seretide Accuhaler IPI 21 TH 04/20 (P).
3. Seretide Evohaler IPI 19 TH 01/19.

PM-TH-FPS-EPNL-210001 Approval Date : 07/21

ใบอนุญาตโฆษณาเลขที่ ฆศ.441/2564
เลขทะเบียนตำรับยาที่ 2C 39/55 (N), 2C 43/54 (N)