Key points

- Stalpex is a branded generic inhaled corticosteroid (ICS) and long-acting β₂ agonist (LABA) alternative to Seretide™ Accuhaler™ available as 50 mcg/500 mcg dose
- **Stalpex provides dosing equivalence to Seretide™ Accuhaler™**, at 50% lower acquisition cost¹²

Drug name

Stalpex (salmeterol xinafoate/fluticasone propionate 50 mcg/500 mcg dose inhalation powder, pre-dispensed)

Indication

- Stalpex is an ICS/LABA indicated for use in:
  - patients ≥12 years with severe asthma where use of a combination product is appropriate
  - patients with chronic obstructive pulmonary disease (COPD), with a FEV₁ <60% predicted normal (pre-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy.

Dosage

- Stalpex is available in one dose strength: salmeterol xinafoate/fluticasone propionate 50 mcg/500 mcg (PIP 4098661)
- For optimum benefit, Stalpex should be used daily, even when asymptomatic⁴
- The recommended dose for asthma and COPD is one inhalation twice daily⁴
- See **Summary of Product Characteristics**⁴ for additional dosage information.

Inhaler

- Stalpex comes in blisters made from polyamide (OPA)/aluminium/polyvinyl chloride (PVC)/aluminium/polyethylene terephthalate (PET)/paper contained in a molded plastic inhaler equipped with a mouthpiece and dose counter⁴
- One inhaler contains 60 inhalations⁴
- The operating principles and pharmaceutical dosage form of Stalpex are equivalent to those of Seretide™ Accuhaler™³

- The handling of the two inhalation devices (Stalpex and reference product) is equivalent.¹

Budgetary implications

- Stalpex (see pricing overleaf) could provide acquisition cost savings of 50% compared to the existing standard of care.²³

Potential cost savings with Stalpex⁵

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost Savings (£ million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current annual cost to NHS for ICS/LABA prescriptions (50 mcg/500 mcg dose)</td>
<td>£24.7</td>
</tr>
<tr>
<td>Potential annual acquisition cost savings to NHS using Stalpex versus Seretide™ Accuhaler™</td>
<td>£12.1</td>
</tr>
</tbody>
</table>

Bioequivalence

- The bioequivalence of Stalpex compared to Seretide™ Accuhaler™ has been confirmed¹
- Equivalence of the two devices was confirmed by a comparative handling study.³

BTS/SIGN recommendations

- ICS are the recommended preventer drug for adults and children to achieve treatment goals⁶
- First choice add-on therapy: LABA in adults; inhaled LABA or leukotriene receptor antagonist (LTRA) in children⁶
- Combination inhalers are recommended to improve treatment adherence⁶
- Patient preference and local cost are the most important factors to consider when prescribing an inhaler⁶
- Generic prescribing of inhalers should be avoided so that patients are not given unfamiliar devices.⁶

References

1. Medicine and Healthcare products Regulatory Agency (MHRA). Public assessment report. Stalpex 50 microgram/500 microgram/dose inhalation powder, pre-dispensed (salmeterol xinafoate and fluticasone propionate). UK/H/6498/03/DC. December 2018. Available at: mhraproducts4853.blob.core.windows.net/docs/77c1431424dd55258ef03d0555b684036cecb9f2e03
5. Glenmark Pharmaceuticals Europe Ltd data on file. GMK/UK/005 v 03.
Stalpex is indicated for the symptomatic treatment of patients with severe asthma where use of a combination product (long-acting β2 agonist and inhaled corticosteroid) is appropriate: patients not adequately controlled on a lower strength corticosteroid combination product, or patients already adequately controlled on an inhaled corticosteroid in a high strength and a long-acting β2 agonist. Chronic Obstructive Pulmonary Disease (COPD): Stalpex is indicated for use in patients with COPD receiving inhaled corticosteroids. Data from one trial suggested African-American patients were at increased risk of serious respiratory-related events or deaths when using salmeterol compared with placebo. Patients of black African or Afro-Caribbean ancestry should therefore be asked to continue treatment but to seek medical advice if asthma symptoms remain uncontrolled or worsen whilst using Stalpex. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be referred to an ophthalmologist for evaluation. Adolescents <16 years taking high doses of fluticasone propionate (typically ≥ 1000 micrograms/day) may be at particular risk. Systemic effects such as Cushing’s syndrome, Cushingoid features, adrenal suppression, acute adrenal crisis and growth retardation in adolescents, decreased bone mineral density, hyperglycaemia, anxiety, sleep disorders, behavioural changes, including psychomotor hyperactivity and irritability (predominantly in adolescents), depression, aggression (predominantly in adolescents), tremor, cataract, glaucoma, blunted vision, Palpitations, tachycardia, cardiac arrhythmias (including supraventricular tachycardia and extrasystoles), atrial fibrillation, angina pectoris, Paradoxical bronchospasm. Please consult the summary of product characteristics for a full list of adverse reactions.

Asthma COPD

Indications: Asthma: Stalpex is indicated for use in patients with severe asthma 12 years of age and older only. Indicated in the regular treatment of patients with severe asthma where use of a combination product (long-acting β2 agonist and inhaled corticosteroid) is appropriate: patients not adequately controlled on a lower strength corticosteroid combination product, or patients already adequately controlled on an inhaled corticosteroid in a high strength and a long-acting β2 agonist. Chronic Obstructive Pulmonary Disease (COPD): Stalpex is indicated for the symptomatic treatment of patients with COPD, with a FEV₁ <60% predicted normal (pre-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy. Dosage and administration: Use daily for optimum benefit, even when asymptomatic. Titrate to the lowest dose at which effective control of symptoms is maintained. Stalpex is only available in one strength therefore when titrating down, change to an alternative lower fixed-dose combination of salmeterol and fluticasone propionate. Asthma: Adults and adolescents 12 years and older: One 50 micrograms salmeterol and 500 micrograms fluticasone propionate inhalation twice daily. Once asthma is controlled, consider stepping down to a lower dose inhaled corticosteroid/ LABA combination or ICS alone. In general, inhaled corticosteroids remain the first line treatment. Stalpex is not intended for the initial management of mild or moderate asthma. Children: Limited data are available. COPD: Adults: One inhalation of 50 micrograms salmeterol and 500 micrograms fluticasone propionate twice daily. Elderly: no dose adjustment required. Renal impairment: no dose adjustment required. Hepatic impairment: no data are available for use of Stalpex in patients with hepatic impairment. Contraindications: Hypersensitivity to the active substances or to any of the excipients. Patients with severe asthma only; not for acute treatment, during an exacerbation or worsening asthma. Increased use of, or decreased response to, reliever medication indicates deterioration warranting physician review. Sudden and progressive deterioration is potentially life-threatening and the patient should undergo urgent medical assessment; consider increasing corticosteroid therapy. Once asthma symptoms are controlled, consideration may be given to gradually reducing the dose of the inhaled corticosteroid and therefore a change to an alternative fixed-dose combination of salmeterol and fluticasone propionate containing a lower dose. The lowest dose of inhaled corticosteroid should be used. Treatment with Stalpex should not be stopped abruptly in patients with asthma due to risk of exacerbation. Therapy should be down-titrated under physician supervision. For patients with COPD, cessation of therapy may also be associated with symptomatic decompensation and should be supervised by a physician. Caution in patients with active or quiescent pulmonary tuberculosis and fungal, viral or other infections of the airway. Stalpex should be used with caution in patients with severe cardiovascular disorders or heart rhythm abnormalities and in patients with diabetes mellitus, thyrotoxicosis, uncorrected hypokalaemia or patients predisposed to low levels of serum potassium. Caution in diabetes mellitus (some reports of hyperglycaemia). If paradoxical bronchospasm develops, Stalpex should be discontinued immediately, the patient assessed and alternative therapy instituted if necessary. Ensure regular review of patients on long term or high dose treatment to obtain lowest effective dose. Prolonged treatment of patients with high doses of inhaled corticosteroids may result in adrenal suppression and acute adrenal crisis. Triggers of acute adrenal crisis include trauma, surgery, infection or any rapid reduction in dosage. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery. Caution in patients transferring from oral steroids as they may remain at risk of impaired adrenal reserve for a considerable time. An increase in the incidence of pneumonia has been observed in patients with COPD receiving inhaled corticosteroids. Data from one trial suggested African-American patients were at increased risk of serious respiratory-related events or deaths when using salmeterol compared with placebo. Patients of black African or Afro-Caribbean ancestry should therefore be asked to continue treatment but to seek medical advice if asthma symptoms remain uncontrolled or worsen whilst using Stalpex. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be referred to an ophthalmologist for evaluation. Adolescents <16 years taking high doses of fluticasone propionate (typically ≥ 1000 micrograms/day) may be at particular risk. Systemic effects such as Cushing’s syndrome, Cushingoid features, adrenal suppression, acute adrenal crisis and growth retardation in adolescents and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression may occur, particularly at high doses prescribed for long periods. Consider referring adolescents to a paediatric respiratory specialist. Regularly monitor the height of adolescents receiving prolonged treatment. Interaction with fluticasone/β2 adrenergic blockers. Avoid non-selective and selective β blockers. Potentially serious hypokalaemia may result from β2 agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics. Avoid ritonavir (can greatly increase plasma concentration of fluticasone propionate). Caution with CYP3A inhibitors and avoid long-term treatment. Interaction with salmeterol: Avoid potent CYP3A4 inhibitors. Pregnancy and lactation: Animal studies have shown reproductive toxicity after administration of β2 adrenoceptor agonists and glucocorticosteroids; data on 300-1000 women indicate no malformative or feto/neonatal toxicity. It is unknown whether salmeterol and fluticasone propionate/metabolites are excreted in human milk and a risk to infants cannot be ruled out. Adverse reactions:

| Common and very common: | Candidiasis of the mouth and throat, pneumonia (in COPD patients), bronchitis, hypokalaemia, headache, nasopharyngitis, throat irritation, hoarseness/dysphonia, sinusitis, Confusions, muscle cramps, traumatic fractures, arthralgia, myalgia. Uncommon, rare and unknown frequency serious reactions: Oesophageal candidiasis, hypersecretory reactions with the following manifestations: cutaneous hypersensitivity reactions, angioedema (mainly facial and oropharyngeal oedema), respiratory symptoms (dyspnoea), respiratory symptoms (bronchospasm), anaphylactic reactions including anaphylactic shock, Cushing’s syndrome, Cushingoid features, adrenal suppression, growth retardation in adolescents, decreased bone mineral density, hyperglycaemia, anxiety, sleep disorders, behavioural changes, including psychomotor hyperactivity and irritability (predominantly in adolescents), depression, aggression (predominantly in adolescents), tremor, cataract, glaucoma, blunted vision, Palpitations, tachycardia, cardiac arrhythmias (including supraventricular tachycardia and extrasystoles), atrial fibrillation, angina pectoris, Paradoxical bronchospasm. Please consult the summary of product characteristics for a full list of adverse reactions. Marketing authorization number: PL: 25258/0296. Marketing Authorization Holder: Glenmark Pharmaceuticals Europe Limited, Laxmi House, 2B Draycott Avenue, Kenton, Middlesex, HA3 0BU, United Kingdom. Distributor: As above. Legal classification: POM. Price: £16.37. Job code: PP-UK-STAL-0037 Date of preparation: September 2020. |