

PRESCRIBING INFORMATION

TRIXEO AEROSPHERE® (formoterol fumarate dihydrate/ glycopyrronium/ budesonide) 5 micrograms/7.2 micrograms/160 micrograms pressurised inhalation, suspension

Consult Summary of Product Characteristics before prescribing.

Indication: Trixeo Aerosphere is indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist or combination of a long-acting beta2-agonist and a long-acting muscarinic antagonist.

Presentation: Each single actuation (delivered dose, ex-actuator) contains 5mcg of formoterol fumarate dihydrate, glycopyrronium bromide 9mcg, equivalent to 7.2mcg of glycopyrronium and budesonide 160mcg. This corresponds to a metered dose of 5.8mcg of formoterol fumarate dihydrate, glycopyrronium bromide 10.4mcg, equivalent to 8.2mcg of glycopyrronium and budesonide 182mcg.

Dosage and Administration: The recommended and maximum dose is two inhalations twice daily (two inhalations morning and evening). If a dose is missed, take as soon as possible and take the next dose at the usual time. A double dose should not be taken to make up for a forgotten dose. **Special populations: Elderly:** No dose adjustments required in elderly patients. **Renal impairment:** Use at recommended dose in patients with mild to moderate renal impairment. Can also be used at the recommended dose in patients with severe renal impairment or end-stage renal disease requiring dialysis, only if expected benefit outweighs the potential risk. **Hepatic impairment:** Use at recommended dose in patients with mild to moderate hepatic impairment. Can also be used at the recommended dose in patients with severe hepatic impairment, only if expected benefit outweighs the potential risk. For inhalation use. To ensure proper administration of the medicinal product, the patient should be shown how to use the inhaler correctly by a physician or other healthcare professional, who should also regularly check the adequacy of the patient's inhalation technique. Patients who find it difficult to coordinate actuation with inhalation may use Trixeo Aerosphere with a spacer to ensure proper administration of the medicinal product.

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

Warnings and Precautions: Not for acute use: Not indicated for treatment of acute episodes of bronchospasm, i.e. as a rescue therapy. **Paradoxical bronchospasm:** Administration of formoterol/glycopyrronium/budesonide may produce paradoxical bronchospasm with an immediate wheezing and shortness of breath after dosing and may be life-threatening. Treatment should be discontinued immediately if paradoxical bronchospasm occurs. Assess patient and alternative therapy instituted if necessary. **Deterioration of disease:** Recommended that treatment should not be stopped abruptly. If patients find the treatment ineffective, continue treatment but seek medical attention. Increasing use of reliever bronchodilators indicates worsening of the underlying condition and warrants reassessment of the therapy. Sudden and progressive deterioration in the symptoms of COPD is potentially life-threatening, patient should undergo urgent medical assessment. **Cardiovascular effects:** Cardiovascular effects, such as cardiac arrhythmias, e.g. atrial fibrillation and

tachycardia, may be seen after the administration of muscarinic receptor antagonists and sympathomimetics, including glycopyrronium and formoterol. Use with caution in patients with clinically significant uncontrolled and severe cardiovascular disease such as unstable ischemic heart disease, acute myocardial infarction, cardiomyopathy, cardiac arrhythmias and severe heart failure. Caution should also be exercised when treating patients with known or suspected prolongation of the QTc interval (QTc > 450 milliseconds for males or > 470 milliseconds for females), either congenital or induced by medicinal products. **Systemic corticosteroid effects:** May occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur with inhalation treatment than with oral corticosteroids. Systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, cataract and glaucoma. Potential effects on bone density should be considered particularly in patients on high doses for prolonged periods that have co-existing risk factors for osteoporosis. **Visual disturbances:** May be reported with systemic and topical corticosteroid use. If patient presents symptoms such as blurred vision or other visual disturbances, consider ophthalmologist referral for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR). **Transfer from oral therapy:** Care is needed in patients transferring from oral steroids, since they may remain at risk of impaired adrenal function for a considerable time. Patients who have required high dose corticosteroid therapy or prolonged treatment at the highest recommended dose of inhaled corticosteroids, may also be at risk. These patients may exhibit signs and symptoms of adrenal insufficiency when exposed to severe stress. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery. **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. 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 include current smoking, older age, low body mass index (BMI) and severe COPD. **Hypokalaemia:** Potentially serious hypokalaemia may result from β_2 -agonist therapy. This has potential to produce adverse cardiovascular effects. Caution is advised in severe COPD as this effect may be potentiated by hypoxia. Hypokalaemia may also be potentiated by concomitant treatment with other medicinal products which can induce hypokalaemia, such as xanthine derivatives, steroids and diuretics. **Hyperglycaemia:** Inhalation of high doses of β_2 -adrenergic agonists may produce increases in plasma glucose. Blood glucose should be monitored during treatment following established guidelines in patients with diabetes. **Co-existing conditions:** Use with caution in patients with thyrotoxicosis. **Anticholinergic activity:** Due to anticholinergic activity, use with caution in patients with symptomatic prostatic hyperplasia, urinary retention or with narrow-angle glaucoma. Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using this medicinal product and to contact their doctor immediately should any of these signs or symptoms develop. Co-administration of this medicinal product with other anticholinergic containing medicinal products is not recommended. **Renal impairment:** Patients with severe renal impairment (creatinine clearance of <30 mL/min), including those with end-stage renal disease requiring dialysis, should only be treated with this medicinal product if the expected benefit outweighs the potential risk. **Hepatic impairment:** In patients with severe hepatic impairment, use only if the expected benefit outweighs the potential risk. These patients should be monitored for potential adverse reactions.

Drug Interactions: Co-treatment with strong CYP3A inhibitors, e.g. itraconazole, ketoconazole, HIV protease inhibitors and cobicistat-containing products are expected to increase the risk of systemic side effects. Should be avoided unless the benefit

outweighs the increased risk, in which case patients should be monitored for systemic corticosteroid adverse reactions. This is of limited clinical importance for short-term (1-2 weeks) treatment. **Other antimuscarinics and sympathomimetics:** Co-administration with other anticholinergic and/or long-acting β_2 -adrenergic agonist containing medicinal products is not recommended as it may potentiate known inhaled muscarinic antagonist or β_2 -adrenergic agonist adverse reactions. Concomitant use of other beta-adrenergic medicinal products can have potentially additive effects, caution required when prescribed concomitantly with formoterol. **Medicinal product-induced hypokalaemia:** Possible initial hypokalaemia may be potentiated by xanthine derivatives, steroids and non-potassium sparing diuretics. Hypokalaemia may increase the disposition towards arrhythmias in patients who are treated with digitalis glycosides. **β -adrenergic blockers:** β -adrenergic blockers (including eye drops) can weaken or inhibit the effect of formoterol. Concurrent use of β -adrenergic blockers should be avoided unless the expected benefit outweighs the potential risk. If required, cardio-selective β -adrenergic blockers are preferred. **Other pharmacodynamic interactions:** Concomitant treatment with quinidine, disopyramide, procainamide, antihistamines, monoamine oxidase inhibitors, tricyclic antidepressants and phenothiazines can prolong QT interval and increase the risk of ventricular arrhythmias. L-dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance towards beta2-sympathomimetics. Concomitant treatment with monoamine oxidase inhibitors, including medicinal products with similar properties such as furazolidone and procarbazine, may precipitate hypertensive reactions. Elevated risk of arrhythmias in patients receiving concomitant anaesthesia with halogenated hydrocarbons.

Pregnancy and Lactation: Administration to pregnant women/women who are breast-feeding should only be considered if the expected benefit to the mother justifies the potential risk to the foetus/child.

Ability to Drive and Use Machines: Dizziness is an uncommon side effect which should be taken into account.

Undesirable events: Consult SmPC for full list of adverse events. **Common ($\geq 1/100$ to $< 1/10$):** Oral candidiasis, pneumonia, hyperglycaemia, anxiety, insomnia, headache, palpitations, dysphonia, cough, nausea, muscle spasms, urinary tract infection. **Uncommon ($\geq 1/1,000$ to $< 1/100$):** Hypersensitivity, depression, agitation, restlessness, nervousness, dizziness, tremor, angina pectoris, tachycardia, cardiac arrhythmias (atrial fibrillation, supraventricular tachycardia and extrasystoles), bronchospasm, bruising, urinary retention, chest pain. **Very Rare ($< 1/10,000$):** Signs or symptoms of systemic glucocorticosteroid effects, e.g. hypofunction of the adrenal gland, abnormal behaviour. **Not known:** Angioedema, vision blurred, cataract, glaucoma.

Legal Category: POM.

Marketing Authorisation Number: EU/1/20/1498/002

Presentation & Basic NHS cost: 1 inhaler x 120 actuations:

Marketing Authorisation Holder: AstraZeneca AB, SE-151 85, Södertälje, Sweden.

Further Information is Available From: AstraZeneca UK Ltd, 600 Capability Green, Luton, LU1 3LU, UK.

TRIXEO and AEROSPHERE are registered trade marks of the AstraZeneca group of companies.

Date of preparation: 10/2020

RSP 20 0059

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to AstraZeneca by visiting <https://aereporting.astrazeneca.com> or by calling 0800 783 0033.