PRESCRIBING INFORMATION - COPD

SYMBICORT® 200 micrograms/6micrograms per actuation, pressurised inhalation, suspension
SYMBICORT® TURBOHALER® 200 micrograms/6 micrograms/inhalation, inhalation powder
SYMBICORT® TURBOHALER® 400 micrograms/12 micrograms/inhalation, inhalation powder

(budesonide/formoterol fumarate dihydrate)

Consult Summary of Product Characteristics before prescribing.

Indication: Symptomatic treatment of adult patients, aged 18 and older with Chronic Obstructive Pulmonary Disease (COPD) with FEV_1 <70% predicted normal (post-bronchodilator) and an exacerbation history despite regular bronchodilator therapy.

Presentation: **Symbicort 200/6 pMDI-** Pressurised inhalation suspension. Each metered dose contains 200mcg budesonide/actuation and 6mcg formoterol fumarate dihydrate/actuation. **Symbicort Turbohaler 200/6-** Inhalation powder. Each metered dose contains 200mcg budesonide/inhalation and 6mcg formoterol fumarate dihydrate/inhalation. **Symbicort Turbohaler 400/12-** Inhalation powder. Each metered dose contains 400mcg budesonide/inhalation and 12mcg formoterol fumarate dihydrate/inhalation.

Dosage and administration: **Symbicort Turbohaler 200/6-** Recommended dose is 2 inhalations twice daily in adults. **Symbicort Turbohaler 400/12-** Recommended dose is 1 inhalation twice daily in adults. **Symbicort 200/6 pMDI-** Recommended dose is 2 actuations twice daily in adults. Use of a spacer device (e.g. AeroChamber Plus Flow Vu and or AeroChamber Plus) with Symbicort 200/6 pMDI is usually recommended, especially in patients who have, or are likely to have, difficulties to coordinate actuation with inhalation. Refer to the SmPC for full details. **Children and adolescents under 18 years:** No relevant use. **Elderly:** No dose adjustment required. **Patients with hepatic or renal impairment:** Increased exposure is expected in patients with severe liver cirrhosis.

Contraindications: Hypersensitivity to active substance(s) or excipients.

Warnings and precautions: Patients should be advised to have their rescue inhaler available at all times. Patients should be reminded to take maintenance dose even if asymptomatic. Treatment should not be stopped abruptly without supervision by a physician. Sudden and progressive deterioration in control is potentially life threatening and requires urgent medical assessment. Consideration should be given for increased therapy with corticosteroids e.g. orally, or antibiotic treatment if infection present. Paradoxical bronchospasm may occur, with immediate increase in wheezing and shortness of breath after dosing. If experienced, Symbicort should be discontinued immediately and alternative therapy instituted. Paradoxical bronchospasm responds to a rapid-acting inhaled bronchodilator and should be treated straightaway. Systemic effects may occur, particularly at high doses prescribed for long periods e.g. Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, 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). Potential effects on bone density should be considered especially for patients on high doses for prolonged periods that have coexisting risk factors for osteoporosis. Care should be taken when transferring patients to Symbicort therapy from previous systemic steroid therapy if adrenal function is impaired. Patients transferring from oral steroids may remain at risk of impaired adrenal reserve for a considerable time, HPA

axis function should be monitored regularly. Prolonged treatment with high doses of inhaled corticosteroids may result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress such as severe infections or elective surgery. Rapid reduction in dose of steroids can induce acute adrenal crisis, symptoms may include anorexia, abdominal pain, weight loss, tiredness, headache, nausea, vomiting, decreased level of consciousness, seizures, hypotension and hypoglycaemia. Treatment with systemic steroids should not be stopped abruptly. Transfer from oral steroid therapy to Symbicort may result in the appearance of allergic or arthritic symptoms such as rhinitis, eczema, muscle and joint pain. Specific treatment should be initiated for these conditions. In rare cases, tiredness, headache, nausea and vomiting can occur due to insufficient glucocorticosteroid effect and temporary increase in the dose of oral glucocorticosteroids may be necessary. To minimise risk of oropharyngeal candida infection, patients should rinse mouth with water after inhaling doses. Concomitant treatment with itraconazole, ritonavir or other potent CYP3A4 inhibitors should be avoided. Observe caution in patients with thyrotoxicosis, phaeochromocytoma, diabetes mellitus, untreated hypokalaemia, hypertrophic obstructive cardiomyopathy, idiopathic subvalvular aortic stenosis, severe hypertension, aneurysm or other severe cardiovascular disorders such as ischaemic heart disease, tachyarrhythmias or severe heart failure. Observe caution when treating patients with prolongation of the QTc-interval. Re-evaluate need for Symbicort in patients with active or quiescent pulmonary tuberculosis, fungal and viral infections in the airways. Hypokalaemia may occur at high doses of beta$_2$-adrenoceptor agonists. Monitor serum potassium levels. As for all beta$_2$-adrenoceptor agonists, consider additional blood glucose monitoring in diabetic patients. Visual disturbances may be reported with systemic and topical corticosteroid use. If a patient presents with these symptoms, consideration to ophthalmologist referral should be given to evaluate possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy. An increase in the incidence of pneumonia, including pneumonia requiring hospitalisation, has been observed in patients with COPD receiving inhaled corticosteroids. Physicians should remain vigilant as clinical features of such infections overlap with symptoms of COPD exacerbations. Risk factors include current smoking, older age, low BMI and severe COPD. The excipient lactose contains small amounts of milk proteins, which may cause allergic reactions.

Drug interactions: Potent CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, clarithromycin, telithromycin, nefazodone and HIV protease inhibitors) are likely to increase plasma levels of budesonide and concomitant use should be avoided. If this is not possible the time interval between administration should be as long as possible. Not to be given together with beta-adrenergic blockers (including eye drops) as can weaken or inhibit the effect of formoterol, unless compelling reasons. Concomitant treatment with quinidine, disopyramide, procainamide, phenothiazines, antihistamines (terfenadine), and TCAs can prolong the QTc-interval and increase the risk of ventricular arrhythmias. L-Dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance towards beta$_2$-sympathomimetics. Concomitant treatment with MAOIs including agents with similar properties such as furazolidone and procarbazine, may precipitate hypertension reactions. Elevated risk of arrhythmias in patients receiving anaesthesia with halogenated hydrocarbons. Concomitant use of other beta-adrenergic drugs or anticholinergic drugs can potentially have an additive bronchodilating effect. Hypokalaemia may increase the disposition towards arrhythmias in patients taking digitalis glycosides.

Pregnancy and lactation: Use only when benefits outweigh potential risks during pregnancy and breastfeeding. Budesonide is excreted in breast milk; at therapeutic doses no effects on child are anticipated. Not known whether formoterol passes into human breast milk.

Undesirable events: Consult SmPC for full list of side effects. **Common:** Candida infections in the oropharynx, headache, tremor, palpitations, mild irritation in the throat, coughing, hoarseness and pneumonia. **Uncommon:** Sleep disorders and tachycardia. **Rare:** Immediate and delayed hypersensitivity reactions, e.g. exanthema, urticaria, pruritus, dermatitis, angioedema and anaphylactic reaction, hypokalaemia, cardiac arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia and extrasystoles, bronchospasm. **Very rare:** Cushing's syndrome, cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, hyperglycaemia, depression, cataract and glaucoma, angina pectoris, prolongation of QTc-interval and variations in blood pressure. Paradoxical bronchospasm may occur in very rare cases.

Legal category: POM

Marketing authorisation number: **Symbicort Turbohaler 200/6** PL 17901/0092, **Symbicort Turbohaler 400/12** PL 17901/0200, **Symbicort 200/6 pMDI** PL 17901/0293.

Basic NHS cost: **Symbicort Turbohaler 200/6** 1 pack x 120 doses, £28.00, **Symbicort Turbohaler 400/12** 1 pack x 60 doses, £28.00, **Symbicort 200/6 pMDI** 200/6 1 pack x 120 doses, £28.00.

Further information is available from the Marketing Authorisation Holder: AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, UK.

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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 on 0800 783 0033.