# Trimbow 87/5/9 Pressurised Metered Dose Inhaler (pMDI) Prescribing Information

Please refer to the full Summary of Product Characteristics (SPC) before prescribing.

**Presentation:** Each Trimbow 87/5/9 pMDI delivered dose contains 87micrograms (mcg) of beclometasone dipropionate (BDP), 5mcg of formoterol fumarate dihydrate (formoterol) and 9mcg of glycopyrronium. This is equivalent to a metered dose of 100mcg BDP, 6mcg formoterol and 10mcg glycopyrronium. **Indications:** Maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) not adequately treated by a combination of an inhaled corticosteroid (ICS) and a long-acting $beta_2$-agonist (for effects on symptoms control and prevention of exacerbations see section 5.1 of SPC). **Dosage and administration:** For inhalation in adult patients (≥18 years). 2 inhalations twice daily (bd). Can be used with the AeroChamber Plus® spacer device. BDP in Trimbow is characterised by an extrafine particle size distribution which results in a more potent effect than formulations of BDP with a non-extrafine particle size distribution (100mcg of BDP extrafine in Trimbow are equivalent to 250mcg of BDP in a non-extrafine formulation). **Contraindications:** Hypersensitivity to the active substances or to any of the excipients. **Warnings and precautions:** Not for acute use in treatment of acute episodes of bronchospasm or to treat COPD exacerbation. Discontinue immediately if hypersensitivity or paradoxical bronchospasm. Deterioration of disease: Trimbow should not be stopped abruptly. Cardiovascular effects: Use with caution in patients with cardiac arrhythmias, aortic stenosis, hypertrophic obstructive cardiomyopathy, severe heart disease, occlusive vascular diseases, arterial hypertension and aneurysm. Caution should also be used 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. Trimbow should not be administered for at least 12 hours before the start of anaesthesia as there is a risk of cardiac arrhythmias. Caution in patients with thyrotoxicosis, diabetes mellitus, phaeochromocytoma and untreated hypokalaemia. Increase in pneumonia and pneumonia hospitalisation in COPD patients receiving ICS observed. Clinical features of pneumonia may overlap with symptoms of COPD exacerbations. Systemic effects of ICS may occur, particularly at high doses for long periods, but are less likely than with oral steroids. These include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation, decrease in bone mineral density, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression and aggression. Use with caution in patients with pulmonary tuberculosis or fungal/viral airway infections. Potentially serious hypokalaemia may result from $beta_2$-agonist therapy. Formoterol may cause a rise in blood glucose levels. Glycopyrronium should be used with caution in patients with narrow-angle glaucoma, prostatic hyperplasia or urinary retention. Use in patients with severe hepatic or renal impairment should only be considered if benefit outweighs the risk. **Interactions:** Since glycopyrronium is eliminated via renal route, potential drug interactions could occur with medicinal products affecting renal excretion mechanisms e.g. with cimetidine (an inhibitor of OCT2 and MATE1 transporters in the kidney) co-administration, glycopyrronium showed a slight decrease in renal excretion (20%) and a limited increase in total systemic exposure (16%). Possibility of systemic effects with concomitant use of strong CYP3A inhibitors (e.g. ritonavir, cobicistat) cannot be excluded and therefore caution and appropriate monitoring is advised. *Related to formoterol*: Non-cardioselective beta-blockers (including eye drops) should be avoided. Concomitant administration of other beta-adrenergic drugs may have potentially additive effects. Concomitant treatment with quinidine, disopyramide, procainamide, antihistamines, monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants and phenothiazines 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. Hypertensive reactions may occur following co-administration with MAOIs including drugs with similar properties (e.g. furazolidone, procarbazine). Risk of arrhythmias in patients receiving concomitant anaesthesia with halogenated hydrocarbons. Concomitant treatment with xanthine derivatives, steroids or diuretics may potentiate a possible hypokalaemic effect of $beta_2$-agonists. Hypokalaemia may increase the likelihood of arrhythmias in patients receiving digitalis glycosides. *Related to glycopyrronium:* Co-administration with other anticholinergic-containing medicinal products *is* not recommended. *Excipients:* Presence of ethanol may cause potential interaction in sensitive patients taking metronidazole or disulfram. **Fertility, pregnancy and lactation:** Should only be used during pregnancy if the expected benefits outweigh the potential risks. Children born to mothers receiving substantial doses should be observed for adrenal suppression. Glucocorticoids and metabolites are excreted in human milk. It is unknown whether formoterol or glycopyrronium (including their metabolites) pass into human breast-milk but they have been detected in the milk of lactating animals. Anticholinergic agents like glycopyrronium could suppress lactation. A risk/benefit decision should be taken to discontinue therapy in the mother or discontinue breastfeeding. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from therapy. **Effects on driving and operating machinery:** None or negligible. **Side effects:** *Common*: pneumonia (in COPD patients), pharyngitis, oral candidiasis, urinary tract infection, nasopharyngitis, headache, dysphonia. *Uncommon:* influenza, oral fungal infection, oropharyngeal candidiasis, oesophageal candidiasis, sinusitis, rhinitis, gastroenteritis, vulvovaginal candidiasis, granulocytopenia, dermatitis allergic, hypokalaemia, hyperglycaemia, restlessness, tremor, dizziness, dysgeusia, hypoaesthesia, otosalpingitis, atrial fibrillation, electrocardiogram QT prolonged, tachycardia, tachyarrhythmia, palpitations, hyperaemia, flushing, cough, productive cough, throat irritation, epistaxis, diarrhoea, dry mouth, dysphagia, nausea, dyspepsia, burning sensation of the lips, dental caries, rash, urticaria, pruritus, hyperhidrosis, muscle spasms, myalgia, pain in extremity, musculoskeletal chest pain, dysuria, urinary retention, fatigue, asthenia, C-reactive protein increased, platelet count increased, free fatty acids increased, blood insulin increased, blood ketone body increased, blood cortisol decreased. *Rare*: Lower respiratory tract infection (fungal), hypersensitivity reactions, including erythema, lips, face, eyes and pharyngeal oedema, decreased appetite, insomnia, hypersomnia, angina pectoris (stable and unstable), ventricular extrasystoles, nodal rhythm, sinus bradycardia, blood extravasation, hypertension, paradoxical bronchospasm, oropharyngeal pain, angioedema, nephritis, blood pressure increased, blood pressure decreased. *Very rare*: thrombocytopenia, adrenal suppression, glaucoma, cataract, dyspnoea, growth retardation, peripheral oedema, bone density decreased. *Unknown frequency*: psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (Refer to SPC for full list of side effects). **Legal category:** POM **Packs and price:** £44.50 1x120 actuations. **Marketing authorisation No:** EU/1/17/1208/002 **UK Distributor:** Chiesi Limited, 333 Styal Road, Manchester, M22 5LG. **Date of preparation:** June 2017. AeroChamber Plus® is a registered trademark of Trudell Medical International.

**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 Chiesi Limited on 0800 0092329 (GB), 1800 817459 (IE).**

# Fostair 100/6 and 200/6 Prescribing Information

Please refer to the full Summary of Product Characteristics (SPC) before prescribing.

**Presentation**: Each Fostair pressurised metered dose inhaler (pMDI) 100/6 dose contains 100 micrograms (mcg) of beclometasone dipropionate (BDP) and 6mcg of formoterol fumarate dihydrate (formoterol). Each Fostair pMDI 200/6 dose contains 200mcg of BDP and 6mcg of formoterol. Each Fostair NEXThaler 100/6 dry powder inhaler (DPI) dose contains 100mcg of BDP anhydrous and 6mcg of formoterol. Each Fostair NEXThaler 200/6 DPI dose contains 200mcg of BDP anhydrous and 6mcg of formoterol. **Indications**: *Asthma*: Regular treatment of asthma where use of an inhaled corticosteroid/long-acting $beta_2$-agonist (ICS/LABA) combination is appropriate: patients not adequately controlled on ICS and 'as needed' (prn) short-acting beta2-agonist, or patients already adequately controlled on both ICS and LABA. ***COPD* (Fostair 100/6 only)**: Symptomatic treatment of patients with severe COPD ($FEV_1$ <50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators. **Dosage and administration**: For inhalation in adult patients (≥18 years). *Asthma*: **Maintenance And Reliever Therapy (Fostair pMDI 100/6 only)** taken as a regular maintenance treatment and prn in response to asthma symptoms: 1 inhalation twice daily (bd) plus 1 additional inhalation prn in response to symptoms. If symptoms persist after a few minutes, an additional inhalation is recommended. The maximum daily dose is 8 inhalations. Fostair pMDI 100/6 may also be used as maintenance therapy (with a separate short-acting bronchodilator prn). Fostair pMDI 200/6 and NEXThaler (100/6 and 200/6) should be used as maintenance therapy only. Maintenance therapy: Fostair pMDI and NEXThaler 100/6: 1-2 inhalations bd. Fostair pMDI and NEXThaler 200/6: 2 inhalations bd. The maximum daily dose is 4 inhalations. Patients should receive the lowest dose that effectively controls their symptoms. ***COPD* (Fostair 100/6 only)**: 2 inhalations bd. Fostair pMDI can be used with the AeroChamber Plus® spacer device. BDP in Fostair is characterised by an extrafine particle size distribution which results in a more potent effect than formulations of BDP with a non-extrafine particle size distribution (100mcg of BDP extrafine in Fostair are equivalent to 250mcg of BDP in a non-extrafine formulation). When switching patients from previous treatments, it should be considered that the recommended total daily dose of BDP for Fostair is lower than that for non-extrafine BDP containing products and should be adjusted to the needs of the individual patient. However, patients who are transferred between Fostair NEXThaler and Fostair pMDI do not need dose adjustment. **Contraindications**: Hypersensitivity to the active substances or to any of the excipients. **Warnings and precautions**: Use with caution in patients with cardiac arrhythmias, aortic stenosis, hypertrophic obstructive cardiomyopathy, ischemic heart disease, severe heart failure, congestive heart failure, occlusive vascular diseases, arterial hypertension, severe arterial hypertension, aneurysm, thyrotoxicosis, diabetes mellitus, phaeochromocytoma and untreated hypokalaemia. Caution should also be used when treating patients with known or suspected prolongation of the QTc interval (QTc > 0.44 seconds). Formoterol itself may induce QTc prolongation. Potentially serious hypokalaemia may result from $beta_2$-agonist therapy and may also be potentiated by concomitant treatments (e.g. xanthine derivatives, steroids and diuretics) and increase the risk of arrhythmias. Formoterol may cause a rise in blood glucose levels. Fostair should not be administered for at least 12 hours before the start of anaesthesia, if halogenated anaesthetics are planned as risk of arrhythmias. Use with caution in patients with pulmonary tuberculosis or fungal/viral airway infections. Increase in pneumonia and pneumonia hospitalisation in COPD patients receiving ICS. Clinical features of pneumonia may overlap with symptoms of COPD exacerbations. Fostair treatment should not be stopped abruptly. Treatment should not be initiated during exacerbations or acutely deteriorating asthma. Fostair treatment should be discontinued immediately if the patient experiences a paradoxical bronchospasm. Fostair not intended for initial management of asthma. Systemic effects of ICS may occur, particularly at high doses for long periods, but are less likely than with oral steroids. These include Cushing's syndrome, Cushingoid features, adrenal suppression, 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 and aggression. Prolonged treatment with high doses of ICS may result in adrenal suppression and acute adrenal crisis. Lactose contains small amounts of milk proteins, which may cause allergic reactions. **Interactions**: Possibility of systemic effects with concomitant use of strong CYP3A inhibitors (e.g. ritonavir, cobicistat) cannot be excluded and therefore caution and appropriate monitoring is advised. Beta-blockers should be avoided in asthma patients. Concomitant administration of other beta-adrenergic drugs may have potentially additive effects. Concomitant treatment with quinidine, disopyramide, procainamide, phenothiazines, antihistamines, monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants 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. Hypertensive reactions may occur following co-administration with MAOIs including agents with similar properties (e.g. furazolidone, procarbazine). Concomitant treatment with xanthine derivatives, steroids or diuretics may potentiate a possible hypokalaemic effect of $beta_2$-agonists. Hypokalaemia may increase the likelihood of arrhythmias in patients receiving digitalis glycosides. Presence of ethanol may cause potential interaction in sensitive patients taking metronidazole or disulfram. **Fertility, pregnancy and lactation**: Fostair should only be used during pregnancy or lactation if the expected benefits outweigh the potential risks. **Effects on driving and operating machinery**: Fostair is unlikely to have any effect on the ability to drive and use machines. **Side effects**: *Common*: pneumonia (in COPD patients), pharyngitis, oral candidiasis, headache, dysphonia, tremor. *Uncommon*: influenza, oral fungal infection, oropharyngeal candidiasis, nasopharyngitis, oesophageal candidiasis, vulvovaginal candidiasis, gastroenteritis, sinusitis, rhinitis, granulocytopenia, allergic dermatitis, hypokalaemia, hyperglycaemia, hypertriglyceridaemia, restlessness, dizziness, otosalpingitis, palpitations, prolongation of QTc interval, ECG change, tachycardia, tachyarrhythmia, atrial fibrillation, sinus bradycardia, angina pectoris, myocardial ischaemia, blood pressure increased, hyperaemia, flushing, cough, productive cough, throat irritation, asthmatic crisis, exacerbation of asthma, dyspnoea, pharyngeal erythema, diarrhoea, dry mouth, dyspepsia, dysphagia, burning sensation of the lips, nausea, dysgeusia, pruritus, rash, hyperhidrosis, urticaria, muscle spasms, myalgia, C-reactive protein increased, platelet count increased, free fatty acids increased, blood insulin increased, blood ketone body increased, blood cortisol decrease, oropharyngeal pain, fatigue, irritability, cortisol free urine decreased, blood potassium increased, blood glucose increased, ECG poor r-wave progression. *Rare*: ventricular extrasystoles, paradoxical bronchospasm, angioedema, nephritis, blood pressure decreased. *Very rare*: thrombocytopenia, hypersensitivity reactions, including erythema, lips, face, eyes and pharyngeal oedema, adrenal suppression, glaucoma, cataract, peripheral oedema, bone density decreased. *Unknown frequency*: psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (Refer to SPC for full list of side effects). **Legal category**: POM **Packs and price**: £29.32 1x120 actuations **Marketing authorisation (MA) Nos**: PL 08829/0156, PL 08829/0175, PL 08829/0173, PL 08829/0174 **MA holder**: Chiesi Ltd, 333 Styal Road, Manchester, M22 5LG. **Date of preparation**: Mar 2017. Aerochamber Plus® is a registered trademark of Trudell Medical International.

**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 Chiesi Limited on 0800 0092329 (GB), 1800 817459 (IE).**