Prescribing Information (UK) SPIRIVA® RESPIMAT® (tiotropium)

Inhalation solution containing 2.5 microgram tiotropium (as bromide monohydrate) per puff. **Indication:** COPD: Tiotropium is indicated as a maintenance bronchodilator treatment to relieve symptoms of patients with chronic obstructive pulmonary disease (COPD). Asthma: Spiriva Respimat is indicated as add-on maintenance bronchodilator treatment in patients aged 6 years and older with severe asthma who experienced one or more severe asthma exacerbations in the preceding year. **Dose and Administration:** COPD Adults only age 18 years or over: 5 microgram tiotropium given as two puffs from the Respimat inhaler once daily, at the same time of the day. Asthma Adults and patients 6 to 17 years of age: 5 microgram tiotropium given as two puffs from the Respimat inhaler once daily, at the same time of the day. In adult patients with severe asthma, tiotropium should be used in addition to inhaled corticosteroids (≥ 800 µg budesonide/day or equivalent) and at least one controller. In adolescents (12 - 17 years) with severe asthma, tiotropium should be used in addition to inhaled corticosteroids (> 800 - 1600 µg budesonide/day or equivalent) and one controller or in addition to inhaled corticosteroids (400 - 800 µg budesonide/day or equivalent) with two controllers. For children (6 - 11 years) with severe asthma, tiotropium should be used in addition to inhaled corticosteroids (> 400 µg budesonide/day or equivalent) and one controller or in addition to inhaled corticosteroids (200 - 400 µg budesonide/day or equivalent) with two controllers. **Contraindications:** Hypersensitivity to tiotropium bromide, atropine or its derivatives, e.g. ipratropium or oxitropium or to any of the excipients; benzalkonium chloride, disodium edetate, purified water, hydrochloric acid 3.6 % (for pH adjustment). **Warnings and Precautions:** Benzalkonium chloride may cause wheezing and breathing difficulties; patients with asthma are at an increased risk for these adverse events. Not for the initial treatment of acute episodes of bronchospasm or for the relief of acute symptoms. Spiriva Respimat should not be used as monotherapy for asthma. Asthma patients must be advised to continue taking anti-inflammatory therapy, i.e. inhaled corticosteroids, unchanged after the introduction of Spiriva Respimat, even when their symptoms improve. Immediate hypersensitivity reactions may occur after administration of tiotropium bromide inhalation solution. Caution in patients with narrow-angle glaucoma, prostatic hyperplasia or bladder-neck obstruction. Inhaled medicines may cause inhalation-induced bronchospasm. Tiotropium should be used with caution in patients with recent myocardial infarction < 6 months; any unstable or life threatening cardiac arrhythmia or cardiac arrhythmia requiring intervention or a change in drug therapy in the past year; hospitalisation of heart failure (NYHA Class III or IV) within the past year. These patients were excluded from the clinical trials and these conditions may be affected by the anticholinergic mechanism of action. In patients with moderate to severe renal impairment (creatinine clearance ≤ 50 ml/min) tiotropium bromide should be used only if the expected benefit outweighs the potential risk. Patients should be cautioned to avoid getting the spray into their eyes. They should be advised that this may result in precipitation or worsening of narrow-angle glaucoma, eye pain or discomfort, temporary blurring of vision, visual halos or coloured images in association with red eyes from conjunctival congestion and corneal oedema. Should any combination of these eye symptoms develop, patients should stop using tiotropium bromide and consult a specialist immediately. Tiotropium bromide should not be used more frequently than once a day. **Interactions:** Although no formal drug interaction studies have been performed, tiotropium bromide has been used concomitantly with other drugs commonly used in the treatment of COPD and asthma, including sympathomimetic bronchodilators, methylxanthines, oral and inhaled steroids, antihistamines, mucolytics, leukotriene modifiers, cromones, anti-IgE treatment without clinical evidence of drug interactions. Use of LABA or ICS was not found to alter the exposure to tiotropium. The co-administration of tiotropium bromide with other anticholinergic-containing drugs has not been studied and is therefore not recommended. **Fertility, Pregnancy and Lactation:** Very limited amount of data in pregnant women. Avoid the use of Spiriva Respimat during pregnancy. It is unknown whether tiotropium bromide is excreted in human breast milk. Use of Spiriva Respimat during breast feeding is not recommended. A decision on whether to continue/discontinue breast feeding or therapy with Spiriva Respimat should be made taking into account the benefit of breast feeding to the child and the benefit of Spiriva Respimat therapy to the woman. Clinical data on fertility are not available for tiotropium. **Effects on ability to drive and use machines:** No studies have been performed. The occurrence of dizziness or blurred vision may influence the ability to drive and use machinery. **Undesirable effects:** COPD: Common (≥ 1/100 to < 1/10) Dry mouth. Uncommon (≥ 1/1,000 to < 1/100) Dizziness, headache, cough, pharyngitis, dysphonia, constipation, oropharyngeal candidiasis, rash, pruritus, urinary retention, dysuria. Rare (≥1/10,000 to <1/1,000): Insomnia, glaucoma, intraocular pressure increased, vision blurred, atrial fibrillation, palpitations, supraventricular tachycardia, tachycardia, epistaxis, bronchospasm, laryngitis, dysphagia, gastrooesophageal reflux disease, dental caries, gingivitis, glossitis, angioneurotic oedema, urticaria, skin infection/ skin ulcer, dry skin, urinary tract infection. Not known (cannot be estimated from the available data): Dehydration, sinusitis, stomatitis, intestinal obstruction including ileus paralytic, nausea, hypersensitivity (including immediate reactions), anaphylactic reaction, joint swelling. Asthma: Uncommon (≥ 1/1,000 to < 1/100) Dizziness, headache, insomnia, palpitations, cough, pharyngitis, dysphonia, bronchospasm, dry mouth, oropharyngeal candidiasis, rash. Rare (≥1/10,000 to <1/1,000): Epistaxis, constipation, gingivitis, stomatitis, pruritus, angioneurotic oedema, urticaria, hypersensitivity (including immediate reactions), urinary tract infection. Not known (cannot be estimated from the available data): Dehydration, glaucoma, intraocular pressure increased, vision blurred, atrial fibrillation, supraventricular tachycardia, tachycardia, laryngitis, sinusitis, dysphagia, gastrooesophageal reflux disease, dental caries, glossitis, intestinal obstruction including ileus paralytic, nausea, skin infection/skin ulcer, dry skin, anaphylactic reaction, joint swelling, urinary retention, dysuria. Serious undesirable effects consistent with anticholinergic effects: glaucoma, constipation, intestinal obstruction including ileus paralytic and urinary retention. An increase in anticholinergic effects may occur with increasing age. Prescribers should consult the Summary of Product Characteristics for further information on undesirable effects. **Pack sizes and NHS price:** Single pack: 1 Respimat re-usable inhaler and 1 cartridge providing 60 puffs (30 medicinal doses) £23.00; Single refill pack: 1 cartridge providing 60 puffs (30 medicinal doses) £23.00. **Legal category:** POM. **MA number:** PL 14598/0084. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** September 2019

Prescribing Information (UK) SPIOLTO® RESPIMAT® (tiotropium and olodaterol)

Inhalation solution containing 2.5 microgram tiotropium (as bromide monohydrate) and 2.5 microgram olodaterol (as hydrochloride) per puff. **Action**: Inhalation solution containing a long acting muscarinic receptor antagonist, tiotropium, and a long acting beta$_2$-adrenergic agonist, olodaterol. **Indication:** Maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). **Dose and Administration:** Adults only aged 18 years or over: 5 microgram tiotropium and 5 microgram of olodaterol given as two puffs from the Respimat inhaler once daily, at the same time of the day.**Contraindications:** Hypersensitivity to tiotropium or olodaterol or any of the excipients; benzalkonium chloride, disodium edetate, purified water, 1M hydrochloric acid (for pH adjustment); atropine or its derivatives e.g. ipratropium or oxitropium. **Warnings and Precautions:** Not for use in asthma or for the treatment of acute episodes of bronchospasm, i.e. as rescue therapy. Inhaled medicines may cause inhalation-induced paradoxical bronchospasm. Caution in patients with narrow-angle glaucoma, prostatic hyperplasia or bladder-neck obstruction. Patients should be cautioned to avoid getting the spray into their eyes. They should be advised that this may result in precipitation or worsening of narrow-angle glaucoma, eye pain or discomfort, temporary blurring of vision, visual halos or coloured images in association with red eyes from conjunctival congestion and corneal oedema. Should any combination of these eye symptoms develop, patients should stop using Spiolto Respimat and consult a specialist immediately. In patients with moderate to severe renal impairment (creatinine clearance ≤ 50ml/min) use only if the expected benefit outweighs the potential risk. Caution in patients with a history of myocardial infarction during the previous year, unstable or life-threatening cardiac arrhythmia, hospitalised for heart failure during the previous year or with a diagnosis of paroxysmal tachycardia (> 100 beats per minute) as these patients were excluded from the clinical trials. In some patients, like other beta-adrenergic agonists, olodaterol may produce a clinically significant cardiovascular effect as measured by increases in pulse rate, blood pressure and/or symptoms. Caution in patients with: cardiovascular disorders, especially ischaemic heart disease, severe cardiac decompensation, cardiac arrhythmias, hypertrophic obstructive cardiomyopathy, hypertension, and aneurysm; convulsive disorders or thyrotoxicosis; known or suspected prolongation of the QT interval (e.g. QT>0.44 s); patients unusually responsive to sympathomimetic amines; in some patients beta$_2$-agonists may produce significant hypokalaemia; increases in plasma glucose after inhalation of high doses. Caution in planned operations with halogenated hydrocarbon anaesthetics due to increased susceptibility of adverse cardiac effects. Should not be used in conjunction with any other long-acting beta$_2$-adrenergic agonists. Immediate hypersensitivity reactions may occur after administration. Should not be used more frequently than once daily. Benzalkonium chloride may cause wheezing and breathing difficulties; patients with asthma are at an increased risk for these adverse events. **Interactions:** Although no formal *in vivo* drug interaction studies have been performed, inhaled Spiolto Respimat has been used concomitantly with other COPD medicinal products, including short acting sympathomimetic bronchodilators and inhaled corticosteroids without clinical evidence of drug interactions. The co-administration of the component tiotropium with other anticholinergic containing drugs has not been studied and therefore is not recommended. Concomitant administration of other adrenergic agents (alone or as part of combination therapy) may potentiate the undesirable effects of Spiolto Respimat. Concomitant treatment with xanthine derivatives, steroids, or non-potassium sparing diuretics may potentiate any hypokalaemic effect of adrenergic agonists. Beta-adrenergic blockers may weaken or antagonise the effect of olodaterol. Cardioselective beta-blockers could be considered, although they should be administered with caution. MAO inhibitors, tricyclic antidepressants or other drugs known to prolong the QTc interval may potentiate the action of Spiolto Respimat on the cardiovascular system. **Fertility, pregnancy and lactation:** There is a very limited amount of data from the use of tiotropium in pregnant women. For olodaterol no clinical data on exposed pregnancies are available. As a precautionary measure, avoid the use of Spiolto Respimat during pregnancy. Like other beta$_2$-adrenergic agonists, olodaterol may inhibit labour due to a relaxant effect on uterine smooth muscle. It is not known whether tiotropium and/or olodaterol pass into human breast milk. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Spiolto Respimat should be made taking into account the benefit of breast-feeding to the child and the benefit of therapy for the woman. Clinical data on fertility are not available for tiotropium or olodaterol or the combination of both components. **Effects on ability to drive and use machines:** No studies have been performed. The occurrence of dizziness or blurred vision may influence the ability to drive and use machinery. **Undesirable effects:** Uncommon (≥ 1/1,000 to <1/100): Dizziness, headache, tachycardia, cough, dysphonia, dry mouth. Rare (≥ 1/10,000 to <1/1,000): Insomnia, vision blurred, atrial fibrillation, palpitations, supraventricular tachycardia, hypertension, laryngitis, pharyngitis, epistaxis, bronchospasm, constipation, oropharyngeal candidiasis, gingivitis, nausea, stomatitis, hypersensitivity, angioedema, urticaria, pruritus, rash, arthralgia, back pain, joint swelling, urinary retention, urinary tract infection, dysuria. Not known (cannot be estimated from the available data): Nasopharyngitis, dehydration, glaucoma, intraocular pressure increased, sinusitis, intestinal obstruction ileus paralytic, dysphagia, gastrooesophageal reflux disease, glossitis, dental caries, anaphylactic reaction, skin infection and skin ulcer, dry skin. Serious undesirable effects consistent with anticholinergic effects: glaucoma, constipation, intestinal obstruction including ileus paralytic and urinary retention. An increase in anticholinergic effects may occur with increasing age. The occurrence of undesirable effects related to beta-adrenergic agonist class should be taken into consideration such as, arrhythmia, myocardial ischaemia, angina pectoris, hypotension, tremor, nervousness, muscle spasms, fatigue, malaise, hypokalaemia, hyperglycaemia and metabolic acidosis. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** Single pack: 1 Respimat re-usable inhaler and 1 cartridge providing 60 puffs (30 medicinal doses) £32.50; Single refill pack: 1 cartridge providing 60 puffs (30 medicinal doses) £32.50 **Legal category:** POM **MA numbers:** PL 14598/0101 **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** September 2020

Prescribing Information (UK) ▼ STRIVERDI® RESPIMAT® (olodaterol)

Inhalation solution containing 2.5 microgram olodaterol (as hydrochloride) per actuation. **Indication:** Maintenance bronchodilator treatment in patients with chronic obstructive pulmonary disease (COPD). **Dose and Administration:** Adults only age 18 years or over: 5 microgram olodaterol given as two actuations (puffs) from the Respimat inhaler once daily, at the same time of the day. **Contraindications:** Hypersensitivity to olodaterol or to any of the excipients; benzalkonium chloride, disodium edetate, purified water or citric acid (anhydrous). **Warnings and Precautions:** Not for use in asthma or the treatment of acute episodes of bronchospasm, i.e. as rescue therapy. Immediate hypersensitivity reactions may occur after administration. Inhaled medicines may cause inhalation-induced paradoxical bronchospasm. Caution in patients with: cardiovascular disorders, especially ischaemic heart disease, severe cardiac decompensation, cardiac arrhythmias, hypertrophic obstructive cardiomyopathy, hypertension and aneurysm; convulsive disorders or thyrotoxicosis; known or suspected prolongation of the QT interval (e.g. QT>0.44 s); patients unusually responsive to sympathomimetic amines. Experience in the following patient groups is limited therefore use with caution in patients: with a history of myocardial infarction during the previous year or unstable or life-threatening cardiac arrhythmia; hospitalised for heart failure during the previous year or with a diagnosis of paroxysmal tachycardia (>100 beats per minute). In some patients, like other beta-adrenergic agonists, olodaterol may produce: clinically significant cardiovascular effects; significant hypokalaemia; increases in plasma glucose after inhalation of high doses. Caution in planned operations with halogenated hydrocarbon anaesthetics due to increased susceptibility of adverse cardiac effects. Benzalkonium chloride may cause wheezing and breathing difficulties; patients with asthma are at an increased risk for these adverse events. Should not be used in conjunction with any other long-acting beta$_2$-adrenergic agonists. **Interactions:** Concomitant administration with other adrenergic agents (alone or in combination therapy) may potentiate the undesirable effects of Striverdi Respimat. Concomitant treatment with xanthine derivatives, steroids, or non-potassium sparing diuretics may potentiate any hypokalemic effect of adrenergic agonists. Beta-adrenergic blockers may weaken or antagonise the effect of Striverdi Respimat which should only be given together if there are compelling reasons for their use. MAO inhibitors, tricyclic antidepressants, or QTc prolonging drugs may potentiate the action of Striverdi Respimat on the cardiovascular system. **Fertility, Pregnancy and Lactation:** No data on the use of Striverdi Respimat in pregnant women are available. As a precautionary measure, it is preferable to avoid use during pregnancy. Like other beta$_2$-adrenergic agonists, olodaterol may inhibit labour due to a relaxant effect on uterine smooth muscle. It is unknown whether olodaterol/metabolites are excreted in human milk. A decision on whether or not to discontinue/abstain from Striverdi Respimat should be made taking into account the benefit of breast feeding to the child or benefit of therapy for the woman. Clinical data on fertility are not available for Striverdi Respimat. **Effects on ability to drive and use machines:** No studies have been performed. The occurrence of dizziness may affect the ability to drive or operate machinery. **Undesirable effects:** Uncommon (≥1/1,000 to <1/100) Nasopharyngitis, dizziness, rash. Rare (≥1/10,000 to <1/1,000) Hypertension, arthralgia. Occurrence of undesirable effects related to the beta-adrenergic agonist class should be taken into account such as tachycardia, arrhythmia, palpitations, myocardial ischaemia, angina pectoris, hypertension or hypotension, hypokalemia, hyperglycemia, tremor, headache, nervousness, insomnia, dizziness, dry mouth, nausea, muscle spasms, fatigue, malaise, and metabolic acidosis. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** Single pack: 1 Respimat re-usable inhaler and 1 cartridge providing 60 actuations (puffs) (30 medicinal doses) £26.35; Single refill pack: 1 cartridge providing 60 actuations (puffs) (30 medicinal doses) £26.35 **Legal category:** POM **MA numbers:** PL 14598/0093 **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** September 2019

Prescribing Information (UK) SPIRIVA® (tiotropium)

Inhalation powder, hard capsules containing 18 microgram tiotropium (as bromide monohydrate). **Indication:** Tiotropium is indicated as a maintenance bronchodilator treatment to relieve symptoms of patients with chronic obstructive pulmonary disease (COPD). **Dose and Administration:** Adults only age 18 years or over: Inhalation of the contents of one capsule once daily from the HandiHaler® device. **Contraindications:** Hypersensitivity to tiotropium bromide or to the excipient lactose monohydrate (which may contain small amounts of milk proteins) or to atropine or its derivatives. **Warnings and Precautions:** Not for the initial treatment of acute episodes of bronchospasm, i.e. rescue therapy. Immediate hypersensitivity reactions may occur after administration of tiotropium bromide inhalation powder. Caution in patients with narrow-angle glaucoma, prostatic hyperplasia or bladder-neck obstruction. Inhaled medicines may cause inhalation-induced bronchospasm. Tiotropium should be used with caution in patients with recent myocardial infarction < 6 months; any unstable or life threatening cardiac arrhythmia or cardiac arrhythmia requiring intervention or a change in drug therapy in the past year; hospitalisation of heart failure (NYHA Class III or IV) within the past year. These patients were excluded from the clinical trials and these conditions may be affected by the anticholinergic mechanism of action. In patients with moderate to severe renal impairment (creatinine clearance ≤ 50 ml/min) tiotropium bromide should be used only if the expected benefit outweighs the potential risk. Patients should be cautioned to avoid getting the drug powder into their eyes. They should be advised that this may result in precipitation or worsening of narrow-angle glaucoma, eye pain or discomfort, temporary blurring of vision, visual halos or coloured images in association with red eyes from conjunctival congestion and corneal oedema. Should any combination of these eye symptoms develop, patients should stop using tiotropium bromide and consult a specialist immediately. Tiotropium bromide should not be used more frequently than once a day. Spiriva capsules contain 5.5mg lactose monohydrate. This amount does not normally cause problems in lactose intolerant patients. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. The excipient lactose monohydrate may contain small amounts of milk proteins which may cause allergic reactions. **Interactions:** Although no formal drug interaction studies have been performed, tiotropium bromide inhalation powder has been used concomitantly with other drugs without clinical evidence of drug interactions. These include sympathomimetic bronchodilators, methylxanthines, oral and inhaled steroids, commonly used in the treatment of COPD. Use of LABA or ICS was not found to alter the exposure to tiotropium. The co-administration of tiotropium bromide with other anticholinergic-containing drugs has not been studied and is therefore not recommended. **Fertility, Pregnancy and Lactation:** There is a very limited amount of data from the use of tiotropium in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity at clinically relevant doses. As a precaution, avoid the use of Spiriva during pregnancy. It is unknown whether tiotropium bromide is excreted in human breast milk. Use of Spiriva is not recommended during breast feeding. A decision on whether to continue or discontinue breast feeding or therapy with Spiriva should be made taking into account the benefit of breast feeding to the child and the benefit of Spiriva therapy to the woman. Clinical data on fertility are not available for tiotropium. **Effects on ability to drive and use machines:** No studies have been performed. The occurrence of dizziness, blurred vision, or headache may influence the ability to drive and use machinery. **Undesirable effects:** Common (≥ 1/100 to <1/10): Dry mouth. Uncommon (≥ 1/1000 to <1/100): Dizziness, headache, taste disorders, vision blurred, atrial fibrillation, pharyngitis, dysphonia, cough, gastrooesophageal reflux disease, constipation, oropharyngeal candidiasis, rash, dysuria, urinary retention. Rare (≥1/10,000 to <1/1,000): Insomnia, glaucoma, intraocular pressure increased, supraventricular tachycardia, tachycardia, palpitations, bronchospasm, epistaxis, laryngitis, sinusitis, intestinal obstruction including ileus paralytic, gingivitis, glossitis, dysphagia, stomatitis, nausea, urticaria, pruritus, hypersensitivity (including immediate reactions), angioedema, urinary tract infection. Not known (frequency cannot be estimated from the available data): Dehydration, dental caries, anaphylactic reaction, skin infection, skin ulcer, dry skin, joint swelling. Serious undesirable effects consistent with anticholinergic effects: glaucoma, constipation and intestinal obstruction including ileus paralytic as well as urinary retention. An increase in anticholinergic effects may occur with increasing age. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** Combopack HandiHaler device and 30 capsules (3 blisters) £34.87 Refill Pack 30 capsules (3 blisters) £33.50; 60 capsules (6 blisters) £67.00. **Legal category:** POM. **MA Number:** PL 14598/0062. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** March 2018

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 Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone).

SPIRIVA® RESPIMAT® (tiotropium)

SPIOLTO® RESPIMAT® TIOTROPIUM & OLODATEROL

STRIVERDI® RESPIMAT® Olodaterol

SPIRIVA® (tiotropium)

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