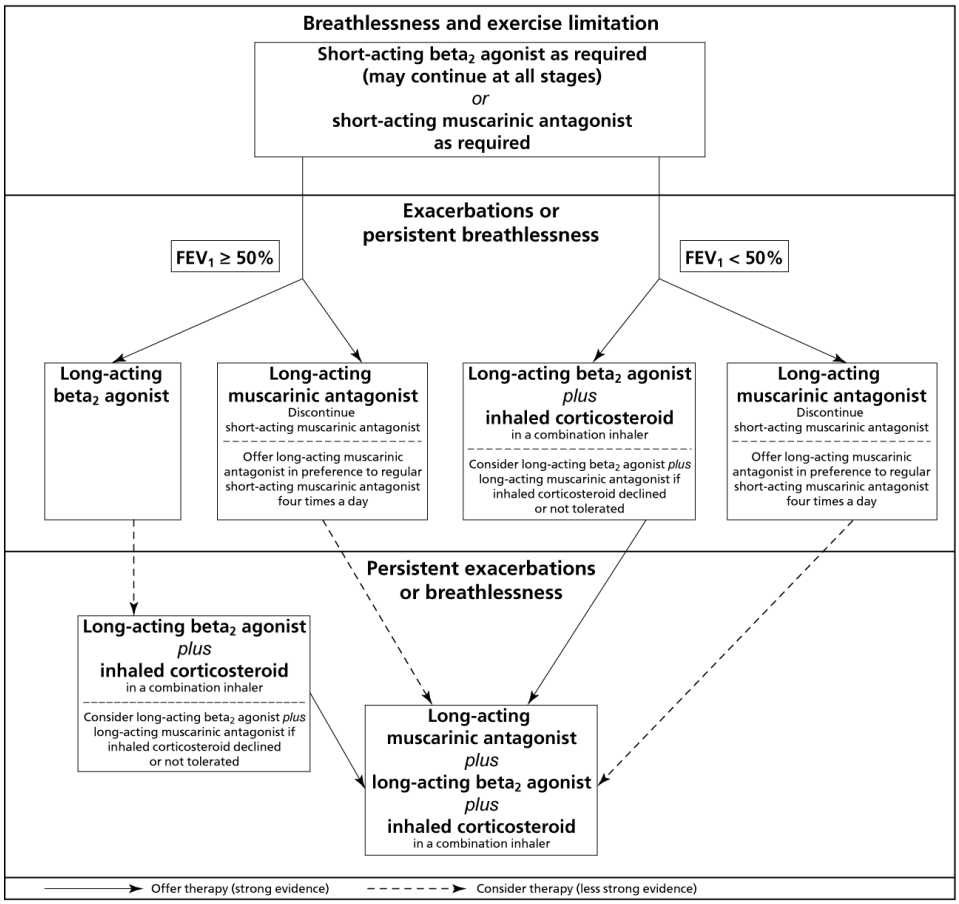
Use of inhaled therapies in chronic obstructive pulmonary disease



Advice on the use of inhaled therapies in chronic obstructive pulmonary disease is based on the recommendations of the National Institute for Health and Care Excellence (2010). Management of chronic obstructive pulmonary disease in adults in primary and secondary care. London: NICE.
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Oxygen

Overview

Oxygen should be regarded as a drug. It is prescribed for hypoxaemic patients to increase alveolar oxygen tension and decrease the work of breathing. The concentration of oxygen required depends on the condition being treated; the administration of an inappropriate concentration of oxygen can have serious or even fatal consequences.

Oxygen is probably the most common drug used in medical emergencies. It should be prescribed initially to achieve a normal or near–normal oxygen saturation; in most acutely ill patients with a normal or low arterial carbon dioxide (P_aCO_2), oxygen saturation should be 94–98% oxygen saturation. However, in some clinical situations such as cardiac arrest and carbon monoxide poisoning it is more appropriate to aim for the highest possible oxygen saturation until the patient is stable. A lower target of 88–92% oxygen saturation is indicated for patients at risk of hypercapnic respiratory failure.

High concentration oxygen therapy is safe in uncomplicated cases of conditions such as pneumonia, pulmonary thromboembolism, pulmonary fibrosis, shock, severe trauma, sepsis, or anaphylaxis. In such conditions low arterial oxygen (P_aO_2) is usually associated with low or normal arterial carbon dioxide (P_aCO_2), and therefore there is little risk of hypoventilation and carbon dioxide retention.

In acute severe asthma, the arterial carbon dioxide (P_aCO_2) is usually subnormal but as asthma deteriorates it may rise steeply (particularly in children). These patients usually require high concentrations of oxygen and if the arterial carbon dioxide (P_aCO_2) remains high despite other treatment, intermittent positive-pressure ventilation needs to be considered urgently.

Low concentration oxygen therapy (controlled oxygen therapy) is reserved for patients at risk of hypercapnic respiratory failure, which is more likely in those with:

- chronic obstructive pulmonary disease;
- advanced cystic fibrosis;
- severe non-cystic fibrosis bronchiectasis;
- severe kyphoscoliosis or severe ankylosing spondylitis;
- severe lung scarring caused by tuberculosis;
- musculoskeletal disorders with respiratory weakness, especially if on home ventilation;

- an overdose of opioids, benzodiazepines, or other drugs causing respiratory depression.

Until blood gases can be measured, initial oxygen should be given using a controlled concentration of 28% or less, titrated towards a target oxygen saturation of 88–92%. The aim is to provide the patient with enough oxygen to achieve an acceptable arterial oxygen tension without worsening carbon dioxide retention and respiratory acidosis. Patients may carry an *oxygen alert card*.

Domiciliary oxygen

Oxygen should only be prescribed for use in the home after careful evaluation in hospital by respiratory experts. Patients should be advised of the risks of continuing to smoke when receiving oxygen therapy, including the risk of fire. Smoking cessation therapy should be recommended before home oxygen prescription.

Air travel

Some patients with arterial hypoxaemia require supplementary oxygen for air travel. The patient's requirement should be discussed with the airline before travel.

Long-term oxygen therapy

Long-term administration of oxygen (usually at least 15 hours daily) prolongs survival in some patients with chronic obstructive pulmonary disease.

Assessment for long-term oxygen therapy requires measurement of arterial blood gas tensions. Measurements should be taken on 2 occasions at least 3 weeks apart to demonstrate clinical stability, and not sooner than 4 weeks after an acute exacerbation of the disease. Long-term oxygen therapy should be considered for patients with:

- chronic obstructive pulmonary disease with P_aO_2 <7.3 kPa when breathing air during a period of clinical stability;
- chronic obstructive pulmonary disease with P_aO_2 7.3–8 kPa in the presence of secondary polycythaemia, nocturnal hypoxaemia, peripheral oedema, or evidence of pulmonary hypertension;
- severe chronic asthma with P_aO_2<7.3 kPa or persistent disabling breathlessness;
- interstitial lung disease with P_aO_2<8 kPa and in patients with P_aO_2>8 kPa with disabling dyspnoea;
- cystic fibrosis when P_aO_2<7.3 kPa or if P_aO_2 7.3–8 kPa in the presence of secondary polycythaemia, nocturnal hypoxaemia, pulmonary hypertension, or peripheral oedema;
- pulmonary hypertension, without parenchymal lung involvement when P_aO_2<8 kPa;
- neuromuscular or skeletal disorders, after specialist assessment;
- obstructive sleep apnoea despite continuous positive airways pressure therapy, after specialist assessment;
- pulmonary malignancy or other terminal disease with disabling dyspnoea;
- heart failure with daytime P_aO_2<7.3 kPa when breathing air or with nocturnal hypoxaemia;
- paediatric respiratory disease, after specialist assessment.

Increased respiratory depression is seldom a problem in patients with stable respiratory failure treated with low concentrations of oxygen although it may occur during exacerbations; patients and relatives should be warned to call for medical help if drowsiness or confusion occur.

Short-burst oxygen therapy

Oxygen is occasionally prescribed for short-burst (intermittent) use for episodes of breathlessness not relieved by other treatment in patients with severe chronic obstructive pulmonary disease, interstitial lung disease, heart failure, and in palliative care. It is important, however, that the patient does not rely on oxygen instead of obtaining medical help or taking more specific treatment. Short-burst oxygen therapy can be used to improve exercise capacity and recovery; it should only be continued if there is proven improvement in breathlessness or exercise tolerance.

Ambulatory oxygen therapy

Ambulatory oxygen is prescribed for patients on long-term oxygen therapy who need to be away from home on a regular basis. Patients who are not on long-term oxygen therapy can be considered for ambulatory oxygen therapy if there is evidence of exercise-induced oxygen desaturation and of improvement in blood oxygen saturation and exercise capacity with oxygen. Ambulatory oxygen therapy is not recommended for patients with heart failure or those who smoke.

Oxygen therapy equipment

Under the NHS oxygen may be supplied as **oxygen cylinders**. Oxygen flow can be adjusted as the cylinders are equipped with an oxygen flow meter with 'medium' (2 litres/minute) and 'high' (4 litres/minute) settings. Oxygen delivered from a cylinder should be passed through a humidifier if used for long periods.

Oxygen concentrators are more economical for patients who require oxygen for long periods, and in England and Wales can be ordered on the NHS on a regional tendering basis. A concentrator is recommended for a patient who requires oxygen for more than 8 hours a day (or 21 cylinders per month). Exceptionally, if a higher concentration of oxygen is required the output of 2 oxygen concentrators can be combined using a 'Y' connection.

A nasal cannula is usually preferred for long-term oxygen therapy from an oxygen concentrator. It can, however, produce dermatitis and mucosal drying in sensitive individuals.

Giving oxygen by nasal cannula allows the patient to talk, eat, and drink, but the concentration of oxygen is not controlled; this may not be appropriate for acute respiratory failure. When oxygen is given through a nasal cannula at a rate of 1–2 litres/minute the inspiratory oxygen concentration is usually low, but it varies with ventilation and can be high if the patient is underventilating.

Arrangements for supplying oxygen

The following oxygen services may be ordered in England and Wales:

- emergency oxygen;
- short-burst (intermittent) oxygen therapy;
- long-term oxygen therapy;
- ambulatory oxygen.

The type of oxygen service (or combination of services) should be ordered on a Home Oxygen Order Form (HOOF); the amount of oxygen required (hours per day) and flow rate should be specified. The clinician will determine the appropriate equipment to be provided. Special needs or preferences should be specified on the HOOF.

The clinician should obtain the patient or carers consent, to pass on the patient's details to the supplier, the fire brigade, and other relevant organisations. The supplier will contact the patient to make arrangements for delivery, installation, and maintenance of the equipment. The supplier will also train the patient or carer to use the equipment.

The clinician should send the HOOF to the supplier who will continue to provide the service until a revised HOOF is received, or until notified that the patient no longer requires the home oxygen service.

- East of England, North East: BOC Medical: Tel: 0800 136 603 Fax: 0800 169 9989
- South West: Air Liquide: Tel: 0808 202 2229 Fax: 0191 497 4340
- London, East Midlands, North West: Air Liquide: Tel: 0500 823 773 Fax: 0800 781 4610

- Yorkshire and Humberside, West Midlands, Wales: Air Products: Tel: 0800 373 580 Fax: 0800 214 709
- South East Coast, South Central: Dolby Vivisol: Tel: 08443 814 402 Fax: 0800 781 4610

In **Scotland** refer the patient for assessment by a respiratory consultant. If the need for a concentrator is confirmed the consultant will arrange for the provision of a concentrator through the Common Services Agency. In **Northern Ireland** oxygen concentrators and cylinders should be prescribed on form HS21; oxygen concentrators are supplied by a local contractor. In **Scotland** and **Northern Ireland** prescriptions for oxygen cylinders and accessories can be dispensed by pharmacists contracted to provide domiciliary oxygen services.

ANTIMUSCARINICS

Antimuscarinics (inhaled)

- **CAUTIONS** Bladder outflow obstruction · prostatic hyperplasia · risk of glaucoma (in children) · susceptibility to angle-closure glaucoma (in adults)
- **INTERACTIONS** See Appendix 1 (antimuscarinics). However, note that interactions do not *generally* apply to antimuscarinics used by inhalation.
- **SIDE-EFFECTS**
  - **Common or very common** Constipation · cough · diarrhoea · dry mouth · gastro-intestinal motility disorder · headache
  - **Uncommon** Angle-closure glaucoma · atrial fibrillation (in adults) · blurred vision (in adults) · bronchospasm · dysphagia (in adults) · dysphonia (in adults) · gastro-oesophageal reflux disease (in adults) · mydriasis · nasopharyngitis (in adults) · nausea (in adults) · palpitation · paradoxical bronchospasm · pharyngitis (in adults) · tachycardia · throat irritation (in adults) · urinary retention
  - **Rare** Dental caries (in adults) · dry skin (in adults)

Aclidinium bromide

- **INDICATIONS AND DOSE**

  Maintenance treatment of chronic obstructive pulmonary disease
  - BY INHALATION OF POWDER
  - Adult: 375 micrograms twice daily

  DOSE EQUIVALENCE AND CONVERSION
  Each 375 microgram inhalation of aclidinium bromide delivers 322 micrograms of aclidinium.

- **CAUTIONS** Hospitalisation with moderate or severe heart failure within last 12 months · myocardial infarction within last 6 months · newly diagnosed arrhythmia within last 3 months · unstable angina
- **SIDE-EFFECTS** Sinusitis
- **PREGNANCY** Manufacturer advises use only if potential benefit outweighs risk.
- **BREAST FEEDING** Manufacturer advises avoid.
- **PATIENT AND CARER ADVICE** Patients or carers should be given advice on how to administer aclidinium bromide powder inhalation.

- **MEDICINAL FORMS**
  There can be variation in the licensing of different medicines containing the same drug.

  Inhalation powder
  - **Eklira** (AstraZeneca UK Ltd) ▼
    Aclidinium bromide 375 microgram per 1 dose Eklira 322micrograms/dose Genuair | 60 dose PoM £28.60

Aclidinium bromide with formoterol

The properties listed below are those particular to the combination only. For the properties of the components please consider, aclidinium bromide above, formoterol fumarate p. 221.

- **INDICATIONS AND DOSE**

  Maintenance treatment of chronic obstructive pulmonary disease
  - BY INHALATION OF POWDER
  - Adult: 1 inhalation twice daily

- **CAUTIONS** Convulsive disorders · phaeochromocytoma · thyrotoxicosis
- **SIDE-EFFECTS**
  - **Common or very common** Raised creatine phosphokinase · tooth abscess · urinary tract infection
- **PATIENT AND CARER ADVICE** Patients or carers should be given advice on how to administer aclidinium bromide with formoterol powder inhalation.

- **MEDICINAL FORMS**
  There can be variation in the licensing of different medicines containing the same drug.

  Inhalation powder
  - **Duaklir** (AstraZeneca UK Ltd) ▼
    Formoterol fumarate dihydrate 11.8 microgram per 1 dose, Aclidinium bromide 396 microgram per 1 dose Duaklir 340micrograms/dose / 12micrograms/dose Genuair | 60 dose PoM £32.50

Glycopyrronium bromide (Glycopyrrolate)

- **INDICATIONS AND DOSE**

  Maintenance treatment of chronic obstructive pulmonary disease
  - BY INHALATION OF POWDER
  - Adult: 50 micrograms once daily

  DOSE EQUIVALENCE AND CONVERSION
  For inhalation of powder, each 50 microgram capsule of glycopyrronium delivers 44 micrograms of glycopyrronium.

- **CAUTIONS** Arrhythmia (excluding chronic stable atrial fibrillation) · history of myocardial infarction · history of QT-interval prolongation · left ventricular failure · unstable ischaemic heart disease
- **SIDE-EFFECTS**
  - **Common or very common** Insomnia
  - **Uncommon** Epistaxis · hyperglycaemia · hypoaesthesia · malaise · rhinitis
- **PREGNANCY** Manufacturer advises use only if potential benefit outweighs risk.
- **BREAST FEEDING** Manufacturer advises use only if potential benefit outweighs risk.
- **RENAL IMPAIRMENT** Use with caution if eGFR less than 30 mL/minute/1.73 m^2.
- **PATIENT AND CARER ADVICE** Patients or carers should be given advice on how to administer glycopyrronium for inhalation.

- **MEDICINAL FORMS**
  There can be variation in the licensing of different medicines containing the same drug.

  Inhalation powder
  - **Glycopyrronium bromide (non-proprietary)** ▼
    Glycopyrronium bromide 55 microgram Glycopyrronium bromide 55microgram inhalation powder capsules with device |

6 capsule PoM no price available | 30 capsule PoM no price available

- Seebri Breezhaler (Novartis Pharmaceuticals UK Ltd) ▼
  Glycopyrronium bromide 55 microgram Seebri Breezhaler 44microgram inhalation powder capsules with device | 6 capsule PoM £5.50 | 30 capsule PoM £27.50

Ipratropium bromide

- **INDICATIONS AND DOSE**

Reversible airways obstruction

- BY INHALATION OF AEROSOL
- Child 1 month–5 years: 20 micrograms 3 times a day
- Child 6–11 years: 20–40 micrograms 3 times a day
- Child 12–17 years: 20–40 micrograms 3–4 times a day

Reversible airways obstruction, particularly in chronic obstructive pulmonary disease

- BY INHALATION OF AEROSOL
- Adult: 20–40 micrograms 3–4 times a day
- BY INHALATION OF NEBULISED SOLUTION
- Adult: 250–500 micrograms 3–4 times a day

Acute bronchospasm

- BY INHALATION OF NEBULISED SOLUTION
- Child 1 month–5 years: 125–250 micrograms as required; maximum 1 mg per day
- Child 6–11 years: 250 micrograms as required; maximum 1 mg per day
- Child 12–17 years: 500 micrograms as required
- Adult: 500 micrograms as required

Severe or life-threatening acute asthma

- BY INHALATION OF NEBULISED SOLUTION
- Child 1 month–11 years: 250 micrograms every 20–30 minutes for the first 2 hours, then 250 micrograms every 4–6 hours as required
- Child 12–17 years: 500 micrograms every 4–6 hours as required
- Adult: 500 micrograms every 4–6 hours as required

PHARMACOKINETICS

The maximal effect of inhaled ipratropium occurs 30–60 minutes after use; its duration of action is 3 to 6 hours and bronchodilation can usually be maintained with treatment 3 times a day.

- **CAUTIONS** Cystic fibrosis

CAUTIONS, FURTHER INFORMATION

- Glaucoma *Acute angle-closure glaucoma* has been reported with nebulised ipratropium, particularly when given with nebulised salbutamol (and possibly other beta$_2$ agonists); care needed to protect the patient's eyes from nebulised drug or from drug powder.

- **SIDE-EFFECTS**
- **Common or very common** Dizziness · nausea (in children)
- **Uncommon** Laryngospasm · pharyngeal oedema (in children) · pruritus · stomatitis · vomiting
- **Rare** Atrial fibrillation (in children) · ocular accommodation disorder (in children)

- **PREGNANCY** Inhaled drugs for asthma can be taken as normal during pregnancy.
- **BREAST FEEDING** Inhaled drugs for asthma can be taken as normal during breast-feeding.
- **DIRECTIONS FOR ADMINISTRATION**
- In adults If dilution of ipratropium bromide nebuliser solution is necessary use only sterile sodium chloride 0.9%.
- **PATIENT AND CARER ADVICE** Advise patient not to exceed prescribed dose and to follow manufacturer's directions.

- **MEDICINAL FORMS**
  There can be variation in the licensing of different medicines containing the same drug.

Pressurised inhalation

- Ipratropium bromide (Non-proprietary)
  Ipratropium bromide 20 microgram per 1 dose Ipratropium bromide 20micrograms/dose inhaler CFC free | 200 dose PoM £5.56 DT price = £5.56
- Atrovent (Boehringer Ingelheim Ltd)
  Ipratropium bromide 20 microgram per 1 dose Atrovent 20micrograms/dose inhaler CFC free | 200 dose PoM £5.56 DT price = £5.56

Nebuliser liquid

- Ipratropium bromide (Non-proprietary)
  Ipratropium bromide 250 microgram per 1 ml Ipratropium bromide 500micrograms/2ml nebuliser liquid unit dose vials | 20 unit dose PoM £6.60 DT price = £3.40
  Ipratropium bromide 250micrograms/1ml nebuliser liquid unit dose vials | 20 unit dose PoM £6.00 DT price = £4.39
- Atrovent UDV (Boehringer Ingelheim Ltd)
  Ipratropium bromide 250 microgram per 1 ml Atrovent 500micrograms/2ml nebuliser liquid UDVs | 20 unit dose PoM £4.87 DT price = £3.40 | 60 unit dose PoM £14.59
  Atrovent 250micrograms/1ml nebuliser liquid UDVs | 20 unit dose PoM £4.14 DT price = £4.39 | 60 unit dose PoM £12.44
- Respontin (GlaxoSmithKline UK Ltd)
  Ipratropium bromide 250 microgram per 1 ml Respontin 250micrograms/1ml Nebules | 20 unit dose PoM £4.78 DT price = £4.39
  Respontin 500micrograms/2ml Nebules | 20 unit dose PoM £5.60 DT price = £3.40

Ipratropium with salbutamol

The properties listed below are those particular to the combination only. For the properties of the components please consider, ipratropium bromide above, salbutamol p. 224.

- **INDICATIONS AND DOSE**

Bronchospasm in chronic obstructive pulmonary disease

- BY INHALATION OF NEBULISED SOLUTION
- Adult: 0.5/2.5 mg 3–4 times a day

- **PRESCRIBING AND DISPENSING INFORMATION** A mixture of ipratropium bromide and salbutamol (as sulphate); the proportions are expressed in the form x/y where x and y are the strengths in milligrams of ipratropium and salbutamol respectively.
- **LESS SUITABLE FOR PRESCRIBING** Ipratropium bromide with salbutamol nebuliser solution is considered less suitable for prescribing.

- **MEDICINAL FORMS**
  There can be variation in the licensing of different medicines containing the same drug.

Nebuliser liquid

- Ipratropium with salbutamol (Non-proprietary)
  Ipratropium bromide 200 microgram per 1 ml, Salbutamol (as Salbutamol sulfate) 1 mg per 1 ml Salbutamol 2.5mg/2.5ml / Ipratropium bromide 500micrograms/2.5ml nebuliser liquid unit dose vials | 60 unit dose PoM no price available
- Combivent (Boehringer Ingelheim Ltd)
  Ipratropium bromide 200 microgram per 1 ml, Salbutamol (as Salbutamol sulfate) 1 mg per 1 ml Combivent nebuliser liquid 2.5ml UDVs | 60 unit dose PoM £24.10
- Ipramol (Teva UK Ltd)
  Ipratropium bromide 200 microgram per 1 ml, Salbutamol (as Salbutamol sulfate) 1 mg per 1 ml Ipramol nebuliser solution 2.5ml Steri-Neb unit dose vials | 60 unit dose PoM £23.83

Tiotropium

INDICATIONS AND DOSE

Maintenance treatment of chronic obstructive pulmonary disease

- BY INHALATION OF POWDER
- Adult: 18 micrograms once daily

SPIRIVA RESPIMAT®

Maintenance treatment of chronic obstructive pulmonary disease | Adjunct to inhaled corticosteroids and long-acting beta$_2$ agonists for the maintenance treatment of patients with asthma who have suffered one or more severe exacerbations in the last year

- BY INHALATION OF AEROSOL
- Adult: 5 micrograms once daily

CAUTIONS Cardiac arrhythmia requiring intervention in the previous 12 months · hospitalisation for moderate to severe heart failure in the previous 12 months · life-threatening cardiac arrhythmia · myocardial infarction in the previous 6 months · unstable cardiac arrhythmia

CAUTIONS, FURTHER INFORMATION

Regularly review treatment in patients at high risk of cardiovascular events.

SIDE-EFFECTS

- **Common or very common** Dizziness · epistaxis · oropharyngeal candidiasis · pruritus · taste disturbance
- **Rare** Gingivitis · glossitis · insomnia · intestinal obstruction · paralytic ileus · sinusitis · stomatitis
- **Frequency not known** Dehydration · joint swelling

PREGNANCY Manufacturer advises use only if potential benefit outweighs risk.

BREAST FEEDING Manufacturer advises avoid—no information available.

RENAL IMPAIRMENT Plasma-tiotropium concentration raised. Manufacturer advises use only if potential benefit outweighs risk if eGFR less than 50 mL/ minute/1.73 m^2.

PRESCRIBING AND DISPENSING INFORMATION

SPIRIVA RESPIMAT® Use *Spiriva Respimat®* only when patient unable to use *Spiriva Handihaler®* device.

PATIENT AND CARER ADVICE

Counselling Advise patients to report any worsening of cardiac symptoms during treatment.

Patients or carers should be given advice on how to administer tiotropium powder inhalation and pressurised inhalation.

NATIONAL FUNDING/ACCESS DECISIONS

SPIRIVA RESPIMAT®

Scottish Medicines Consortium (SMC) Decisions

The *Scottish Medicines Consortium* has advised (November 2007) that *Spiriva Respimat®* is restricted for use in chronic obstructive pulmonary disease in patients who have poor manual dexterity and difficulty using the *Handihaler®* device.

MEDICINAL FORMS

There can be variation in the licensing of different medicines containing the same drug.

Pressurised inhalation

- **Spiriva Respimat** (Boehringer Ingelheim Ltd)
  Tiotropium (as Tiotropium bromide) 2.5 microgram per 1 dose Spiriva Respimat 2.5micrograms/dose solution for inhalation cartridge with device | 60 dose PoM £33.50 DT price = £33.50

Inhalation powder

- **Spiriva** (Boehringer Ingelheim Ltd)
  Tiotropium (as Tiotropium bromide) 18 microgram Spiriva 18microgram inhalation powder capsules with HandiHaler | 30 capsule PoM £34.87 DT price = £34.87
  Spiriva 18microgram inhalation powder capsules | 30 capsule PoM £33.50 DT price = £33.50 | 60 capsule PoM £67.00

Umeclidinium

INDICATIONS AND DOSE

Maintenance treatment of chronic obstructive pulmonary disease

- BY INHALATION OF POWDER
- Adult: 55 micrograms once daily

DOSE EQUIVALENCE AND CONVERSION

Each 65 microgram inhalation of umeclidinium bromide delivers 55 micrograms of umeclidinium.

CAUTIONS Cardiac disorders (particularly cardiac rhythm disorders)

SIDE-EFFECTS

- **Uncommon** Arrhythmias · rash · sinusitis · urinary tract infection

PREGNANCY Manufacturer advises use only if potential benefit outweighs risk.

BREAST FEEDING Manufacturer advises avoid—no information available.

HEPATIC IMPAIRMENT Use with caution in severe impairment.

PATIENT AND CARER ADVICE Patient or carers should be given advice on how to administer umeclidinium inhalation powder.

MEDICINAL FORMS

There can be variation in the licensing of different medicines containing the same drug.

Inhalation powder

- **Incruse Ellipta** (GlaxoSmithKline UK Ltd) ▼
  Umeclidinium bromide 65 microgram per 1 dose Incruse Ellipta 55micrograms/dose dry powder inhaler | 30 dose PoM £27.50 DT price = £27.50

Umeclidinium with vilanterol

The properties listed below are those particular to the combination only. For the properties of the components please consider, umeclidinium above.

INDICATIONS AND DOSE

Maintenance treatment of chronic obstructive pulmonary disease

- BY INHALATION OF POWDER
- Adult: 1 inhalation once daily

CAUTIONS Arrhythmias · bladder outflow obstruction · cardiac disorders · convulsive disorders · diabetes—monitor blood glucose (risk of ketoacidosis) · hypertension · hyperthyroidism · hypokalaemia · prostatic hyperplasia · severe cardiovascular disease · severe hepatic impairment · susceptability to angle-closure glaucoma · susceptibility to QT-interval prolongation

INTERACTIONS → Appendix 1 (antimuscarinics, sympathomimetics beta$_2$).

SIDE-EFFECTS

- **Common or very common** Constipation · cough · dry mouth · headache · nasopharyngitis · oropharyngeal pain · pharyngitis · sinusitis · upper respiratory tract infection · urinary tract infection
- **Uncommon** Atrial fibrillation · rash · rhythm idioventricular · supraventricular extrasystoles · supraventricular tachycardia · tachycardia
- **Frequency not known** Angle-closure glaucoma · arrhythmias · fine tremor (particularly in the hands) · hyperglycaemia · hypokalaemia (when in high doses) · paradoxical bronchospasm · urinary retention

SIDE-EFFECTS, FURTHER INFORMATION

- **Hypokalaemia** Potentially serious hypokalaemia may result from beta$_2$ agonist therapy.

- **PREGNANCY** Manufacturer advises use only if potential benefit outweighs risk.
- **BREAST FEEDING** Manufacturer advises avoid—no information available.
- **PATIENT AND CARER ADVICE** Patient or carers should be given advice on how to administer umeclidinium with vilanterol dry powder inhaler.

- **MEDICINAL FORMS**
There can be variation in the licensing of different medicines containing the same drug.

Inhalation powder

- **Anoro Ellipta** (GlaxoSmithKline UK Ltd) ▼
Vilanterol (as Vilanterol trifenatate) 22 microgram per 1 dose, Umeclidinium bromide 65 microgram per 1 dose Anoro Ellipta 55micrograms/dose / 22micrograms/dose dry powder inhaler | 30 dose PoM £32.50

BETA$_2$-ADRENOCEPTOR AGONISTS, SELECTIVE

Selective beta$_2$ agonists

- **CONTRA-INDICATIONS** Severe pre-eclampsia
- **CAUTIONS** Arrhythmias · cardiovascular disease · diabetes (risk of hyperglycaemia and ketoacidosis, especially with intravenous use) · high doses of beta$_2$ agonists can be dangerous in some children · hypertension · hyperthyroidism · hypokalaemia · susceptibility to QT-interval prolongation

CAUTIONS, FURTHER INFORMATION

- Hypokalaemia Potentially serious hypokalaemia may result from beta$_2$ agonist therapy. Particular caution is required in severe asthma, because this effect may be potentiated by concomitant treatment with theophylline and its derivatives, corticosteroids, diuretics, and by hypoxia.
- **INTERACTIONS** → Appendix 1 (sympathomimetics, beta$_2$). Hypokalaemia may be potentiated by concomitant treatment with theophylline and its derivatives, corticosteroids, and diuretics.
- **SIDE-EFFECTS** Angioedema · arrhythmias · behavioural disturbances · collapse · fine tremor (particularly in the hands) · headache · hyperglycaemia (especially when given intravenously) · hypersensitivity reactions · hypokalaemia (with high doses) · hypotension · ketoacidosis (especially when given intravenously) · muscle cramps · myocardial ischaemia · nervous tension · palpitation · paradoxical bronchospasm (occasionally severe) · peripheral vasodilation · rash · sleep disturbances · tachycardia · urticaria
- **PREGNANCY** Women planning to become pregnant should be counselled about the importance of taking their asthma medication regularly to maintain good control.
- **MONITORING REQUIREMENTS**
- In severe asthma, plasma-potassium concentration should be monitored (risk of hypokalaemia).
- In patients with diabetes, monitor blood glucose (risk of hyperglycaemia and ketoacidosis, especially when beta$_2$ agonist given intravenously).
- **PATIENT AND CARER ADVICE**
- When used by inhalation The **dose**, the frequency, and the maximum number of inhalations in 24 hours of the beta$_2$ agonist should be **stated explicitly** to the patient or their carer. The patient or their carer should be advised to seek medical advice when the prescribed dose of beta$_2$ agonist fails to provide the usual degree of symptomatic relief because this usually indicates a worsening of the asthma and the patient may require a prophylactic drug. Patients or their carers should be advised to follow manufacturers' instructions on the care and cleansing of inhaler devices.

SELECTIVE BETA$_2$-AGONISTS (LONG-ACTING)

Bambuterol hydrochloride

- **DRUG ACTION** Bambuterol is a pro-drug of terbutaline.

- **INDICATIONS AND DOSE**

Asthma (patients who have previously tolerated beta$_2$-agonists) | Other conditions associated with reversible airways obstruction (patients who have previously tolerated beta$_2$-agonists)

- BY MOUTH
- Adult: 20 mg once daily, dose to be taken at bedtime

Asthma (patients who have not previously tolerated beta$_2$-agonists) | Other conditions associated with reversible airways obstruction (patients who have not previously tolerated beta$_2$-agonists)

- BY MOUTH
- Adult: Initially 10 mg once daily for 1–2 weeks, then increased if necessary to 20 mg once daily, dose to be taken at bedtime

- **PREGNANCY** Manufacturer advises avoid—no information available.
- **BREAST FEEDING** Manufacturer advises avoid—no information available.
- **HEPATIC IMPAIRMENT** Avoid in severe impairment.
- **RENAL IMPAIRMENT** Reduce initial dose by half if eGFR less than 50 mL/minute/1.73 m^2.

- **MEDICINAL FORMS**
There can be variation in the licensing of different medicines containing the same drug.

Tablet

- **Bambec** (AstraZeneca UK Ltd)
Bambuterol hydrochloride 10 mg Bambec 10mg tablets | 28 tablet PoM £14.46 DT price = £14.46
Bambuterol hydrochloride 20 mg Bambec 20mg tablets | 28 tablet PoM £15.77 DT price = £15.77

Formoterol fumarate

(Eformoterol fumarate)

- **INDICATIONS AND DOSE**

Reversible airways obstruction in patients requiring long-term regular bronchodilator therapy | Nocturnal asthma in patients requiring long-term regular bronchodilator therapy | Prophylaxis of exercise-induced bronchospasm in patients requiring long-term regular bronchodilator therapy | Chronic asthma in patients who regularly use an inhaled corticosteroid

- BY INHALATION OF POWDER
- Child 6-11 years: 12 micrograms twice daily, a daily dose of 24 micrograms of formoterol should be sufficient for the majority of children, particularly for younger age-groups; higher doses should be used rarely, and only when control is not maintained on the lower dose
- Child 12-17 years: 12 micrograms twice daily, dose may be increased in more severe airway obstruction; increased to 24 micrograms twice daily, a daily dose of 24 micrograms of formoterol should be sufficient for the majority of children, particularly for younger age-groups; higher doses should be used rarely, and only when control is not maintained on the lower dose
- Adult: 12 micrograms twice daily, dose may be increased in more severe airway obstruction; increased to 24 micrograms twice daily
- BY INHALATION OF AEROSOL
- Child 12-17 years: 12 micrograms twice daily, dose may be increased in more severe airway continued →