# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Salamol Easi-Breathe CFC-Free Inhaler

100 micrograms Pressurised Inhalation, suspension.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered dose contains salbutamol sulfate equivalent to 100 micrograms salbutamol.

Excipient with known effect:
Each metered dose contains 3.93 mg alcohol (ethanol).

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Pressurised inhalation, suspension.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

The symptomatic treatment of asthma and other conditions with associated reversible airways obstruction. For relief of wheezing and shortness of breath, Salamol Easi-Breathe CFC-Free Inhaler should be used on an 'as required' basis.
Prevention of asthma attacks induced by exercise or exposure to allergens.

Salamol Easi-Breathe CFC-Free Inhaler can be used as relief medication to manage mild, moderate and severe asthma, provided its use does not delay the introduction and regular use of inhaled corticosteroid therapy, where necessary.

Salamol Easi-Breathe CFC-Free Inhaler is indicated in adults, adolescents and children aged 4 to 11 years. For infants and children under 4 years of age, see section 5.1.

### 4.2. Posology and method of administration

Posology

For optimum results in most patients Salamol Easi-Breathe CFC-Free Inhaler should be used as required.

*Adults (including the elderly)*

**Relief of acute asthma symptoms including bronchospasm**
One inhalation (100 micrograms) may be administered as a single minimum starting dose. This may be increased to two inhalations (200 micrograms) if necessary.

**Prevention of allergen or exercise-induced bronchospasm**
Two inhalations (200 micrograms) should be taken 10-15 minutes before challenge.

On demand use of Salamol Easi-Breathe CFC-Free Inhaler should not exceed 8 inhalations (800 micrograms) in any 24 hours. Inhalations should not usually be repeated more often than every 4 hours. Reliance on such frequent supplementary use, or a sudden increase in dose indicates poorly controlled or deteriorating asthma.

For all patients, four hours should be allowed between each dose.

*Paediatric population*

**Relief of acute asthma symptoms including bronchospasm**
The usual dosage for children under the age of 12 years: one inhalation (100 micrograms). The dose may be increased to two inhalations (200 micrograms) if required.

Children aged 12 years and over: Dose as per adult population.

**Prevention of allergen or exercise-induced bronchospasm**
The usual dosage for children under the age of 12 years: one inhalation (100 micrograms) before challenge or exertion. The dose may be increased to two inhalations (200 micrograms) if required.

Children aged 12 years and over: Dose as per adult population.

The usual dosage for children under the age of 12 years: up to two inhalations 4 times daily.

Children aged 12 years and over: Dose as per adult population.

*Patients with Hepatic or Renal Impairment*
No need to adjust the dose.

Method of administration
Inhalation use.

Salamol Easi-Breathe® administration in children should be supervised by an adult.
Patients should wait four hours between doses.
Patients should sit, or stand, upright during inhalation. It is also important that the inhaler should be held in an upright position, as the inhaler works correctly only in a vertical position.

The aerosol spray is inhaled through the mouth into the lungs. The inhaler should be tested by spraying the inhaler by firing two shots into the air before first use, and if the inhaler has not been used for a period of five days or longer.

Use of the inhaler

1. Patients should shake the inhaler vigorously.

2. The inhaler must be held upright. Patients should open it by folding down the cap which fits over the mouthpiece.

3. Patients should exhale normally, and place the mouthpiece in their mouth with their lips closed around it. They should hold the inhaler upright and make sure that their hand is not blocking the airholes. Inhalation through the mouthpiece should be slow and deep. Patients should be advised not to stop breathing when the inhaler puffs the dose into their mouth. After that, they should carry on until they have taken a deep breath.

4. Patients should remove the inhaler from their mouth and hold their breath for 10 seconds or as long as they comfortably can. Then, exhale slowly.

5. After using the inhaler, patients should hold it upright and close the cap immediately.
6. If more than one puff is needed, patients should close the cap, wait about one minute and then start again from step 1.

Patients should be advised to clean the inhaler once a week, especially in the mouthpiece to prevent deposits from the aerosol building up.

As with most inhaled medicinal products in pressurised containers, the therapeutic effect of this medicinal product may decrease when the container is cold.

The container should not be punctured, broken or burnt, even when apparently empty.

The metal container must not be put into water.

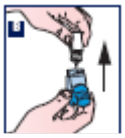
**Full instructions for use are given in the Patient Information Leaflet which should be read carefully by the patient before use.**

Cleaning of the inhaler

Patients must clean the inhaler once a week.

A Unscrew and remove the top of the inhaler. Patients should be advised to keep this top dry all the time.

B Remove the metal from the bottom of the inhaler. Patients should be advised not to put the container into water



C Rinse the bottom of the inhaler with warm running water for at least 30 seconds

D Shake off any excess water and dry the bottom of the inhaler thoroughly (overnight if possible). It is important to advise patients not to use direct heat. Patients should put the can back into the bottom of the inhaler. Then, close the cap and screw the top and bottom parts of their inhaler back together.

## 4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Salbutamol inhalation is contraindicated in treatment of threatened abortion or premature labour.

## 4.4. Special warnings and precautions for use

Salbutamol should be used with caution and only when strictly indicated in the following cases:

- hypersensitivity to other sympathomimetics
- hyperthyroidism/thyrotoxicosis
- coronary insufficiency
- hypertrophic obstructive cardiomyopathy
- recent heart attack
- severe and untreated arterial hypertension
- tachycardia and known tachyarrhythmias
- Phaeochromocytoma
- Aneurysms
- concomitant use of cardiac glycosides
- difficult-to-control diabetes mellitus.

Patients should be instructed in the proper use of the inhaler and their technique checked, to ensure that the active substance reaches the target areas within the lungs.

The management of asthma should normally follow a stepwise programme, and the patient's response should be monitored clinically and by lung function tests.

Patients who are prescribed regular anti-inflammatory therapy (e.g., inhaled corticosteroids) should be advised to continue taking their anti-inflammatory medication even when symptoms decrease, and they do not require Salamol Easi-Breathe CFC-Free Inhaler.

Increasing use of short-acting inhaled bronchodilators, in particular ß$_2$-agonists to control symptoms, indicates deterioration of asthma control, and patients should be warned to seek medical advice as soon as possible. If, despite therapy, there is no satisfactory improvement or even exacerbation of the disease, the treatment plan must be reviewed by the physician and, if necessary, reformulated by combining it with anti-inflammatories, adjusting the dose of pre-existing anti-inflammatory therapy or co-administering other medicinal products.

Overuse of short-acting beta-agonists may mask the progression of the underlying disease and contribute to deteriorating asthma control, leading to an increased risk of severe asthma exacerbations and mortality.

Patients who take more than twice a week “as needed” salbutamol, not counting prophylactic use prior to exercise, should be re-evaluated (i.e., daytime symptoms, night-time awakening, and activity limitation due to asthma) for proper treatment adjustment as these patients are at risk for overuse of salbutamol.

Salbutamol should not be used as monotherapy in patients with persistent asthma.

The dosage or frequency of administration should only be increased on medical advice.

Patients requiring long term management with Salamol Easi-Breathe CFC-Free Inhaler should be kept under regular surveillance.

Care should be taken when treating acute asthma attacks or exacerbation of severe asthma as increased serum lactate levels, and rarely, lactic acidosis have been reported after the use of high doses of salbutamol have been used in emergency situations this is reversible on reducing the dose of salbutamol

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmias or severe heart failure) who are receiving salbutamol should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be either respiratory or cardiac in origin.

Potentially serious hypokalaemia may result from ß$_2$-agonist therapy mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.
Significantly exceeding the recommended doses (in particular the single doses used in an acute attack, but also the total daily dose) can be dangerous because of possible cardiac side effects, especially in association with electrolyte imbalances (e.g., hypokalaemia), and must therefore be avoided.

As with other beta-adrenoceptor agonists, salbutamol can induce reversible metabolic changes such as increased blood glucose levels. Diabetic patients may be unable to compensate for the increase in blood glucose and the development of ketoacidosis has been reported. Concurrent administration of glucocorticoids can exaggerate this effect.

If treatment with Salamol Easi-Breathe CFC-Free Inhaler is initiated in diabetics, additional blood glucose monitoring is recommended as $beta_2$-agonists increase the risk of hyperglycaemia.As with other inhalation therapies, the potential for paradoxical bronchospasm with immediate exacerbation of wheezing should be considered. If it occurs the preparation should be discontinued immediately and alternative therapy given. In such cases, treatment should be switched immediately to a different dosage form or to another fast-acting inhaled bronchodilator.
Solutions which are not of neutral pH may rarely cause paradoxical bronchospasm in some patients. Salbutamol and non-selective beta blocking drugs such as propranolol should not usually be prescribed together.

Excipient(s)

*Ethanol*
This medicine contains 3.93 mg of alcohol (ethanol) in each metered dose. The amount in each metered dose of this medicine is equivalent to less than 0.1 ml beer or wine.
The small amount of alcohol in this medicine will not have any noticeable effects.

## 4.5. Interaction with other medicinal products and other forms of interaction

Concomitant use of salbutamol and beta-receptor antagonists leads to a mutual attenuation of effect, whereby the administration of beta-receptor antagonists in patients with bronchial asthma carries the risk of triggering severe bronchospasm.
Furthermore, the hypoglycaemic effect of antidiabetics can be reduced during treatment with salbutamol. However, this is generally only to be expected at higher doses that are usual in systemic administration (as tablets or injection/infusion).

Mutual potentiation of the effects and an increased risk of adverse reactions are possible if salbutamol is co-administered with theophylline (and theophylline derivatives) or other sympathomimetics.

An increased risk of adverse reactions is possible if salbutamol is co-administered with antiarrhythmic agents (e.g. digitalis glycosides/quinidine).

In addition, substances which themselves potentiate sympathomimetic effects, such as L dopa, L thyroxine, oxytocin or alcohol, can have an effect on cardiovascular regulation in interaction with salbutamol.

Concomitant treatment of salbutamol and substances of the ergot alkaloid type, such as ergotamine, should be carried out only with caution, since the reciprocal influence on vasomotor activity is difficult to predict on an individual basis and can lead to vasoconstrictor as well as vasodilator reactions.
Concomitant use of salbutamol and monoamine oxidase inhibitors or tricyclic antidepressants can induce an increased effect of salbutamol on the cardiovascular system.

Hypertensive reactions may occur if procarbazine is co-administered.

The use of halogenated anaesthetics, such as halothane, methoxyflurane or enflurane, must be expected to increase the risk of severe cardiac arrhythmias and hypotension in patients treated with salbutamol (see Notes).

Notes:
When anaesthesia using halogenated anaesthetics is scheduled, it should be ensured that, wherever possible, salbutamol is no longer used for at least 6 hours before the start of anaesthesia.

Hypokalaemia may occur during high-dose therapy with salbutamol.
This can be further exacerbated with concomitant use of other medicinal products, especially methylxanthines (e.g. theophylline), corticosteroids, diuretics or digitalis glycosides, or if hypoxaemia is also present. Blood electrolyte monitoring is indicated, so that potassium can be administered if necessary.
Because of the content of ethanol, there is theoretical potential for interaction in patients taking disulfiram or metronidazole

## 4.6. Fertility, pregnancy and lactation

Pregnancy

Salbutamol crosses the placental barrier. For humans, insufficient experience is available on use during pregnancy. Animal studies have shown reproductive toxicity at high doses (see section 5.3). The potential risk to humans is not known.
Salamol Easi-Breathe CFC-Free Inhaler during pregnancy should only be used in situations where the expected benefit to the mother is thought to outweigh any risk to the foetus.

Salamol Easi-Breathe CFC-Free Inhaler should be used during pregnancy, especially during the first three months, only in situations where the expected benefit to the mother is expected to outweigh any risk to the foetus. The same applies to use at the end of pregnancy because of the labour-inhibiting effect.
***Salamol Easi-Breathe CFC-Free Inhaler***
There is no documented evidence of the use of salbutamol formulated with propellant HFA-134a in pregnant women.

*Propellant HFA-134a*
There is no documented evidence of the use of propellant HFA-134a in pregnant women. Pregnant animals exposed to high levels of HFA-134a showed no evidence of any adverse effects.

*Salbutamol*
Experience on the use of beta-sympathomimetics during early pregnancy indicates no harmful effect at the doses ordinarily used for inhalation therapy. High systemic doses at the end of pregnancy can cause inhibition of labour and may induce $\beta_2$-specific foetal/neonatal effects like tachycardia and hypoglycaemia. Inhalation therapy at recommended doses is not expected to induce these harmful side effects at the end of pregnancy.

Breast-feeding

Salamol Easi-Breathe CFC-Free Inhaler should only be used in lactation in situations where the expected benefit to the mother is thought to outweigh any risk to the neonate.

*Salamol Easi-Breathe CFC-Free Inhaler*
There is no documented evidence of the use of salbutamol formulated with propellant HFA-134a in lactating women.

*Propellant HFA-134a*
There is no documented evidence of the use of propellant HFA-134a in lactating women. Lactating animals exposed to high levels of HFA-134a showed no evidence of any adverse effects.

*Salbutamol*
Salbutamol may be secreted in breast milk. It is not known whether salbutamol has a harmful effect on the neonate.

Fertility

There is no information on the effects of salbutamol on human fertility. In animals, there were no negative effects on fertility (see section 5.3).

## 4.7. Effects on ability to drive and use machines

No studies have been carried out on the effects on the ability to drive and operate machinery.

## 4.8. Undesirable effects

Based on the MedDRA system organ class and frequencies, adverse events are listed in the table below.

Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000), not known (cannot be estimated from the available data).

| System Organ Class | Frequency | Adverse Event |
|---|---|---|
| Immune system disorders | Very rare | Hypersensitivity reactions (including angioedema, urticaria, exanthema bronchospasm, hypotension and collapse) |
| Metabolism and nutrition disorders | Common<br><br>Rare | Hyperglycaemia<br><br>Hypokalaemia*, increased serum lactate levels and acidosis lactic |
| Psychiatric disorders | Common<br><br>Rare<br><br><br>Very rare | Tenseness<br><br>Sleep disturbances and hallucinations (especially in children), hyperactivity in children<br><br>Insomnia |
| Nervous system disorders | Common<br><br>Uncommon | Tremor muscle, headache**, dizziness<br><br>Restlessness** |
| Cardiac disorders | Common<br><br>Uncommon<br><br><br>Very rare | Tachycardia<br><br>Palpitations, myocardial ischaemia (see section 4.4)<br><br>Cardiac arrhythmia including atrial fibrillation, supraventricular tachycardia and (ventricular) extrasystoles and anginal complaints – especially if used concomitantly with other $\beta_2$- agonists |
| Vascular disorders | Rare | Peripheral vasodilatation |
| Respiratory, thoracic and mediastinal disorders | Uncommon<br><br>Very rare | Throat irritation<br><br>Paradoxical bronchospasm (with an immediate increase in wheezing after dosing)[§] |
| Gastrointestinal disorders | Uncommon<br><br><br>Rare | Mouth irritation, changes in the sense of taste<br><br>Nausea, vomiting, dry mouth, sore mouth |
| Skin and subcutaneous tissue disorders | Very rare | Pruritus |
| Musculoskeletal and connective tissue disorders | Uncommon<br><br>Very rare | Myalgia, muscle cramps<br><br>Fine tremor (particularly of hands) |

[*] Very marked hypokalaemia may possibly occur during therapy with beta$_2$-agonists.
[**] Mild tremor and restlessness, as well as headache and muscle spasms, may resolve over the course of 1 to 2 weeks with continued treatment.

[§] As with other inhalation therapies, paradoxical bronchospasm may occur immediately after dosing. Salamol Easi-Breathe CFC-Free Inhaler should be discontinued immediately, the patient reassessed and treated immediately with another presentation or a different fast-acting inhaled bronchodilator.
Treatment with Salamol Easi-Breathe CFC-Free Inhaler must be discontinued without delay, the patient examined and, if necessary, another form of therapy instituted (see also section 4.4).

Rarely, micturition disorders, heartburn and increases or decreases in blood pressure can occur.

Paediatric population
There have been isolated reports of a stimulant effect on the central nervous system after inhalation of salbutamol, which manifested as hyperexcitability, conspicuous hyperactive behaviour, sleep disorders and hallucinations. These observations were mainly made (90%) in children and adolescents up to 12 years of age.

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9. Overdose

Symptoms of an overdose
In the event of an overdose, the above-mentioned adverse reactions appear very rapidly and possibly in exaggerated form.

Typical symptoms are:
Tachycardia, palpitations, arrhythmias, restlessness, sleep disorders, chest pain and severe tremor, especially of the hands, but also the entire body. Uncommonly, psychotic reactions have been observed after excessive salbutamol doses.

Gastrointestinal complaints, including nausea, can occur, especially after oral intoxication.

In the event of an overdose with salbutamol, there may be increased shifts of potassium into the intracellular space, resulting in hypokalaemia, as well as hyperglycaemia, hyperlipidaemia and hyperketonaemia.

Lactic acidosis has been reported with high therapeutic doses and overdoses of short-acting beta-agonists. Thus, monitoring of patients for the development of elevated serum lactate levels and subsequent metabolic acidosis may be indicated (particularly if tachypnoea persists or worsens despite resolution of other signs of bronchospasm, such as wheezing).

Therapeutic measures in the event of overdose
Treatment after a beta-agonist overdose is mainly symptomatic and should also take into account the additive effect from any previous treatment with other medicinal products that can cause hypokalaemia.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

Pharmacotherapeutic group:
Selective beta$_2$ adrenoreceptor agonists,

ATC code: R03AC02

Mechanism of action

Salbutamol is a direct-acting beta-agonist with predominant $\beta_2$ selectivity, with $\beta_1$ receptor stimulation expressed only at higher doses.

Salbutamol causes relaxation of smooth muscle in the bronchi and blood vessels, as well as relaxation of the uterine muscles. Salbutamol also inhibits mediator release from mast cells.

Furthermore, an increase in mucociliary clearance is detectable in the bronchial system, though the mechanism of action has not yet been fully clarified.

These effects are mediated by activation of adenylate cyclase, resulting in accumulation of cyclic 3',5'-adenosine monophosphate (c-AMP), which in turn inhibits the contractile elements of smooth muscle.

Influence on lipid and sugar metabolism (lipolysis, glycogenolysis and hyperglycaemia) and relative hypokalaemia due to increased $K^+$ uptake in the skeletal muscle are pharmacological effects that come into play only at higher doses.

Salbutamol has high bronchoselectivity. Its effects on the heart - such as increased contractility, increase in heart rate (positive inotropic and chronotropic effect) - can be explained mainly by direct activity on beta$_1$ receptors and by reflex stimulation due to peripheral vasodilation.

Pharmacodynamic effects

Salbutamol provides short acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

Data on the potential for a loss of efficacy (tachyphylaxis) during long-term use of salbutamol are contradictory. It seems that such a loss of efficacy may occur on an individual basis. In such cases, combination with glucocorticoids can normalise the reduced responsiveness of beta$_2$ receptors.

Paediatric population

Paediatric clinical studies conducted at the recommended dose (SB020001. SB030001. SB030002) in patients < 4 years with bronchospasm associated with reversible obstructive airways disease, show that Salbutamol CFC-Free Inhaler has a safety profile comparable to that in children > 4 years, adolescents and adults.

## 5.2. Pharmacokinetic properties

Salamol Easi-Breathe CFC-Free Inhaler has been shown to be therapeutically equivalent to salbutamol metered dose inhaler formulated with chlorofluorocarbon (CFC) propellants.

Absorption
Absorption and metabolism of salbutamol differ depending on the route of administration (oral or inhalation).
Following inhalation from a metered-dose inhaler, around 10 to 20% of salbutamol reaches the deeper bronchial segments, whilst the remainder of the dose is deposited in the upper part of the respiratory tract and in the mouth, and is subsequently swallowed.

Distribution

Salbutamol is subject to first pass metabolism in the liver, about half is excreted in the urine as an inactive sulfate conjugate following oral administration (the rest being unchanged salbutamol). Salbutamol does not appear to be metabolised in the lung, therefore its behaviour following inhalation depends upon the delivery method used which determines the proportion of inhaled salbutamol relative to the proportion inadvertently swallowed.

Biotransformation
Salbutamol is well absorbed after oral administration and is partially metabolised in the gastrointestinal tract and in the liver. In the plasma, the substance is present as free salbutamol and in metabolite form. Free salbutamol is fully effective, while the metabolite shows hardly any beta-stimulating properties.

Elimination
In studies with radioactively labelled salbutamol, 64 to 98% of the administered doses were excreted within 72 hours in the urine and 10 to 12% in the faeces. About 55% of the radioactivity in urine derives from the sulphate ester, which has been identified as the main metabolite of salbutamol in humans. This high excretion rate shows that salbutamol is not stored in the body.

The biological steady-state half-life of salbutamol in serum after intravenous infusion is approximately 6 hours.

Salbutamol crosses the placental barrier.

Pharmacokinetic/pharmacodynamic relationship
Since the plasma level after inhalation is mainly the result of enteral absorption of the swallowed fraction, the serum level does not correlate with the pharmacodynamic time-effect curve. Compared to equipotent oral doses, inhalation plasma levels are 500 to 1,000 times lower and show a delayed time course similar to that after oral administration. In contrast, onset of the inhalation effect is significantly more rapid.

## 5.3. Preclinical safety data

The non-CFC propellant, norflurane (HFA 134a), has been shown to have no toxicological effect at very high vapour concentrations far in excess of those to which patients are normally exposed, in a large number of animal species exposed daily over periods of more than 2 years.
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. The effects observed in toxicity studies are related to the β-adrenergic activity of salbutamol. Reproductive toxicity studies in rats showed no effects on fertility at therapeutically relevant doses. In mice, cleft palate was seen in fetuses at doses four times the maximum oral dose of some salbutamol preparations in humans. No teratogenic effect was demonstrated at relevant doses in rats and rabbits.

# 6. PHARMACEUTICAL PARTICULARS

## 6.1. List of excipients

Ethanol, anhydrous
Norflurane (Propellant HFA-134a)
Salamol Easi-Breathe CFC-Free Inhaler contains a new propellant (HFA-134a) and does not contain any chlorofluorocarbon (CFC) propellants.

## 6.2. Incompatibilities

Not applicable.

## 6.3. Shelf-life

3 years

## 6.4. Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze.

## 6.5. Nature and contents of container

A pressurised aluminium container with a metering valve and breath-operated actuator.
Each pack contains:
Single pack with one Easi-Breathe MDI with 200 metered doses
Twin pack with one Easi-Breathe MDI and one refill container, each containing 200 metered doses (2 x 200).
Not all pack sizes may be marketed.

## 6.6. Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

Norton Healthcare Ltd.,
T/A IVAX Pharmaceuticals UK,
Ridings Point, Whistler Drive,
Castleford, West Yorkshire,
WF10 5HX, United Kingdom

## 8. MARKETING AUTHORISATION NUMBER

PL 00530/0556

## 9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 April 2000
Date of latest renewal: 14 April 2010

## 10 DATE OF REVISION OF THE TEXT

29/02/2024