# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Asthalin 100 micrograms Inhaler

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered dose (ex-valve) contains 100 micrograms salbutamol (as sulphate).

Each delivered dose (ex-actuator) contains 85micrograms salbutamol (as sulphate).

Excipient with known effect

Each metered dose (ex-valve) contains 1.516 mg of ethanol.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Pressurised inhalation, suspension.

The inhaler comprises an aluminium canister fitted with a metering valve, which is inserted into a light blue standard plastic actuator fitted with a removable blue plastic mouthpiece cover, embossed with "Cipla" logo and " Asthalin CFC-Free Salbutamol 100 mcg".

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Asthalin Inhaler is indicated in adults, adolescents and children aged 4 to 11 years.

For babies and children under 4 years of age, see section 4.2 and 5.1.

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

It is particularly suitable for the relief and prevention of asthma symptoms. It should be used to relieve symptoms when they occur, and to prevent them in those circumstances recognised by the patient to precipitate an asthma attack (e.g. before exercise or unavoidable allergen exposure).

Asthalin Inhaler may also be used in the treatment of the reversible component of airways obstruction.

## 4.2 Posology and method of administration

Posology

*Adults*

For the relief of acute asthma symptoms including bronchospasm, wheezing, shortness of breath and attacks of acute dyspnoea, or the reversible component of airways obstruction, one inhalation (100 micrograms) may be administered as a single starting dose. This may be increased to two inhalations if necessary. To prevent allergen or exercise induced symptoms, two inhalations should be taken 10-15 minutes before challenge.

For chronic therapy, two inhalations up to four times a day.

*Paediatric population*

*Relief of acute bronchospasm*

The usual dosage for children under the age of 12 years: one inhalation (100 micrograms). The dose may be increased to two inhalations 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 if required.

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

*Chronic therapy*

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

*Elderly*

No special dosage recommendations are made for older patients.

For all patients, the maximum recommended dose should not exceed 8 inhalations in 24 hours. Each repetitive dosing, 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 (see section 4.4).

Asthalin Inhaler **cannot be used with any spacing device at this time. If a patient needs a spacing device an alternative product, which can be used with such a device, will need to be prescribed instead of Asthalin Inhaler.**

Instructions for use

1. The mouthpiece cover should be removed and the patient should check inside and outside to make sure that the mouthpiece is clean and that there is no dust, dirt or foreign objects. If it needs cleaning the instructions for cleaning outlined below should be followed. If the inhaler gets very cold, patients should be instructed to take the metal canister out of the plastic actuator and warm it in their hands for a few minutes before use. Patients should never use anything else to warm it up. The inhaler should be shaken prior to use.

2. The inhaler should be held upright with the thumb on the base, below the mouthpiece. Patients should breathe out as far as is comfortable and then.

3. **Immediately** place the mouthpiece in the mouth between the teeth, and close their lips around it. Patients should be instructed to be careful not to bite the mouthpiece.

4. **Breathe in slowly.** Just after starting to breathe in through the mouth, patients should press down on the top of the inhaler to release a spray, while still breathing in steadily and deeply.

5. Patients should hold their breath, remove the inhaler from the mouth, and take their finger from the top of the inhaler. Patients should continue holding their breath for about 10 seconds, or as long as is comfortable, prior to breathing out slowly.

Patients should be instructed not to rush stages 3, 4 and 5.

It is important that patients breathe in as slowly as possible just before using the inhaler. Patients should be instructed to try practising in front of a mirror for the first few times. If patients see mist or spray coming from the inhaler or the sides of the mouth, they should start again from stage 2.

6. If patients are to take another spray, they should keep the inhaler upright, and wait about half a minute before repeating steps 2 to 5.

7. Once patients have finished using the inhaler, they should be instructed to always replace the mouthpiece cover to keep out dust and fluff and should make sure to replace the cover firmly and snap it into position.

People with weak hands may find it easier to operate the inhaler with both hands, by putting both forefingers on the top of the inhaler, and both thumbs on the bottom below the mouthpiece.

For detailed instructions for use, the patient should be referred to the Patient Information Leaflet included in each pack, with specific reference to the pictograms which accompany the instructions for use.

The inhaler should be cleaned at least once a week as described below, as it can become blocked, which will affect the way in which the inhaler works and will affect the amount of salbutamol which is inhaled.

1. First remove the metal can from the plastic actuator and take off the mouthpiece cover.
2. Rinse the plastic actuator, mouthpiece and mouthpiece cover in tap water; DO NOT place the metal can into water or clean the can using water. Make sure the water runs through the actuator from both ends to ensure that the actuator orifice is clear and not blocked.
3. The plastic components (actuator and mouthpiece cover) should be placed in a warm place to dry thoroughly before re-assembling the inhaler. Avoid drying near direct or excessive heat.

The patient should follow the cleaning instructions described in the Patient Information Leaflet carefully in order to ensure that the inhaler continues to work properly.

At first use of a new inhaler, or after a period when the inhaler has not been used (7 days or more), the inhaler should be shaken well and two sprays should be discharged prior to use, to prime the inhaler.

Method of Administration:

For inhalation use.

## 4.3 Contraindications

Hypersensitivity to salbutamol or to any of the excipients listed in section 6.1.

Non i.v. formulations of salbutamol are contraindicated for use in arresting uncomplicated premature labour and threatened abortion.

## 4.4 Special warnings and precautions for use

Patients should be instructed in the proper use of the inhaler and their technique checked, to ensure that aerosol actuation is synchronised with inspiration of breath for the optimum delivery of the active substance to the lungs. Patients should be warned that they may experience a different taste upon inhalation compared to their previous inhaler.

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 Asthalin Inhaler

Increasing use of short-acting 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. Under these conditions, the patient's therapy plan should be reassessed. Patients with persistent asthma should receive optimal anti-inflammatory basic therapy with corticosteroids. Sudden and progressive deterioration in asthma control is potentially life threatening and consideration should be given to increasing or starting oral and/or inhaler corticosteroid therapy. In patients considered at risk, daily peak flow monitoring may be instituted.

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.

The patient should be advised to seek medical advice if a previously effective dose ceases to be effective for at least three hours, and/or their asthma seems to be worsening.

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

Patients requiring long-term management with salbutamol device should be kept under regular surveillance.

Salbutamol should be administered cautiously to patients with thyrotoxicosis, coronary insufficiency, hypertrophic obstructive cardiomyopathy, arterial hypertension, tachyarrhythmias, in concomitant use of cardiac glycosides or diabetes mellitus.

Potentially serious hypokalaemia has been reported in patients taking $\beta_2$ 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, diuretics, long-term laxatives and by hypoxia. Extra care should therefore be taken if $\beta_2$-agonist are used in these groups of patients and it is recommended that serum potassium levels should be monitored in such situations.

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 high doses of salbutamol have been used in emergency situations. This is reversible on reducing the dose of salbutamol (see section 4.9).

Unwanted stimulation of cardiac adrenoceptors can occur in patients taking $\beta_2$ agonist therapy.

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 ß-agonists. 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.

As with other inhalation therapy, the potential for paradoxical bronchospasm should be considered. If this occurs, the salbutamol should be discontinued immediately and an alternative presentation or a different fast acting inhaled bronchodilator given. Solutions which are not of neutral pH may rarely cause paradoxical bronchospam in some patients.

Salbutamol and non-selective ß-antagonists such as propranolol should not usually be prescribed together.

In common with other ß-agonists, salbutamol can induce reversible metabolic changes such as increased blood glucose levels. Patients with diabetes 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.

Severe exacerbations of asthma must be treated in the normal way.

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

Salbutamol and non-selective β-blocking drugs such as propranolol, should not usually be prescribed together.

Monoamine oxidase inhibitors, tricyclic antidepressants and digoxin increase the risk of cardiovascular effects.

Patients should be instructed to discontinue salbutamol for at least 6 hours before an intended anaesthesia with halogenic anaesthetics, wherever possible.

Hypokalaemia occurring with β2 agonist therapy may be exacerbated by treatment with xanthines, steroids, diuretics and long-term laxatives.

Because Asthalin Inhaler contains ethanol there is a theoretical potential for interaction in patients taking disulfiram or metronidazole. The amount of ethanol is small but it may be enough to precipitate a reaction in some sensitive patients.

## 4.6 Fertility, Pregnancy and lactation

### Pregnancy

There is no experience of this product in pregnancy and lactation in humans. Safety in pregnant women has not been established. No controlled clinical trials with salbutamol have been conducted in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). An inhalation reproductive study with a salbutamol sulphate CFC-free formulation in rats did not exhibit any teratogenic effects. It should not be used in pregnancy and lactation unless the expected benefit to the mother is thought to outweigh any risk to the fetus or neonate.

**Propellant HFA 134a**
There is no documented evidence of the use of salbutamol formulated with propellant

HFA-134a in pregnant or lactating women.Studies of propellant HFA 134a administered to pregnant and lactating rats and rabbits have not revealed any special hazard.

### Salbutamol

The safe use of inhaled salbutamol during pregnancy has not been established but it has been in widespread use for many years in human beings without apparent ill consequence. Rare reports of various congenital anomalies following intrauterine exposure to salbutamol (including cleft palate, limb defects and cardiac disorders) have been received. Some of the mothers were taking multiple medications during their pregnancies. However, in animal studies there was evidence of some harmful effects on the fetus at very high dose levels. In mice and rabbits large doses of salbutamol have been shown to be teratogenic.

Experience on the use of ß-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 ß2-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

As salbutamol is probably secreted in breast milk, its use in nursing mothers requires careful consideration. It is not known whether salbutamol has a harmful effect on the neonate, and so its use should be restricted to situations where it is felt that the expected benefit to the mother is likely to outweigh any potential risk to the neonate.

Fertility

There is no information on the effects of salbutamol on human fertility. There were no adverse effects on fertility in animals (see section 5.3).

## 4.7 Effects on ability to drive and use machines

Salbutamol may cause dizziness. If you are affected do not drive or operate machinery.

## 4.8 Undesirable effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) including isolated reports and not known (cannot be estimated from the available data). Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown events were generally determined from spontaneous data.

Immune system disorders

*Very rare:* Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse.

Metabolism and nutrition disorders

*Rare:* Hypokalaemia (especially in combination with xanthine derivatives, corticosteroids and diuretics) increased serum lactate levels and acidosis lactic.

Psychiatric disorders

*Common:* Tenseness
*Rare:* Sleep disturbances and hallucinations (especially in children)
*Very rare*: Insomnia, Hyperactivity

Nervous system disorders

*Common:* Headache, Dizziness, Fine tremor (particularly in hands)

Cardiac disorders

*Common:* Tachycardia
*Uncommon:* Palpitations,
*Very rare*: Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles) –especially if used concomitantly with other ß$_2$-agonists
*Not known*: Myocardial ischaemia, chest pain (see section 4.4)

Vascular disorders

*Rare:* Peripheral vasodilatation.

Respiratory, thoracic and mediastinal disorders

*Uncommon:* Throat irritation
*Very rare:* Paradoxical bronchospasm (with an immediate increase in wheezing after dosing). (As with other inhalation therapy, paradoxical bronchospasm may occur immediately after dosing. If this occurs, salbutamol should be discontinued immediately and, if needed, an alternative therapy instituted).

Gastrointestinal disorders

*Uncommon*: Mouth irritation
*Rare*: nausea, vomiting, dry mouth, sore mouth.

Skin and subcutaneous tissue disorders
*Very rare:* Pruritus

Musculoskeletal and connective tissue disorders

Uncommon: Myalgia, muscle cramps

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: https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

Symptoms:

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events, including skeletal muscle tremor, tachycardia, tenseness, headache, hyperactivity, peripheral vasodilatation and metabolic effects including hypokalaemia.

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

Hyperglycaemia, agitation and hyperactivity have also been reported following overdose with salbutamol.

Lactic acidosis has been reported in association with high therapeutic doses as well as overdoses of shortacting beta-agonist therapy, therefore monitoring for elevated serum lactate and consequent metabolic acidosis (particularly if there is persistence or worsening of tachypnea despite resolution of other signs of bronchospasm such as wheezing) may be indicated in the setting of overdose.

Management:

*Asthmatic patients*:

Consideration should be given to discontinuation of treatment.

Monitor biochemical abnormalities, particularly hypokalaemia which should be treated with potassium replacement where necessary. ß-adrenoceptor antagonists, even $ß_1$-selective antagonists, are potentially life-threatening and should be avoided.

*Non-asthmatic patients*:

Monitor and correct biochemical abnormalities, particularly hypokalaemia.

The preferred antidote for overdosage with salbutamol is a cardioselective β-adrenoceptor blocking agent but due care and attention should be used in administering beta-blocking drugs in patients with a history of bronchospasm, as these drugs are potentially life-threatening. A non-selective ß-adrenoceptor antagonist (e.g. nadolol, propranolol) will competitively reverse both hypokalaemia and tachycardia ($ß_1$-selective drugs will be largely ineffective).

The treatment of lactic acidosis in cases of salbutamol overdose should be undertaken in a specialist intensive care unit. Salbutamol therapy should be discontinued and appropriate supportive therapy should be commenced to treat the underlying condition. Lactic acidosis is treated indirectly by correcting the underlying causes and not by any treatment aimed directly at correction of lactic acidosis itself.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Andrenergics, inhalants. Selective beta-2-andrenoreceptor agonists

ATC code R03A C02

Salbutamol is a sympathomimetic agent which has a selective action on $ß_2$-adrenoceptors of bronchial muscle. At therapeutic doses, it acts on the $β_2$-adrenoceptors of bronchial muscle with little or no action on the $ß_2$-adrenoceptors of cardiac muscle. Salbutamol provides short-acting (4-6 hour) bronchodilatation with a fast onset (within 5 minutes) in reversible airways obstruction.

*Special Patient Populations*

*Children < 4 years of age*

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 has a safety profile comparable to that in children > 4 years, adolescents and adults.

## 5.2 Pharmacokinetic properties

Pharmacotherapeutic group: Andrenergics, inhalants. Selective beta-2-andrenoreceptor agonists

ATC code R03A C02

Salbutamol is a sympathomimetic agent which has a selective action on ß$_2$-adrenoceptors of bronchial muscle. At therapeutic doses, it acts on the β$_2$-adrenoceptors of bronchial muscle with little or no action on the ß$_2$-adrenoceptors of cardiac muscle. Salbutamol provides short-acting (4-6 hour) bronchodilatation with a fast onset (within 5 minutes) in reversible airways obstruction.

*Special Patient Populations*

*Children < 4 years of age*

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 has a safety profile comparable to that in children > 4 years, adolescents and adults.

## 5.3 Preclinical safety data

**Salbutamol**
In common with other potent selective ß$_2$ agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of fetuses were found to have cleft palate at 2.5mg/kg dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50mg/kg/day orally throughout pregnancy resulted in no significant fetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. Reproductive studies in the rabbit at doses of 50mg/kg/day orally (i.e. much higher than the normal human dose) have shown fetuses with treatment related changes;

these included open eyelids (ablepharia), secondary palate clefts (palatoschisis), changes in ossification of the frontal bones of the cranium (cranioschisis) and limb flexure.

In an oral fertility and general reproductive performance study in rats at doses of 2 and 50 mg/kg/day, with the exception of a reduction in number of weanlings surviving to day 21 post partum at 50 mg/kg/day, there were no adverse effects on fertility, embryofetal development, litter size, birth weight or growth rate.

**Propellant HFA 134a**
In animal studies propellant HFA 134a has been shown to have no significant pharmacological effects other than at very high exposure concentrations, when narcosis and a relatively weak cardiac sensitising effect were found. The potency of the cardiac sensitisation was less than that of CFC-11 (trichlorofluoromethane).

In studies to detect toxicity, repeated high dose levels of propellant HFA 134a indicated that safety margins based on systemic exposure would be of the order 2200, 1314 and 381 for mouse, rat and dog with respect to humans.

There are no reasons to consider propellant HFA 134a as a potential mutagen, clastogen or carcinogen judged from *in vitro* and *in vivo* studies including long-term administration by inhalation in rodents.

**Salbutamol sulphate – a CFC-free formulation**
Safety studies with a salbutamol sulphate CFC-free formulation in rat and dog showed few adverse effects. These occurred at high doses and were consistent with the known effects of salbutamol inhalation.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Norflurane (HFA 134a) – this is a hydrofluoroalkane, non-chlorofluorocarbon (non-CFC) propellant; this product does not contain CFCs.

Ethanol

Oleic Acid

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

2 years.

### 6.4 Special precautions for storage

Do not store above 30ºC.

The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C. Do not pierce the canister.

### 6.5 Nature and contents of container

An inhaler comprising an aluminium canister sealed with a metering valve, inserted into a polypropylene actuator with a polypropylene mouthpiece cover. Each canister contains 200 metered actuations.

### 6.6 Special precautions for disposal

As the canister is pressurised, it should not be punctured or disposed of by burning.

## 7 MARKETING AUTHORISATION HOLDER

Cipla (EU) Limited,

Dixcart House, Addlestone Road,

Bourne Business Park, Addlestone,

Surrey, KT15 2LE,

United Kingdom

## 8 MARKETING AUTHORISATION NUMBER(S)

PLGB 36390/0330

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

16/12/2024

## 10 DATE OF REVISION OF THE TEXT

16/12/2024