Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

VENTOMOL (Salbutamol Sulfate, Bromhexine Hydrochloride & Guaifenesin Syrup)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml contains:

Salbutamol Sulfate BP

Eq to Salbutamol.....2mg

Bromhexine Hydrochloride BP.....4mg

Guaifenesin USP.....100mg

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Orange coloured, viscous liquid filled in amber colour bottle.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic relief in the treatment of productive cough associated with bronchospasm.

4.2 Posology and method of administration

Adults and Children >12 years: 10 mL (2 tsp) 3 times a day.

Children 6-12 years: 5 mL (1 tsp) 3 times a day; 2-5 years: 2.5 mL (½ tsp) 3 times a day;

<2 years: Not recommended.

4.3 Contraindications

Known or suspected hypersensitivity to any of the ingredients of VENTOMOL.

4.4 Special warnings and precautions for use

Salbutamol, as with all sympathomimetic amines, should be used with caution in patients with convulsive disorders, hyperthyroidism or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines. Clinically significant changes in systolic and diastolic blood pressure have been seen and could be expected to occur in some patients after use of any β-adrenergic bronchodilator.

Salbutamol, like all other β-adrenergic agonists, can produce a clinically significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, and/or symptoms. In addition, β-agonists have been reported to produce electrocardiogram (ECG) changes eg, flattening of the T-wave, prolongation of the QTc interval and ST segment depression. Therefore, salbutamol should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias and hypertension.

Asthma may deteriorate acutely over a period of hours or chronically over several days or longer. If the patient needs more doses of salbutamol than usual, this may be a marker of destabilization of asthma and requires re-evaluation of the patient and the treatment regimen, giving special consideration to the possible need for anti-inflammatory treatment eg, corticosteroids.

Salbutamol can produce paradoxical bronchospasm, which may be life-threatening. If paradoxical bronchospasm occurs, salbutamol should be discontinued immediately and alternative therapy instituted.

Immediate hypersensitivity reactions may occur after administration of salbutamol, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm and oropharyngeal edema. Rarely, erythema multiforme and Stevens-Johnson syndrome have been associated with the administration of oral salbutamol in children.

Precaution should be taken while using guaifenesin in treatment of cough accompanied by too much mucous or persistent or chronic cough such as that which occurs with smoking, asthma, chronic bronchitis or emphysema.

Bromhexine should be used cautiously in patients with gastric or duodenal ulcer.

4.5 Interaction with other medicinal products and other forms of interaction

Diuretics: The ECG changes and/or hypokalemia that may result from the administration of nonpotassium-sparing diuretics (eg, loop or thiazide diuretics) can be acutely worsened by β-agonists. Beta-Blockers: Beta-adrenergic receptor blocking agents not only block the pulmonary effect of β-

agonists eg, salbutamol, but may produce severe bronchospasm in asthmatic patients. Therefore, patients with asthma should not normally be treated with β-blockers.

Monoamine Oxidase Inhibitors: Hypertensive crises and other adverse effects occur frequently with the concurrent use of indirect-acting sympathomimetics. Direct-acting β-adrenergic agonist drugs should theoretically not interact with monoamine oxidase (MAO) inhibitors. However, 2 case reports have described adverse effects, including tachycardia and hypomania, attributed to such an interaction.

Digoxin: Decreases of 16-22% in serum digoxin levels were seen after single-dose administration of salbutamol to healthy volunteers who had been receiving digoxin for 10 days. The concomitant use of salbutamol and other oral sympathomimetic agents is not recommended since such combined use may lead to deleterious cardiovascular effects.

4.6 Pregnancy and lactation

Use in pregnancy: Animal reproduction studies have not been conducted with VENTOMOL Expectorant. It is also not known whether it can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. VENTOMOL Expectorant should be used in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Use in lactation: VENTOMOL Expectorant is not recommended in lactating mothers.

4.7 Effects on ability to drive and use machines

One should not drive a vehicle if using the medicine makes you drowsy, dizzy.

4.8 Undesirable effects

VENTOMOL Expectorant is generally well tolerated and adverse events are generally mild and transient. The adverse events reported with the individual ingredients are the following:

Salbutamol: The adverse reactions to salbutamol are similar in nature to reactions to other sympathomimetic agents. The reactions are generally transient in nature. The most frequent adverse reactions to salbutamol are nervousness, tremor, headache, tachycardia and palpitations. Less frequent adverse reactions are muscle cramps, insomnia, nausea, weakness, dizziness, drowsiness, flushing, restlessness, irritability, chest discomfort and difficulty in micturition. Rare cases of urticaria, angioedema, rash, bronchospasm and oropharyngeal edema have been reported after the use of salbutamol. In addition, salbutamol, like other sympathomimetic agents, can cause adverse reactions eg, hypertension, angina, vomiting, vertigo, central nervous system stimulation, unusual taste and drying or irritation of the oropharynx.

Bromhexine: Adverse effects of bromhexine include GI symptoms (nausea, epigastric pain, vomiting), headache, dizziness and skin rash; elevations in liver

function tests have been reported in a few patients.

Guaifenesin: Adverse effects are primarily minor GI complaints. Urolithiasis has been associated with excessive use of guaifenesin.

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 requested to report any suspected adverse reactions via the Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose

Nausea, vomiting and hyperglycaemia have been reported, predominantly in children and when salbutamol overdose has been taken via the oral route.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cough suppressants and expectorants

ATC code: R05FB02

Mechanism of action:

Pharmacology: Pharmacodynamics: Salbutamol: Salbutamol is a direct-acting sympathomimetic agent which demonstrates relatively selective action on β2-adrenoceptors. The prime action of β-adrenergic drugs is to stimulate adenyl cyclase, the enzyme which catalyzes the formation of cyclic-3, 5-adenosine monophosphate (cyclic AMP) from adenosine triphosphate (ATP). Increased cyclic AMP levels are associated with relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells. Salbutamol relaxes the smooth muscle of the bronchi, uterus and skeletal muscle vascular bed. It is more potent and longer acting β2-adrenoceptor agonist as compared to isoproterenol. It may also reduce chemical mediator release from pulmonary mast cells and improve mucociliary transport mechanisms.

Bromhexine: Bromhexine is an expectorant/mucolytic agent. It is a benzylamine derivative and also a derivative of vasicine and adhatodic acid, alkaloids obtained from the plant Adhatoda vasica. Following oral administration, bromhexine has increased sputum volume and reduced the viscosity of bronchial secretions in chronic bronchitis patients. The drug has been reported to induce hydrolytic depolymerization of mucoprotein fibers and stimulate activity of the ciliated epithelium. An increase in lysosomal activity facilitated by bromhexine has been postulated. Improvements in pulmonary function in bronchitis patients appear secondary to easier expectoration.

Other pharmacological effects of bromhexine have been reported, including enhancement of secretion from exocrine glands (eg, tear production) and an increase in pulmonary surfactant production. An effect of bromhexine on increasing sputum concentrations of various antibiotics (eg, oxytetracycline, erythromycin, ampicillin, amoxicillin) has also been reported. It has been

suggested that a metabolite of bromhexine, ambroxol (NA-872), may contribute to enhanced secretion from exocrine glands during bromhexine administration.

Guaifenesin: Guaifenesin is an expectorant which is thought to act by irritating the gastric mucosa and subsequently stimulating respiratory tract secretions. This increase in fluid increases the volume and decreases the viscosity of bronchial secretions.

Menthol: Menthol is chiefly used to relieve symptoms of bronchitis, sinusitis and similar conditions. It exerts soothing and counter-irritant effects on upper respiratory mucosa. It has been suggested that the apparent benefits of menthol in nasal congestion may be due to an effect on calcium channels of sensory nerves.

5.2 Pharmacokinetic properties Salbutamol:

Salbutamol is well absorbed from the gastrointestinal tract with bioavailability of approximately 50-85%. Peak plasma concentrations (Cmax) occur 1-4 hrs (Tmax) after oral administration of salbutamol. Food does not affect the bioavailability of salbutamol. Plasma protein-binding for salbutamol is 10% and volume of distribution (Vd) is 156±38 L. Salbutamol is metabolized in the liver to form active metabolite, 4-O-sulfate ester. Excretion of salbutamol is primarily renal. Approximately 64-98% of the dose is recovered in the urine and 1.2-7% eliminated in feces. The elimination t½ of salbutamol is 3-6.5 hrs.

Bromhexine:

Bromhexine is well absorbed from the GIT. Peak serum concentrations of bromhexine occur approximately 1 hr following oral administration. Bromhexine is extensively metabolized in the liver to form active metabolite, ambroxol. Bromhexine is excreted primarily in the urine as metabolites. Only small amounts appear as unchanged drug. The elimination t½ of bromhexine is 6.5 hrs.

Guaifenesin:

Guaifenesin is well absorbed from the GIT. Sixty percent (60%) of guaifenesin is hydrolyzed in blood within 7 hrs with the formation of β-2-methoxyphenoxy-lactic acid. Excessive use of guaifenesin may result in urolithiasis; the resultant stones contain the metabolite of guaifenesin, β-2- methoxyphenoxy-lactic acid. Guaifenesin is excreted in the urine in the form of metabolites. The plasma t½ of guaifenesin is 1 hr.

Preclinical safety data

No data available

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Menthol, Sucrose, Glycerine, Methyl Paraben Sodium, Propyl Paraben Sodium, Propylene Glycol, Disodium edentate, Colour: Sunset yellow Supra, and Citric Acid Monohydrate.

Flavour: Vanilla No.1, Flavour: Sweet Orange.

6.2 Incompatibilities

None known

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C. Protect from light & moisture.

6.5 Nature and contents of container

100ml Amber colour PET Bottle.

6.6 Special precautions for disposal and other handling No special requirement

7. Marketing Authorization Holder

Dagon Pharmaceuticals Pvt. Ltd.
Baddi-Nalagarh Road, Village & Post: Manpura,
Distt. Solan, Himachal Pradesh-174 101,
India

8. Marketing Authorization Number

H2022/CTD9091/17575

9. Date of first authorization/renewal of the authorization

10/10/2023

10. Date of revision of the text

10/10/2023