Kofarest-LS JUNIOR

1. **Generic Names**

Levosalbutamol

Ambroxol

Guaiphenesin

2. **Qualitative and Quantitative Composition**

Each 5ml contains

Levosalbutamol	0.5mg
Ambroxol	15mg
Guaiphenesin	50 mg

3. **Dosage form and strength**

Oral Syrup containing Levosalbutamol 0.5mg, Ambroxol 15mg, Guaiphenesin 50 mg.

4. **Clinical particulars**

4.1 Therapeutic indication

KOFAREST-LS Junior Syrup is indicated for the treatment of symptomatic relief of bronchospasm in bronchial asthma & chronic bronchitis.

4.2 Posology and method of administration

The usual recommended dose of KOFAREST-LS Junior for:

- 2-5 years: 5 ml twice daily
- 6-12 years: 10 ml twice daily

4.3 Contraindication

KOFAREST-LS Junior Syrup is contraindicated in patients with hypersensitivity to any ingredient of the formulation.

4.4 Special warnings and precautions for use

- While treating cough as a symptom, it is important to make every effort to determine and treat appropriately the underlying cause, such as a specific infection.
- Caution should be observed while prescribing KOFAREST-LS Syrup to children with hypertension, cardiovascular disease, uncontrolled juvenile diabetes mellitus, hyperthyroidism, and seizures or in patients who are unusually hypersensitive to sympathomimetic amines.

4.5 Drug interactions

- Hypokalaemia with high doses of ß2 -agonists may result in increased susceptibility to digitalis induced cardiac arrhythmias.
- Hypokalaemia may be enhanced by concomitant administration of aminophylline or other xanthine, corticosteroids or by diuretic therapy.
- Other sympathomimetic bronchodilators or epinephrine should not be used concomitantly with salbutamol, since their combined effect on the cardiovascular system may be deleterious to the patient.
- Salbutamol should be administered with caution in patients being treated with monoamine oxidase (MAO) inhibitors or tricyclic antidepressants, since the action of salbutamol on the vascular system may be potentiated.

4.6 Use in special population

- Pediatric**:** Safe in children.
- Geriatric: Clinical studies did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently from younger subjects. If clinically warranted due to insufficient bronchodilator response, the dose may be increased in elderly patients as tolerated, in

conjunction with frequent clinical and laboratory monitoring, to the maximum recommended daily dose.

- Liver impairment: Use with caution.
- Renal failure: Use with caution.
- Pregnancy and lactation: Category C: Either studies in animals have revealed adverse effects on the foetus (teratogenic or embryocidal or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the foetus. No studies available for use during breast feeding.

4.7 Effects on ability to drive and use machine

Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to Kofarest LS Junior Syrup is known.

4.8 Undesirable effects

An adverse drug reaction includes Tachycardia, Palpitations, Hypoacusis, Vision blurred, Nausea, Vomiting, Drug ineffective, Drug hypersensitivity, Pneumonia, Medication error, Hear rate increased, Hypokalaemia, Tremor, Dizziness, Headache, Nervousness, Insomnia, Dyspnoea, Asthma, Pruritus, Thrombocytopenia, Eosinophilia, Cardiac flutter, Vascular malformation, Vertigo, Tinnitus, Eyelid edema, Diarrhoea, Chest pain, Chills, Hepatic function abnormal, Anaphylactic shock, Conjunctivitis, Infusion related reaction, Blood pressure increased, Decreased appetite, Pain in extremity, Dysuria, Genital erosion, Rash, Flushing, Anemia, Incorrect product administration duration, Accidental overdose, Muscle spasm, Vaginal haemorrhage, Prostatomegaly.

4.9 Overdose

There is limited experience of overdose with Kofarest LS Junior syrup. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

5.1 Mechanism of action

- Activation of β2 adrenergic receptors on airway smooth muscle leads to the activation of adenylate cyclase and to an increase in the intracellular concentration of 3',5'-cyclic adenosine monophosphate (cyclic AMP). The increase in cyclic AMP is associated with the activation of protein kinase A, which in turn, inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in muscle relaxation. Levosalbutamol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles. Increased cyclic AMP concentrations are also associated with the inhibition of the release of mediators from mast cells in the airways. Levosalbutamol acts as a functional agonist that relaxes the airway irrespective of the spasmogen involved, thereby protecting against all Broncho constrictor challenges.
- Ambroxol is a mucolytic agent. Excessive Nitric oxide (NO) is associated with inflammatory and some other disturbances of airways function. NO enhances the activation of soluble guanylate cyclase and cGMP accumulation. Ambroxol has been shown to inhibit the NO-dependent activation of soluble guanylate cyclase. It is also possible that the inhibition of NO-dependent activation of soluble guanylate cyclase can suppress the excessive mucus secretion; therefore it lowers the phlegm viscosity and improves the mucociliary transport of bronchial secretions.
- Guaifenesin may act as an irritant to gastric vagal receptors, and recruit efferent parasympathetic reflexes that cause glandular exocytosis of a less viscous mucus mixture. Cough may be provoked. This combination may flush tenacious, congealed mucopurulent material from obstructed small airways and lead to a temporary improvement in dyspnea or the work of breathing.

5.2 Pharmacodynamics properties

- Like other bronchodilators, Levosalbutamol acts by relaxing smooth muscle in the bronchial tubes, and thus shortening or reversing an acute "attack" of shortness of breath or difficulty breathing.

- Guaifenesin is an expectorant which increases the output of phlegm (sputum) and bronchial secretions by reducing adhesiveness and surface tension. The increased flow of less viscous secretions promotes ciliary action and changes a dry, unproductive cough to one that is more productive and less frequent. By reducing the viscosity and adhesiveness of secretions, Guaifenesin increases the efficacy of the mucociliary mechanism in removing accumulated secretions from the upper and lower airway.

5.3 Pharmacokinetic properties

There is some systemic absorption of inhaled Levosalbutamol. After a single dose Levosalbutamol has a half-life of 3.3 hours. Levosalbutamol is rapidly excreted, mainly in the urine, as metabolites and unchanged drug; a smaller proportion is excreted in the faeces.

Guaifenesin is well absorbed from the gastrointestinal tract. It is metabolised and then excreted in the urine.

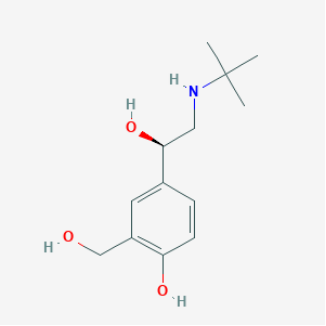
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

NA.

7. Description

Levosalbutamol is a short-acting sympathomimetic beta-2 adrenergic receptor agonist with bronchodilator activity. Its chemical name is 4-[(1*R*)-2-(*tert*-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol and its chemical structure is:

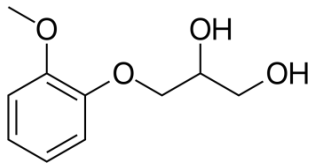


Its empirical formula is $C_{13}H_{21}NO_3$ and its molecular weight is 239.31 g/mol.

Ambroxol belongs to a group of medications called mucolytics. Its chemical name is (1r,4r)-4-{[(2-amino-3,5-dibromophenyl)methyl]amino}cyclohexan-1-ol hydrochloride and its structure is:

Its empirical formula is $C_{13}H_{19}Br_2ClN_2O$ and its molecular weight is 414.56 g/mol.

Guaiphenesin is in a class of medications called expectorants. Its chemical name is 3-(2-methoxyphenoxy)propane-1,2-diol and its chemical structure is:



Its empirical formula is C10H14O4 and its molecular weight is 198.216 g/mol.

8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 months.

8.3 Packaging Information

Kofarest LS Junior syrup is available in 60ml bottle.

8.4 Storage and handling instructions

Store below 25^{o}c. Protect from light.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by Rivpra Formulation Pvt. Ltd.

11. Details of permission or license number with date

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12. Date of revision: January 2022.

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