# Kofarest™-PD
Drops

## 1. Composition

Each ml contains

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| Levosalbutamol | 0.25g |
| Ambroxol | 7.5mg |
| Guaiphenesin | 12.5 mg |

## 2. Dosage form and strength

Kofarest-PD drops is available bottle of 15 ml with calibrated dropper.

## 3. Clinical particulars

### 3.1 Therapeutic indication

Kofarest-PD drops is indicated for the treatment of productive cough associated with bronchospasm in conditions such as bronchitis and bronchial asthma as well as all conditions associated with tenacious mucus, wheezing and chest congestion.

### 3.2 Posology and method of administration

The usual recommended dose of KOFAREST-PD Drops in children is:

- 1-2 years age: 0.8 ml thrice a day
- 2-3 years age: 1.2 ml thrice a day.

### 3.3 Contraindication

Kofarest-PD drops are contraindicated in patients with hypersensitivity to any ingredient of the formulation.

### 3.4 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-PD drops to children with hypertension, cardiovascular disease, uncontrolled juvenile diabetes mellitus, hyperthyroidism, and seizures or in patients who are unusually hypersensitive to sympathomimetic amines.

### 3.5 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.

### 3.6 Use in special population

- Pediatric: safe in children.
- Geriatric: Safety is not evaluated in elderly patients.
- Liver impairment: use with caution.
- Renal failure: use with caution.
- Pregnancy and lactation: Kofarest PD drops is not recommended for use in pregnant and lactating women unless absolutely necessary.

### 3.7 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 PD drops is known.

### 3.8 Undesirable effects

- The adverse reactions to Levosalbutamol are similar in nature to those of other sympathomimetic agents and include nervousness and tremor. The frequency of these side effects appears to diminish with continued therapy. Other commonly reported reactions include increased heart rate, palpitations, dizziness, headache, drowsiness, vomiting, nausea, sweating and muscle cramps. These reactions are generally transient and usually do not require treatment.
- With Ambroxol gastrointestinal side effects may occur occasionally and a transient rise in serum aminotransferase values has been reported.
- Gastrointestinal discomfort has occasionally been reported with Guaiphenesin.

### 3.9 Overdose

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

## 4. Pharmacological properties

### 4.1 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.

### 4.2 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.

### 4.3 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.

## 5. Nonclinical properties

### 5.1 Animal Toxicology or Pharmacology

Not required.

## 6. Description

Already mentioned and covered in the above points.

## 7. Pharmaceutical particulars

### 7.1 Incompatibilities

There are no known incompatibilities.

### 7.2 Shelf-life

24 months.

### 7.3 Storage and handling instructions

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