

Kofarest-PD SYRUP

1. Generic Name

Terbutaline, Ambroxol HCl, Guaiphenesin, Menthol

2. Qualitative and Quantitative composition

Terbutaline..... 1.25mg

Ambroxol HCl. 15mg

Guaiphenesin 50 mg

Menthol.....5mg

3. Dosage form and strength

Oral syrup containing Terbutaline 1.25mg, Ambroxol HCl 15mg, Guaiphenesin 50 mg.

4. Clinical particulars

4.1 Therapeutic indication

Kofarest PD syrup is indicated for the treatment of symptomatic relief of bronchospasm in bronchial asthma & chronic bronchitis.

4.2 Posology and method of administration

Recommended oral dose for Kofarest PD Syrup is:

Age	Dose
2-4 years	2.5 ml twice/ thrice a day
4-6 years	5ml twice/ thrice a day
6-12 years	5-10ml twice/ thrice a day

4.3 Contraindication

Kofarest PD 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 PD syrup to children with hypertension, cardiovascular disease, uncontrolled diabetes mellitus, hyperthyroidism, seizures or in patients who are unusually hypersensitive to sympathomimetic amines.
- Since mucolytics, such as Ambroxol, may disrupt the gastric mucosal barrier, Kofarest PD Syrup should be used with care in patients with a history of peptic ulceration.

4.5 Drug interactions

- Hypokalemia with high doses of β_2 -agonists may result in increased susceptibility to digitalis induced cardiac arrhythmias. Hypokalemia may be enhanced by concomitant administration of aminophylline or other xanthines, 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.
- Terbutaline should be administered with caution in patients being treated with monoamine oxidase (NAO) inhibitors or tricyclic antidepressants, since the action of Terbutaline 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

of 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: Safety of Kofarest PD Syrup has not been studied in pregnancy and lactation. Therefore, probable benefits should be weighed against possible risks, before prescribing.

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 PD Syrup is known.

4.8 Undesirable effects

An adverse drug reaction includes Thrombocytopenia, Palpitations, Tachycardia, Congenital anomaly, Vertigo, Tinnitus, Periorbital oedema, Nausea, Vomiting, Chest pain, Chills, Hepatic function abnormal, Anaphylactoid reaction, Hypersensitivity, Anaphylactic reaction, Anaphylactic shock, Pharyngitis, Pneumonia, Exposure during pregnancy, Blood pressure increased, Heart rate increased, Hypokalaemia, Muscle spasms, Myalgia, Tremor, Dizziness, Headache, Nervousness, Insomnia, Urinary retention, Cough, Dyspnoea, Rash, Pruritus, Flushing, Hypotension.

4.9 Overdose

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

5. Pharmacological properties

5.1 Mechanism of action

Terbutaline is a relatively selective beta2-adrenergic bronchodilator that has little or no effect on alpha-adrenergic receptors. The drug has exerts a preferential effect on beta2-adrenergic receptors but stimulates beta-adrenergic receptors less selectively than relatively selective beta2-agonists. Terbutaline appears to have a greater stimulating effect on beta-receptors of the bronchial, vascular, and uterine smooth muscles (beta2 receptors) than on the beta-receptors of the heart (beta1 receptors). This drug relaxes smooth muscle and inhibits uterine contractions, but may also cause some cardiostimulatory effects and CNS stimulation.

Guaiphenesin 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, Guaiphenesin increases the efficacy of the mucociliary mechanism in removing accumulated secretions from the upper and lower airway.

5.2 Pharmacodynamic properties

The pharmacologic effects of Terbutaline are at least in part attributable to stimulation through beta-adrenergic receptors of intracellular adenylyl cyclase, the enzyme that catalyzes the conversion of adenosine triphosphate (ATP) to cyclic- 3',5'- adenosine monophosphate (c-AMP). Increased c-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.

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.

Guaiphenesin 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.

Menthol has a cooling effect on the throat. It has been suggested that the benefits of menthol may be due to an effect on calcium channels of sensory nerves.

5.3 Pharmacokinetic properties

On inhalation of Terbutaline, less than 10% of the drug is absorbed from the airways. The remainder is swallowed where it is variably absorbed from the gastrointestinal tract. Fasting bioavailability after oral doses is reported to be about 14 to 15% and is reduced by food. Terbutaline undergoes extensive first-pass metabolism by sulfate (and some glucuronide) conjugation in the liver and the gut wall. It is excreted in the urine and faeces partly as the inactive sulfate conjugate and partly as unchanged Terbutaline, the ratio depending upon the route by which it is given. The terminal half-life after single and multiple dosing is reported to be between 16 and 20 hours. There is some placental transfer. Trace amounts are distributed into breast milk.

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

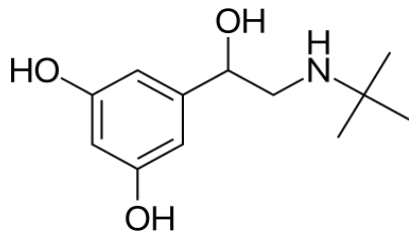
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

NA.

7. Description

Terbutaline is in a class of medications called beta agonists. Its chemical name is 5-[2-(tert-butylamino)-1-hydroxyethyl]benzene-1,3-diol; sulfuric acid and its chemical structure is:



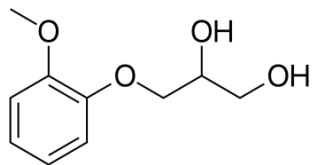
Its empirical formula is C₁₂H₁₉NO₃ and its molecular weight is 225.284 g/mol.

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 C₁₃H₁₉Br₂ClN₂O 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 PD Syrup is available in bottle of 60ml.

8.4 Storage and handling instructions

Store below 25°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

CENTAUR PHARMACEUTICALS PVT. LTD. , Lab Daffodil and Goa Antibiotics

11. Details of permission or license number with date

158(248)/MFG/DFDA/2013/878 dated. 10.06.2013 for export to Nigeria.

158(248)/MFG/DFDA/2013/4579 dated. 07.01.2013 for export to Cambodia.

158(248)/MFG/DFDA/2012/6397 dated. 29.02.2012 for export to Macau.

158(248)/MFG/DFDA/2011/4573 dated. 15.11.2011 for export to Mozambique.

158(248)/MFG/DFDA/2014/5724 dated. 13.03.2014 for export to Tajikistan.

158(248)/MFG/DFDA/2017/1590 dated. 14.06.2017 for export to Ethipoia.

158(248)/MFG/DFDA/2003/6749 dated. 20.01.2004 for export .

158(248)/MFG/DFDA/2020/1215 dated. 10.08.2020 for export to Zambia.

158(289)/MFG/DFDA/2006/14384 dated. 25.01.2010 for domestic.

Date of revision: January 2022.