

PLZ MAKE CORRECTION WITHIN 30 MIN

Proposed Art work for Registrations Purpose only
Actual size 100 %

FRONT SIDE 105 X 297 MM**BACK SIDE 105 X 297 MM****RESPIMAX**

Ambroxol hydrochloride, Salbutamol sulphate, Guaiphenesin

COMPOSITION

Each 5 ml contain:
 Ambroxol Hydrochloride BP.....15 mg
 Salbutamol Sulfate BP
 Eq. To Salbutamol.....1mg
 Guaiphenesin.....50 mg
 Mentholated Syrup Base.....Q.S

INDICATIONS

RESPIMAX is indicated in productive cough associated with asthmatic bronchitis, bronchospasm, chronic obstructive pulmonary disease (COPD), Smokers cough.

MECHANISM OF ACTION

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.

Salbutamol is a beta(2)-adrenergic agonist and thus it stimulates beta(2)-adrenergic receptors. Binding of albuterol to beta(2)-receptors in the lungs results in relaxation of bronchial smooth muscles. It is believed that salbutamol increases cAMP production by activating adenylate cyclase, and the actions of salbutamol are mediated by cAMP. Increased intracellular cyclic AMP increases the activity of cAMP-dependent protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular calcium concentrations. A lowered intracellular calcium concentration leads to a smooth muscle relaxation and bronchodilation. In addition to bronchodilation, salbutamol inhibits the release of bronchoconstricting agents from mast cells, inhibits microvascular leakage, and enhances mucociliary clearance.

Guaifenesin is thought to act as an expectorant by increasing the volume and reducing the viscosity of secretions in the trachea and bronchi. It has been said to aid in the flow of respiratory tract secretions, allowing ciliary movement to carry the loosened secretions upward toward the pharynx. Thus, it may increase the efficiency of the cough reflex and facilitate removal of the secretions. Guaifenesin has muscle relaxant and anticonvulsant properties and may be acting as an NMDA receptor antagonist.

PHARMACOKINETICS

Ambroxol hydrochloride:

Absorption: Ambroxol hydrochloride is rapidly absorbed (70-80%) after oral administration. The time to reach peak plasma concentration is approximately 2 hours.

Distribution: The distribution half-life of ambroxol hydrochloride is around 1.3 hours.

Metabolism: Metabolite is dibromoanthranilic acid (activity unspecified).

Excretion: Primarily via the kidneys. Renal clearance (rate) is approximately 53 ml/minute; approximately 5-6% of a dose is excreted unchanged in the urine. The elimination half-life of ambroxol hydrochloride is biphasic, with an alpha half-life of 1.3 hours and a beta half-life of 8.8 hours.

Salbutamol:

After oral administration, approximately 50% of salbutamol is absorbed from the intestinal tract with a slower onset of action, reaching a peak at about 2 hours after intake. After inhalation, salbutamol reaches the lungs directly and acts within 3-5 minutes with a peak at 15-20 minutes. Overall duration of action of salbutamol is 4-6 hours. It is metabolized in the intestinal tract and in the liver and is excreted via the urine.

Guaifenesin:

Guaifenesin is well absorbed from the gastrointestinal tract. It is metabolised and then excreted in the urine. The half-life in plasma is approximately 1 hour.

ADVERSE REACTIONS

Most common adverse reactions may include tachycardia, arrhythmia, flushing, myocardial ischemia, disturbances of sleep and behaviour.

Ambroxol include gastrointestinal side effects may occur but these are mild.

Salbutamol include fine tremor, anxiety, headache, muscle cramp, dry mouth and palpitation.

WARNINGS/PRECAUTIONS

Ambroxol hydrochloride has not been shown to have any teratogenic or toxic effects on the foetus. It is advisable to avoid use during the first trimester of pregnancy.

Salbutamol should be used with caution in patients with cardiac arrhythmia, hypertension, hyperthyroidism, convulsive disorders and diabetes mellitus. It should be taken with extreme caution in persons taking tricyclic antidepressants, monoamine oxidase inhibitors, loop diuretics or thiazide diuretics. Beta-receptor blocking drugs should be avoided during salbutamol therapy because these drugs block the bronchodilator effect of salbutamol.

Guaifenesin should not use in excessive amount because may cause nausea and vomiting. If cough persists for more than one week, accompanied by high fever, rash or headache, consult the physician. Use caution when driving, operating machinery, or performing other hazardous activities. Guaifenesin may cause dizziness. If you experience dizziness, avoid these activities.

DRUG INTERACTIONS

Ambroxol hydrochloride:

Drug interactions for ambroxol hydrochloride are not known.

Salbutamol:

Diuretics, corticosteroids and xanthines may augment hypokalaemia. CV effects potentiated by MAOIs, TCAs, sympathomimetics. Increases absorption of sulfamethoxazole when used together. May markedly increase heart rate and BP when used with atomoxetine. Reduces serum levels of digoxin. Hypokalaemia induced by salbutamol increases the risk of digitalis toxicity. BP should be closely monitored if linezolid is used concurrently with salbutamol.

Guaifenesin:

No medications are expected to react with guaifenesin when taken alone. However, this does not mean that drug interactions can be dismissed when taking guaifenesin. Because it is often combined with other medicines in cold and cough products, those other medicines could cause drug interactions. Check the ingredient list, and consult your healthcare provider before taking guaifenesin with any medications.

CONTRAINDICATIONS

Contraindicated in patients with a history of hypersensitivity to any of the component of the product or its parent compounds.

Ambroxol is also contraindicated in patients with completely impaired renal function and with gastric ulceration.

Salbutamol is also contraindicated in patients with pre-existing cardiac tachyarrhythmias.

PREGNANCY AND LACTATION

Ambroxol hydrochloride has not been shown to have any teratogenic or toxic effects on the foetus. It is advisable to avoid use during the first trimester of pregnancy.

Salbutamol is a pregnancy category C drug. It should be used during pregnancy only if absolutely essential. During pregnancy, inhalation of salbutamol has particular advantage as the therapeutic action can be achieved without the requirement for such plasma concentration liable to have an effect on the fetus. Guaifenesin available evidence and/or expert consensus is inconclusive or is inadequate for determining infant risk when used during pregnancy and breastfeeding. Weigh the potential benefits of drug treatment against potential risks before taking this drug during pregnancy and breastfeeding.

DOSE

Adult dose: 5 ml to be taken 3-4 times daily.

Children : 2.5-5 ml 3-4 times daily or as directed by the physician.

OVERDOSE AND TREATMENT

Ambroxol hydrochloride:

No information is available on overdosage with ambroxol hydrochloride.

Salbutamol:

The most common symptoms of overdose with salbutamol are tremor, palpitation and tachycardia. It may also produce arrhythmias, hypertension, angina, seizures, nervousness, fatigue, malaise, headache, dizziness, sleeplessness, dry mouth and even cardiac arrest.

Treatment is symptomatic with discontinuation of salbutamol is needed. A cardio-selective beta receptor blocking drug may be given by intravenous injection in patients presenting with tachycardia and palpitation. In general, beta receptor blocking drugs should be used cautiously as they may cause bronchospasm in sensitive persons. Hypokalaemia may occur following overdose with salbutamol. Serum potassium level should be monitored.

Guaifenesin:

Nausea and vomiting may occur.

In the event of overdosage, discontinue medication and seek medical help immediate.

PRESENTATION

100ml Amber Color Bottle Pack

STORAGE

Store in a dry place at a temperature below 30°C.

Manufactured By:
 West-Coast Pharmaceutical Works Ltd.
 FP No. 17 & 16/5, Meldi Estate,
 B/S. Meldi Mata Temple,
 Nr. Gota Railway Crossing,
 At: Gota, Ahmedabad-382 481, Gujarat.

Titulaire de l'AMM/MA Holder:
BEKRA PHARMA UK LTD
 13, LAVINGTON
 LONDON, UNITED KINGDOM.

ARTWORK SPECIFICATION :**DESIGN DEVELOPED BY :**

DESIGN DATE :

PRODUCT NAME : **RESPIMAX**

PRODUCT FOR : EXPORT

PACKING FOR : Insert

ARTWORK CHECKED : SIZE W H L CMYK BLK CLR K100 CONVERT Code : 00000000**DESIGN APPROVED BY :**

PRO.DEV. SIGN.

Q.A. SIGN.

Q.C. SIGN.

FDA SING.

PRO. CO.

PLANT. HEAD

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Dt.

RESPIMAX®

Ambroxol, Salbutamol & Guaïfénésine

COMPOSITION

Chaque 5 ml de **RESPIMAX®** contient:
Ambroxol HCl BP.....15 mg
Sulfate de Salbutamol BP
Eq. à Salbutamol BP..... 1 mg
Guaïfénésine 50 mg
Base de sirop mentholée.....Q.S

INDICATIONS

RESPIMAX® est indiqué pour le traitement de la toux productive associée à un asthme bronchique, un bronchospasme, les maladies pulmonaires obstructives chroniques, la toux du fumeur.

MÉCANISME D'ACTION

L'ambroxol possède des propriétés mucokinétiques et expectorantes. Par son action sur les cellules sécrétrices, il stimule la sécrétion bronchique et favorise la production d'un mucus plus mobilisable. Il augmente également l'activité ciliaire.

Le salbutamol est un agoniste des récepteurs bêta-adrénergiques présentant une action beaucoup plus sélective sur les récepteurs bêta-2. Il va intervenir sur le muscle lisse bronchique assurant ainsi une bronchodilatation rapide et persistante.

La guaïfénésine intervient également dans la régulation des troubles de la sécrétion bronchique.

PHARMACOCINÉTIQUE

Ambroxol Hcl:

Absorption: Rapide (70-80%) après une administration orale. Le pic plasmatique est atteint après environ 2 heures.

Distribution: Elle est rapide et le taux de fixation aux protéines plasmatiques est d'environ 90%.

Excrétion: Elle est principalement rénale. Sa demi vie d'élimination est biphasique, avec une demi-vie alpha de 1.3 heures et une demi-vie Béta de 8.8 heures.

Salbutamol:

Après une administration orale, sa biodisponibilité est d'environ 50%. Le salbutamol est absorbé au niveau du tractus intestinal, atteint son pic plasmatique après 2 heures et son élimination est urinaire.

Guaïfénésine:

La guaïfénésine est bien absorbée au niveau du tractus gastro-intestinal. Après métabolisation, son élimination est urinaire. Sa demi-vie plasmatique est d'environ 1 heure.

EFFETS SECONDAIRES

Les plus courantes sont: la tachycardie, les arythmies, rougeur, ischémie myocardiale, troubles du sommeil et du comportement. Des troubles gastro-intestinaux peuvent également être causées par l'Ambroxol..

Salbutamol est responsable de tremblement, anxiété, céphalées, crampes musculaires, sécheresse de la bouche et palpitations.

PRÉCAUTIONS D'EMPLOI

Ambroxol Hcl n'a pas montré d'effet tératogène ou toxique sur le foetus. Néanmoins il est préférable d'éviter son utilisation au cours du premier trimestre de la grossesse.

RESPIMAX® doit être utilisé avec précaution:

- chez les patients avec troubles du rythme cardiaque, hypertension, hyperthyroïdie, désordre convulsif et diabète.
- chez les patients sous antidépresseurs tricycliques, inhibiteurs de la monoamine oxydase, diurétiques de l'anse ou thiazidiques. Les Béta-bloquant doivent être évité lors du traitement car ceux-ci bloquent l'effet bronchodilatateur de celui-ci.

L'utilisation excessive de la guaïfénésine est susceptible de causer des nausées et vomissements.

Consulter le médecin en cas de persistance de la toux au delà d'une semaine accompagnée de la fièvre, manifestations cutanées ou céphalées.

Une prudence est requise lors de la conduite et utilisation des machines, la guaïfénésine pouvant être responsable de la survenue des vertiges.

INTERACTIONS MÉDICAMENTEUSES

Liées à l'ambroxol:

Les interactions médicamenteuses avec l'ambroxol ne sont pas connues.

Liées au salbutamol:

Les diurétiques, corticostéroïdes et xanthines peuvent augmenter l'hypokaliémie. Les effets cardio-vasculaires sont potentiellement avec les IMAO, les antidépresseurs tricycliques et sympathomimétiques.

L'augmentation de l'absorption du sulfaméthoxazole, augmentation du risque de toxicité digitale. La pression sanguine doit être surveillée si le linezolid est administré avec le salbutamol.

Liées à la guaïfénésine:

Aucun médicament ne devrait réagir avec la guaïfénésine. Les interactions rencontrées proviennent le plus souvent des médicaments combinés à la guaïfénésine lors du traitement de la toux..

CONTRE-INDICATIONS

RESPIMAX® est contre indiqué:

- en cas d'hypersensibilité à l'une de ses composantes;
- chez les insuffisants rénaux et ceux avec ulcération gastrique(Ambroxol);
- chez les patients avec troubles du rythme cardiaque préexistant(Salbutamol).

GROSSESSE ET ALLAITEMENT

RESPIMAX® n'a montré aucun effet tératogène ou toxique sur le foetus. Il est cependant conseillé d'éviter son utilisation au cours du premier trimestre de la grossesse.
RESPIMAX® devra être utilisé avec prudence au cours de la grossesse et de l'allaitement.

POSOLOGIE

La posologie de **RESPIMAX®** est la suivante:

- Enfants : 2.5 ml à 5 ml en 3-4 prises.
- Adulte: 5 ml en 3-4 prises journalières.

SURDOSAGE

Les symptômes les plus courants en cas de surdosage au salbutamol sont: tremblements, palpitations et tachycardie. Les arythmies, hypertension, angines, nervosité, fatigue, vertige, céphalées, insomnie, sécheresse buccale. Le traitement est symptomatique, un bêta-bloquant cardiosélectif peut être administré chez les patients présentant une tachycardie ou des palpitations. Une surveillance se fera pour prévenir l'hypokaliémie. Des nausées et vomissements peuvent caractériser une surcharge en guaïfénésine.

Un arrêt du traitement s'impose en plus d'un avis médical.

PRÉSENTATION

Flacon de 100ml dans un carton

STORAGE

Conserver au frais à une température ne dépassant pas 30°C.

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