1.6. PRODUCT INFORMATION

1.6.1.SUMMARY OF PRODUCT CHARACTERISTICS FOR PHARMACEUTICAL PRODUCTS

1 NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

PAIDOTERIN DECONGESTANT, liquid.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Per 5 ml of syrup: Phenylephrine hydrochloride (I.C.D.), 5 mg; Diphenhydramine hydrochloride (I.C.D.), 5 mg; Chlorpheniramine maleate (I.C.D.), 0.75 mg.

Excipients with known effect:

Each doses of 5 ml contains 1666.67 mg saccharin, 5,72 mg methyl parahydroxybenzoate (E 219) and 150.55 µg amaranth (E 123).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Syrup

4 CLINICAL PARTICULARS

4.1. *Therapeutic indications*

Relief of the symptoms of congestion of the mucosa of the upper airways that accompanies perennial or seasonal allergic rhinitis.

4.2. *Posology and method of administration*

The recommended doses are the following:

Children aged 2 to 6 years: 5 ml every 6 or 8 hours.

Children aged 6 to 12 years: 10-15 ml every 6 or 8 hours.

Adults: 15-20 ml every 6 or 8 hours.

It should be administered preferably after meals. 1 teaspoonful is equivalent to 5 ml. As an alternative option, the medicinal product can be dosed using the dosing cup (with marks at 2.5, 5, 10, 15 and 20 ml) included in the presentation.

Each of the doses should never be greater than twice the indicated dose.

4.3. Method of administration

Oral administration.

4.4. Contraindications

-Hypersensitivity to any of the components of this medicinal product.

-Children under 2 years of age.

The speciality PAIDOTERIN DECONGESTANT should be administered with caution in patients with hypertension, severe cardiovascular conditions, glaucoma, prostatic hypertrophy, bladder neck obstruction and urinary retention.

4.5. Special warnings and precautions for use

Patients who are sensitive to a certain antihistamine can be also sensitive to others. This medicinal product contains 1.665 g of sucrose in 5 ml, this should be taken into account by patients with hereditary intolerance to fructose, glucose/galactose malabsorption, sucrase-isomaltase deficiency and by diabetic patients. Sportspeople should be informed of the fact that this medicinal product contains a component that may give a positive result in the analytical doping control. The use of this medicinal product is not recommended in children under 1 year. Newborns and premature infants are more likely to suffer anticholinergic side effects. A paradoxical reaction characterized by hyperexcitability may occur in older children under treatment with antihistamines.
Use in elderly patients: anticholinergic effects and CNS-stimulating effects are likely to occur and there is risk of precipitating an undiagnosed glaucoma.

4.6. Interaction with other medicinal products and others forms of interaction

Medicinal products that cause CNS depression: the simultaneous use may enhance the CNS depressant effects of these medicinal products or of antihistamines.
Tricyclic antidepressants: the simultaneous use of antihistamines may enhance the CNS depressant effects as well as the anticholinergic effects of tricyclic antidepressants or antihistamines contained in these associations. They may also enhance the cardiovascular effects of phenylephrine.
Maprotiline: the simultaneous use of these medicinal products may enhance the SNC depressant effects of either maprotiline or antihistamines, as well as the anticholinergic effects of antihistamines. The cardiovascular effects of phenylephrine can also be enhanced.
Monoamine-oxidase Inhibitors (MAOIs) including furazolidone, pargyline and procarbazine: the simultaneous use with antihistamines may prolong and potentiate the antimuscarinic and CNS depressant effects of antihistamines.
Anticholinergic drugs or other medicinal products with anticholinergic actions: the anticholinergic effects may be enhanced.
Alcohol: the simultaneous use may potentiate the CNS depressant effects of alcohol or of antihistamines.
Sympathomimetic amines: the simultaneous use of sympathomimetic amines may prolong and potentiate their cardiac stimulant and vasopressor effects.
Alpha-adrenergic blockers: when administered before phenylephrine, they may block the pressor response to phenylephrine and cause severe hypotension. They may also diminish the pressor effect and shorten the duration of action of phenylephrine.
Inhaled halogenated hydrocarbon anesthetics: when used simultaneously with phenylephrine they can increase the risk of severe ventricular arrhythmias.
Local anesthetics: phenylephrine should not be used in combination with a local anesthetic for the anesthesia of areas irrigated by terminal arteries due to the risk of ischemia.
Beta-adrenergic blocking agents: the therapeutic effects of these drugs can be inhibited when they are used simultaneously with phenylephrine; likewise, the adrenergic beta-blocker can cause alpha-adrenergic activity without opposition, with risk of hypertension and excessive bradycardia.
Digitalic glucosides: when they are used simultaneously with phenylephrine the risk of cardiac arrhythmias can be increased.
Hay ergot alkaloids and methysergide: the simultaneous use of dihydroergotamine, ergometrine, methylergometrine or methysergide with phenylephrine can cause an increase in vasoconstriction. Phenylephrine also interacts with ergoloid mesylates or ergotamines so the simultaneous use is not recommended.
Doxapram: the simultaneous use with phenylephrine can increase their pressor effects.
Methyldopa or trimethaphan: their simultaneous use with phenylephrine can enhance the pressor response of phenylephrine.

4.7. Fertility, pregnancy and lactation

The innocuousness of the speciality PAIDOTERIN DECONGESTANT in pregnancy has not been established. Its use is not recommended in nursing women since there is risk of appearing side effects in

the baby, such as unusual excitement or irritability, as small quantities of antihistamines are excreted in milk.

4.8. Effects on ability to drive and use machines

Due to the fact that this medicinal product can cause somnolence, it can have an effect on the ability to drive vehicles and use machines, as it could be dangerous.

4.9. Undesirable effects

Exceptionally, somnolence can occur. Rarely, blood dyscrasias, increase in the skin's sensitivity to the sun, increase in sweating and loss of appetite can occur. Rarely, a paradoxical reaction can also occur (nightmares, excitement, nervousness, etc.), it is more likely to occur in children and in elderly patients; these patients are also more likely to suffer confusion, difficulty or pain during micturition, somnolence, dizziness and dry mouth, nose and throat.

4.10. Overdose

Should acute intoxication due to overdose occur, the treatment consists of the administration of an emetic or gastric lavage with solution of sodium bicarbonate at 5%, activated charcoal and catharsis. Should ventricular tachycardia occur lidocaine should be administered and propranolol if there is no response. In case of seizures diazepam should be administered. In case of severe hypertension nitroprusside or phentolamine should be administered. If the anticholinergic effects are intractable physostigmine should be administered. Hemodialysis and hemoperfusion are not very useful. In case of heart failure vasopressor support should be provided and in case it fails intra-aortic balloon should be used. Electrocardiographic and vital signs monitoring should be carried out. In symptomatic patients urine controls and electrolytes in blood determinations should be carried out.

5 PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Therapeutic group: R01BA53.

The speciality PAIDOTERIN DECONGESTANT is an association of three active ingredients: diphenhydramine hydrochloride (ethanolamine derivative), chlorphenamine maleate (propylamine derivative) and phenylephrine hydrochloride. Diphenhydramine hydrochloride and chlorphenamine maleate are antihistamines that act by competing with the histamine released from mast cells in the mucous membranes by the H1 receptors located in the target organs. They prevent the histamine-mediated responses, but they do not revert them. The antimuscarinic actions of antihistamines provide a drying effect on the nasal mucosa. Phenylephrine is a sympathomimetic amine that acts on alpha-adrenergic receptors of the respiratory tract mucosa causing vasoconstriction, that reduces temporarily the swelling associated to the inflammation of the mucous membranes that cover the nasal cavities, acting as a decongestant.

5.2. Pharmacokinetic properties

Phenylephrine hydrochloride is absorbed in an irregular way in the gastrointestinal tract and it undergoes an extensive first-pass metabolism that takes place in the intestine and in the liver through monoaminooxidase. Diphenhydramine hydrochloride is easily absorbed after its oral administration, the effects appear in 15-60 minutes. The maximum drug concentration is reached in about 2 hours. Its biotransformation is mainly hepatic and renal in a small proportion. The elimination is renal. Chlorphenamine maleate is absorbed slowly from the gastrointestinal tract and the maximum plasmatic concentrations appear 2 to 6 hours after the oral administration. Chlorphenamine seems to undergo a considerable first-pass metabolism. It is excreted mainly in urine.

5.3. Preclinical safety data

Phenylephrine: The LD_{50} in rats is 17±1.1 mg/K administered by the intraperitoneal route and it is 33±2 mg/Kg administered by the subcutaneous route. The estimated minimum lethal dose for adults it is 1 g.

Diphenhydramine: The LD_{50} in rats is 500 mg/Kg administered by the oral route. The estimated minimum lethal dose is 3 g. The toxic effects can be caused by plasmatic concentrations greater than 1 μg/ml.

Chlorphenamine: The LD_{50} in rats is 162 mg/Kg administered by the oral route. The toxic effects can appear with plasmatic concentrations greater than 20 μg/ml.

6 PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Citric acid, saccharin sodium, saccharose, amaranth (E 123), methyl parahydroxybenzoate (E 219), glycerin, sodium citrate, strawberry essence and deionised water.

6.2. Incompatibilities

MAO inhibitors (monoaminooxidase).

6.3. Shelf life

The shelf life of the product packaged for its commercialization is 3 years.

6.4. Special precautions for storage

It does not require special precautions for storage. The bottle should be protected from light and from very low temperatures.

6.5. Nature and contents of container

Polyethylene bottle and polypropylene cap. A polypropylene dosing cup is also included in the packaging (with marks at 2.5, 5, 10, 15 and 20 ml). The volume of syrup per bottle is 100 ml.

6.6. Special precautions for disposal and other handling

No special instructions required.

7 MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

Laboratorio ALDO-UNIÓN, S.L.

Baronesa de Maldá, 73

08950 Esplugues de Llobregat (Barcelona)

8 MARKETING AUTHORISATION NUMBER

For Spain: 37.653

9 DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

10 DATE OF REVISION OF THE TEXT

March 2012