SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Medovent Elixir, 15mg/5 ml, oral solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of oral solution contains 15 mg ambroxol hydrochloride.

Excipients with known effect: propylene glycol 1.5g/5ml, sucrose 1.75g/5ml, sorbitol 250mg/ml, and ethanol 50mg/ml.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.
The solution is clear, transparent with a fruity odour.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Mucolytic treatment of acute and chronic bronchopulmonary diseases, which are associated with abnormal mucus secretion and impaired transport.

Medovent Elixir is indicated for the treatment of adults, children up to 12 years of age and adolescents from 12 years of age.

4.2. Posology and method of administration

In the treatment of acute respiratory diseases, a doctor should be consulted if symptoms do not improve or worsen during treatment.

Posology

Adults

10 ml 3 times a day.

Paediatric population

Adolescents over 12 years: 10 ml 3 times a day

When treating children under 12 years of age, the following dosage scheme is recommended depending on the severity of the disease:
Children 6 - 12 years: 5 ml 2 - 3 times a day
Children 2 - 5 years: 2.5 ml 3 times a day
Children under 2 years: 2.5 ml 2 times a day

Impaired liver or kidney function
No dosage adjustment is necessary in patients with impaired liver or kidney function.

Method of administration
Medovent Elixir can be taken with or without food.

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Taking this drug is contraindicated if you have rare hereditary diseases which can cause an incompatibility with one of the excipients (see section 4.4).

4.4. Special warnings and precautions for use

There have been reports of severe skin reactions such as erythema multiforme, Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) and acute generalised exanthematous pustulosis (AGEP) associated with the administration of ambroxol. If symptoms or signs of a progressive skin rash (sometimes associated with blisters or mucosal lesions) are present, ambroxol treatment should be discontinued immediately and medical advice should be sought.

In case of severe renal or liver impairment, ambroxol hydrochloride should be used only on medical advice.
In severe renal impairment ambroxol accumulation of metabolites formed in the liver is expected.

This medicine contains 1.5 g propylene glycol in each 5 ml oral solution.
Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates and children less than 5 years old.
While propylene glycol has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis.

Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

This medicine contains 3.17% ethanol (alcohol), i.e. up to 250 mg per 5 ml oral solution, equivalent to 6.32 ml beer, 2.64 ml wine per dose.
The small amount of alcohol in this medicine will not have any noticeable effects.

This medicine contains 1250 mg sorbitol in each 5 ml oral solution.
Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.
Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

This medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5. Interaction with other medicinal products and other forms of interaction

Administering ambroxol hydrochloride together with antibiotics (amoxicillin, cefuroxime, erythromycin) leads to an increase in the concentration of antibiotics in bronchopulmonary secretions and sputum.
No clinically significant adverse interactions with other drugs have been reported.

4.6. Fertility, pregnancy and lactation

Pregnancy
Ambroxol hydrochloride crosses the placental barrier. Preclinical studies do not indicate direct or indirect harmful effects with regard to pregnancy, embryo-fetal development, parturition or postnatal development.

Extensive clinical experience beyond the 28th week of pregnancy has not revealed any evidence of harmful effects to the fetus. Nevertheless, the general principles of medication use during pregnancy should be followed. Especially in the 1st trimester, the use of ambroxol preparations is not recommended.

Breast-feeding
Ambroxol hydrochloride is excreted in human milk. Although occurrence of harm to breastfed infants is not expected, ambroxol hydrochloride is not recommended for nursing mothers.

Fertility

Preclinical studies do not indicate direct or indirect harmful effects on fertility.

4.7. Effects on ability to drive and use machines

There are no data on the occurrence of any effects on the ability to drive and use machines. No studies regarding ambroxol hydrochloride effect on the ability to drive and use machines have been conducted.

4.8. Undesirable effects

Adverse reactions are classified using the following frequency convention: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1000 to <1/100), rare (≥ 1/10000 to <1/1000), very rare (<1/10000), not known (cannot be estimated from the available data).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Immune system disorders

Rare: hypersensitivity reactions

Not known: anaphylactic reactions including anaphylactic shock, angioedema and pruritus

Nervous system disorders

Common: dysgeusia (taste disturbance e.g.)

Respiratory, thoracic and mediastinal disorders

Common: pharyngeal hypoaesthesia

Gastrointestinal disorders

Common: nausea, oral hypoaesthesia

Uncommon: diarrhea, vomiting, dyspepsia, dry mouth, abdominal pain

Not known: dry throat

Skin and subcutaneous tissue disorders

Rare: rash, urticaria

Not known: angioedema, pruritus, severe cutaneous adverse reactions (including erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis and acute generalized exanthematous pustulosis).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions is an important way to gather more information to continuously monitor the benefit / risk balance of the medicinal product. Any suspected adverse reactions should be reported via the national reporting system.

4.9. Overdose

There are no described overdosing effects in man. Based on reports of accidental overdoses or / and errors in administration, observed symptoms are similar to known side effects at recommended doses and if they occur, symptomatic treatment should be administrated.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: mucolytics, ATC code: R05CB06

Ambroxol hydrochloride, the active ingredient of Medovent Elixir has been shown to increase respiratory tract secretion. It increases the secretion of surfactant in the lung and increases the ciliary activity. These actions result in improved mucus secretion and transport (mucociliary clearance). Mucociliary clearance improvement has been shown in clinical pharmacology studies. Stimulation of the secretion and mucociliary clearance facilitates expectoration and smoothes cough.

A local anesthetic effect was observed in the rabbit eye test, which can be explained by ambroxol properties of blocking the sodium channel. It has been shown in vitro that ambroxol hydrochloride blocks sodium channels in neurons; binding was reversible and dose dependent.

It has been demonstrated in vitro that cytokine released from blood mononuclear cells but also from polymorphonuclear cells and delineating tissue was significantly reduced by ambroxol hydrochloride. In clinical trials in patients with angina, pharyngeal pain and redness were reduced significantly. These pharmacological properties are consistent with additional observations from clinical trials regarding the efficacy of ambroxol hydrochloride on symptoms of upper respiratory tract, leading to rapid relief of pain and discomfort related to pain in ENT after inhalation.

Concomitant use of ambroxol hydrochloride and antibiotics (amoxicillin, cefuroxime, erythromycin) leads to an increase in the concentration of antibiotic in lung tissue (bronchopulmonary secretions and sputum).

5.2. Pharmacokinetic properties

Absorption

Ambroxol hydrochloride is rapidly and completely absorbed after oral formulations whose mechanism of transfer / release is unchanged dose dependent. Peak plasma concentrations occurred approximately 1 to 2.5 hours after administration of immediate release pharmaceutical forms after an average of 6.5 hours after oral extended release pharmaceutical forms / modified. The absolute bioavailability after administration of a 30 mg tablet was 79%. Showed that the relative bioavailability of extended-release capsules was 95% compared to a total daily dose of 60 mg (30 mg twice daily) administered as immediate release tablets.

Distribution

Distribution of ambroxol hydrochloride from blood to tissues is rapid and strong, the highest concentration of active substance is in the lung. The volume of distribution after oral administration was estimated at 552 l plasma protein binding is approximately 90% at therapeutic doses.

Biotransformation and elimination

About 30% of the oral administrated substance dose is metabolized to first-pass metabolism / first metabolic passage. Otherwise, ambroxol hydrochloride is metabolised primarily in the liver by glucuronidation and a small portion is metabolised in dibromanthranilic acid (about 10% of dose), except for minor metabolites.

Studies in human liver cells microsomes have shown that CYP3A4 is the predominant isoform responsible for the metabolism of ambroxol hydrochloride in dibromanthranilic acid.

After 3 days of oral administration, approximately 6% of the dose is recovered unmodified, while about 26% of the dose is recovered in urine in conjugated form. Elimination half-life of ambroxol hydrochloride is approximately 10 hours. Total elimination has an average of 660 ml / min, while the renal clearance represents about 8% of the total clearance.

Special Populations

In patients with hepatic impairment, ambroxol hydrochloride elimination is reduced, resulting in higher plasmatic concentrations of 1.3 to 2 times. Because of the high therapeutic concentrations, no dose adjustment is required.

Other groups

There is no evidence that age and sex affect from a clinically significant point of view the pharmacokinetics of ambroxol in significant and therefore there is no need for changing the dose.

There is no evidence that foods affect the bioavailability of ambroxol hydrochloride.

5.3. Preclinical safety data

Ambroxol hydrochloride has a low acute toxicity.
After oral doses of 150 mg / kg / day administration (mice, 4 weeks), 50 mg / kg / day (rat, 52 and 78 weeks), 40 mg / kg / day (rabbit, 26 weeks) and 10 mg / kg / day (dog, 52 weeks) no adverse effect was seen, therefore the product was included in NOAEL class ("No Observed Adverse Effect Level - NOAEL"). For ambroxol, no target organ regarding toxicologically was found.
Four weeks studies with repeated toxic doses of intravenous ambroxol hydrochloride in rats (4, 14 and 64 mg / kg / day) and dogs (45, 90 and 120 mg / kg / day (3 hours infusion / day)) did not show the occurrence of severe local or systemic toxicity, including histopathology. All side effects were reversible.
There was no evidence that ambroxol hydrochloride may be embryotoxic or teratogenic in studies with oral administrated doses up to 3000 mg / kg / day in rats and up to 200 mg / kg / day in rabbits. At doses up to 500 mg / kg / day, fertility of male and female rats was not affected.
Dose without adverse effect level ("NOAEL") during peri-and postnatal development was 50 mg / kg, whereas the dose of 500 mg / kg was slightly toxic to female and puppies, as resulted by delayed increase in weight and size reduction.
Ambroxol hydrochloride has no mutagenic properties, according to the studies of genotoxicity *in vitro* (Ames test and chromosomal aberration test) and *in vivo* (micronucleus test).
There is no evidence of carcinogenicity in mice studies (50, 200 and 800 mg / kg / day) and rats (65, 250 and 1000 mg / kg / day), after being subjects of a diet of 105 and 116 weeks respectively.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Medovent Elixir also contains: tartaric acid, benzoic acid, propylene glycol, sorbitol (E420), ethanol, sodium hydroxide, commercial cherry and orange flavours, sucrose, and purified water.
Sucrose content is 35 % w / v. Ethanol content is 5 % w / v.

6.2. Incompatibilities

None known.

6.3. Shelf life

5 years.

6.4. Special precautions for storage

Store below 25°C, in the original package in order to protect from light.

6.5. Nature and contents of container

Amber, type III glass bottles, sealed with a tamper evident aluminium cap or a plastic tamper evident cap or a plastic child proof cap. Bottles are supplied with a measuring spoon or a measuring cup, and a patient information leaflet in a card carton.
Bottles containing 100 ml, 150ml and 200ml are available.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

Use the provided medicines measuring spoon for administration of the dose. Immediately after use wash the spoon in warm soapy water, rinse and dry. Keep the spoon, with the bottle of medicine in the carton provided.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7. MARKETING AUTHORISATION HOLDER

MEDOCHEMIE LTD, 1-10 Constantinoupoleos street, 3011 Limassol, Cyprus

8. MARKETING AUTHORISATION NUMBER

04517/06871/REN/2018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08/01/2015
Date of latest renewal: 28/04/2020

10. DATE OF REVISION OF THE TEXT

07/2023