SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
MUCICLAR 15 mg/5 ml syrup
MUCICLAR 75 mg slow-release capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
MUCICLAR 15 mg/5 ml syrup
100 ml of syrup contains:
Active ingredient: Ambroxol hydrochloride 300 mg

MUCICLAR 75 mg slow-release capsules
One capsule contains:
Active ingredient: Ambroxol hydrochloride 75 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Syrup; Slow-release capsule.

4. CLINICAL INFORMATION
4.1. Therapeutic indications
Secretion problems in acute and chronic bronchopulmonary disorders.

4.2. Posology and method of administration
Muciclar 15 mg/5 ml syrup: adults: 5-10 ml syrup 3 times a day, children over two years old: 5 ml of syrup 2 or 3 times a day.
Muciclar 75 mg slow-release capsule: adults: we recommend 2 capsules in a single administration after breakfast in the morning for 8 days (treatment of attack). Thereafter, the dose can be reduced to a single capsule until the end of the treatment.

4.3. Contraindications
Hypersensitivity to ambroxol hydrochloride or to any of the excipients. Serious changes to liver and/or kidney function.
Taking the medicinal product is contraindicated in the case of rare hereditary disorders that may be incompatible with one of the excipients (see para. 4.4.).
The drug is contraindicated in children under the age of 2 years (for oral forms).

4.4. Special warnings and precautions for use
Ambroxol must be administered with caution in patients with peptic ulcer disease.
In very few cases, while taking mucolytic substances such as ambroxol, serious skin lesions were observed such as Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN). Most of these could be explained by the severity of underlying diseases or other concomitant medications.
Also, in the initial phase of Stevens-Johnson syndrome or toxic epidermal necrolysis (TEN), patients may initially feel non-specific symptoms similar to those of flu, such as, for example fever, chills, rhinitis, cough and sore throat. Due to these misleading symptoms a symptomatic treatment can be taken with a cough and cold treatment.
If you experience new lesions of the skin or mucous membranes consult your doctor immediately and stop treatment with ambroxol as a precaution.
During the administration of the solution to be sprayed, since a cough due to irritation from inspiring aerosols too deeply may occur, you should try to breathe in and out normally during inhalation. In particularly sensitive patients, a pre-heating of that inhaled to body temperature may be recommended.

Patients suffering from bronchial asthma should use a bronchial spasmolytic before inhalation.

In the case of mild or moderate kidney failure, Muciclar may only be used after consulting your doctor. As with all medicinal products subject to hepatic metabolism and subsequent renal elimination, an accumulation of ambroxol metabolites in the liver in the presence of severe kidney failure is expected.

Mucolytics can cause bronchial obstructions in children under the age of 2. In fact, the drainage capacity of bronchial mucus is limited in this age range, due to the physiological characteristics of the respiratory tract.
They should not be used in children under 2 years of age (for the oral form) (see para. 4.3.).

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.

The syrup contains:
- **para-hydroxybenzoates**: can cause allergic reactions (even delayed).
- **sorbitol**: unsuitable in hereditary fructose intolerance. May cause upset stomach and diarrhoea.
- **glycerol**: dangerous in high doses. May cause headaches, upset stomach and diarrhoea.

The syrup also contains 3% vol. of **ethanol (alcohol),** e.g. up to 300 mg per dose (maximum dose), equivalent to 6 ml of beer, 2.5 ml of wine per dose.
It could be harmful to alcoholics.
This should be taken into account in pregnant or breast-feeding women, children and high-risk groups, such as those with liver diseases or epilepsy.
The capsules and granules for oral solution contain **sucrose**, therefore patients affected by rare genetic problems involving intolerance to fructose, malabsorption of glucose-galactose, or insufficiency of sucrase-isomaltase should not take this drug.

4.5. Interactions with other medicinal products and other forms of interaction
Following the administration of ambroxol, concentrations of antibiotics (amoxicillin, cefuroxime, erythromycin) in bronchopulmonary secretions and saliva increase.
No interactions with other medicines have been reported.

4.6. Pregnancy and breast-feeding
Ambroxol crosses the placental barrier. Animal studies have shown no directly or indirectly harmful effects to pregnancy, embryo/foetal development, birth or postnatal development.
Although preclinical studies and the wealth of clinical experience have shown no harmful effects on the foetus after the 28th week of gestation, it is recommended that you take the normal precautions when taking medicines in pregnancy. Taking ambroxol during the first trimester is particularly not recommended.
This medicine is excreted in breast milk, therefore the use of ambroxol is not recommended during breast-feeding. However, no negative effect for on a nursing infant is expected.
In pregnancy and while breast-feeding, the medicinal product is only administered in case of effective need and under the direct control of a doctor.

4.7. Effects on ability to drive and use machines
There are no demonstrated effects on the ability to drive and use machines. No studies have been carried out on the effects on the ability to drive and use machines.

4.8. Side effects
The side effects listed by frequency are indicated, using the following convention: Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000), frequency unknown (the frequency cannot be defined based on the data

available).

Immune system disorders
Rare: hypersensitivity reactions
Not known: Anaphylactic reactions, including anaphylactic shock, angioedema, itching and pruritus

Nervous system disorders
Common: Dysgeusia (e.g. alterations of the sense of taste)
Rare: Headache

Respiratory, thoracic and mediastinal disorders
Common: Hypoesthesia of the oral cavity and pharynx
Rare: Rhinorrhea
Not known: Bronchial obstruction

Gastrointestinal disorders
Common: Nausea
Uncommon: Vomiting, diarrhoea, dyspepsia, abdominal pain, dryness of mouth
Rare: Heartburn, constipation
Not known: Dry throat

Skin and subcutaneous tissue disorders
Rare: Skin rashes, urticaria, contact dermatitis
Not known: Severe cutaneous adverse reactions (including erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis and acute generalized exanthematous pustulosis).

Renal and urinary disorders
Rare: Dysuria

General disorders and administration site conditions
Rare: Fatigue

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via *http://medicinesauthority.gov.mt/reportingadversereactions*.

4.9. Overdose
So far specific symptoms of overdose have not been reported in humans. The symptoms observed in cases of accidental overdose and/or in cases of errors in the administration of medicines are consistent with the expected side effects of Muciclar in the recommended doses and may require symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Expectorants, excluding combinations with cough sedatives; mucolytic - ATC Code: R05CB06.
Ambroxol acts by regulating the transport of secretions throughout the respiratory tract. It has a marked mucolytic and mucus regulating activity. The pharmacological effect is exerted on the quality of the mucus, on ciliary function and on the production of alveolar surfactant.
Quality of the mucus: ambroxol stimulates the activity of serous glandular cells, it discharges mucus granules already formed, normalises the viscosity of that secreted and finally regularises the activity

of the tubuloacinar glands of the respiratory tract.
Ciliary function: ambroxol increases both the number of the microvilli of the vibratile epithelium, and the frequency of ciliary movements with a consequent increase in the transport speed of the secreted product and finally leads to normalisation of respiratory tone improving expectoration.
Increase in the production of surfactant: ambroxol stimulates type II pneumocyte to a greater production of alveolar surfactant thereby ensuring the stability of the lung tissue, enabling proper bronchioloalveolar purification and finally by facilitating respiratory mechanics and encouraging gaseous exchanges.

5.2. Pharmacokinetic Properties
The bioavailability of ambroxol was assessed in humans after oral administration of the medicinal product in healthy volunteers. It has been deduced that ambroxol is rapidly absorbed through the enteric tract. The half-life is approximately 10 hours and maximum serum levels are reached around the 2nd hour. The medicinal product is almost completely eliminated by the kidneys in the form of metabolites or unchanged. At the 24th hour the plasma level is still higher than 25 ng/ml.

5.3. Preclinical safety data
Ambroxol hydrochloride has a low acute toxicity index. In studies with repeated dosing, oral doses of 150 mg/kg/day (mouse 4 weeks), 50 mg/kg/day (rats 52 and 78 weeks), 40 mg/kg/day (rabbits 26 weeks) and 10 mg/kg/day (dogs 52 weeks) corresponded to dose levels without observable adverse effects ($NOAEL_S$). No target organ for toxicological effects has been identified.
Toxicity studies intravenously with ambroxol hydrochloride in rats, using 4, 16 and 64 mg/kg/day, and dogs using 45, 90 and 120 mg/kg/day (infusions 3 h/day), showed no serious systemic and oral toxicity including histopathology. Any adverse effects were reversible.
Ambroxol hydrochloride was not embryotoxic or teratogenic in studies in rats and rabbits when tested in oral doses up to 3,000 mg/kg/day and 200 mg/kg/day, respectively. Fertility in rats, both male and female, remained altered from doses up to 500 mg/kg/day. The "no observed adverse effect level" (NOAEL) during peri- and post-natal development is equal to 50 mg/kg/day, while doses of 500 mg/kg/day demonstrated a slight toxicity in pregnant women and the small, which manifested in a delay in the increase of body weight and with a reduction in the number of babies born.
Studies of in vitro (Ames and chromosome aberration test) and in vivo (rat micronucleus test) genotoxicity did not reveal any mutagenic potential of ambroxol hydrochloride. Ambroxol hydrochloride was not proven to be potentially carcinogenic in carcinogenesis studies in mice (50, 200 and 800 mg/kg/day) and rats (65, 250 and 1,000 mg/kg/day) when treated with a diet for 105 and 116 weeks respectively.

6. PHARMACEUTICAL INFORMATION
Syrup: sorbitol solution, glycerin, methyl p-hydroxybenzoate, propyl p-hydroxybenzoate, hydroxyethylcellulose, alcohol, saccharin, raspberry essence, purified water.
Capsules: sucrose, starch, natural and artificial resins, talc, polyvinylpyrrolidone.

6.2. Incompatibilities
There are no known incompatibilities with other medicinal substances.

6.3. Validity period
Syrup: 3 years;
Capsules: 5 years.

6.4. Special storage precautions
Syrup, capsules
Store at a temperature not exceeding 25°C.

6.5. Nature and contents of the container
Syrup: polyethylene terephthalate 200 ml bottle.

6.6. Special precautions for disposal and handling

Syrup: 5 ml of syrup corresponds to 15 mg of ambroxol; a dosing cup is attached to the package that has notches at a volume of 2.5 ml, 5 ml and 10 ml.

7. MARKETING AUTHORISATION HOLDER

PIAM FARMACEUTICI S.P.A. - Via XII Ottobre, 10 - 16121 Genoa

8. MARKETING AUTHORISATION NUMBER

MUCICLAR 15 mg/5 ml syrup - 200 ml bottle – MA037/00301
MUCICLAR 75 mg slow-release capsule - 20 capsules - MA037/00302

9. DATE OF FIRST AUTHORISATION/AUTHORISATION RENEWAL

MUCICLAR 15 mg/5 ml syrup - 9th August 2006 / 20th October 2011
MUCICLAR 75 mg slow-release capsule – 14th September 2006 / 20th October 2011

10. TEXT REVISION DATE

7th February 2025