Product Trade Name	**SEKROL® 15 mg/5 ml**
Drug Product name , strength and pharmaceutical form	**Ambroxol hydrochloride 15 mg/5 mL, Syrup**
Dossier ID	**CPR-RAD-SSEKRS15-RW**
Module 1.6.1	**Product information – Prescribing information (SmPC)**

MODULE 1 ADMINISTRATIVE INFORMATION AND PRODUCT INFORMATION

1.6 Product Information

1.6.1 Prescribing information (SmPC)

Enclosed is the section 1.5.1 Summary of Product Characteristics (SmPC) from the dossier CPR-RAD-SSEKRS15-V.2.0_31.10.2018.

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT (FPP)

Sekrol

Ambroxol hydrochloride

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 15 mg of ambroxol.

Each ml contains 3 mg ambroxol hydrochloride

Excipients with known effect :

Sodium metabisulphite (E223): 1 mg / 5ml

Benzoic acid (E210): 1 mg / 5ml

Sorbitol (E420): 2.5 g / 5ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup.

Colorless viscous solution with characteristic odor.

Bottle of 100 ml.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Sekrol is proposed for the symptomatic adjuvant treatment of airway congestion states related to stagnation of secretions in the tracheobronchial tree, occurring during chronic bronchitis.

4.2. Posology and mode of administration

4.2.1. Posology

Age	Dose in mg	Volume of syrup Sekrol 15mg/5ml
2 to years	7 to 15 mg 2 times a day	2,5 to 5 ml 2 times a day
5 to 12 years	15 to 30 mg 2 times a day	5 to 10 ml 2 times a day
12 years and older	30 to 60 mg 2 times a day	10 to 20 ml 2 times a day

For children under 2 years old, the use of Sekrol is strongly advised against.

4.2.2. Special populations

No special dosage recommandations

4.2.3. Pediatric population

Sekrol is contraindicated in children under 12 years of age.

4.2.4. Method of administration

Oral administration.

Sekrol can be administered with or without food.

4.3. Contraindications

- Sekrol is contraindicated in patients who are hypersensitive to the active substance or to any of the excipients listed in section 6.1 and also in children under 12 years of age.

- Patients with fructose intolerance must not take this medicine.

4.4. Special warning and precautions for use

-Sekrol syrup contains sorbitol. Patients with fructose intolerance must not take this medicine.

- Cases of severe skin reactions such as erythema multiforme, Stevens-Johnson syndrome (SSJ) / Lyell syndrome, and acute generalized exanthematous pustulosis (PEAG) associated with ambroxol hydrochloride have been reported. If signs or symptoms of progressive skin rash (sometimes associated with blisters or mucosal lesions) are present, treatment with ambroxol hydrochloride should be discontinued immediately and a physician should be consulted.

- In the presence of renal insufficiency or severe hepatopathy, Sekrol will only be given after consulting a doctor. As with all drugs metabolized by the liver and subsequently eliminated by the kidneys, severe kidney failure may produce an accumulation of metabolites generated by the liver.

- 5 ml of syrup contains 1 mg of sodium metabisulphite which can, in rare cases, cause hypersensitivity reactions and bronchospasm.

- 5 ml of syrup contains 1 mg of benzoic acid. Benzoic acid may increase jaundice risk in neonates (up to 4 weeks).

4.5. Interactions with other medicinal products and other forms of interactions

4.5.1. General information

No adverse clinical interactions between Sekrol and other drugs have been reported. The combination of a mucolytic with an antitussive is irrational.

4.5.2. Paediatric population

Sekrol is contraindicated in children under 12 years of age.

4.6. Fertility, pregnancy and lactation

4.6.1. Pregnancy

Ambroxol hydrochloride crosses the placental barrier. Nonclinical studies do not directly or indirectly indicate adverse effects on pregnancy, embryonic or foetal development, childbirth or postnatal development.
Extensive clinical experience with ambroxol hydrochloride after 28 weeks of pregnancy has not been shown to have deleterious effects on the foetus.
Nevertheless, the usual precautions regarding the use of drugs during pregnancy should be observed. Especially during the first trimester, the use of Sekrol is not recommended.

4.6.2. Lactation

Ambroxol hydrochloride is excreted in breast milk. Although no adverse effects are expected from breastfed infants, administration of Sekrol is not recommended during the lactation period.

4.6.3 Fertility

Non-clinical studies do not directly or indirectly indicate any adverse effects on fertility.

4.7. Effects on the ability to drive and use machines

Sekrol may cause drowsiness and dizziness, and may therefore have a minor influence on the ability to drive and use machines.
Post-marketing data showed no effect on the ability to drive and use machines. No studies on the effects on the ability to drive and use machines have been performed.

4.8. Undesirable effects

Summary of the security profile

The most commonly reported adverse reactions are gastrointestinal system effects such as nausea, vomiting, hypoaesthesia, and diarrhea. Hypoesthesia (oral / pharyngeal) and dysgeusia may also occur frequently. Itching and rash are reported more rarely.
Adverse reactions such as anaphylactic reactions, anaphylactic shock and angioedema may occur sporadically.

The frequencies of adverse reactions reported with ambroxol are defined as:

- very common (≥ 1/10)
- common (≥ 1/100 to < 1/10)
- uncommon (≥ 1/1,000 to < 1/100)
- rare (≥ 1/10,000 to < 1/1,000)
- very rare (< 1/10,000)
- not known (cannot be estimated from the available data)

Immune system disorders	
Hypersensitivity reactions	rare
Anaphylactic reactions, including anaphylactic shock	indeterminate frequency
Skin and subcutaneous tissue disorders	
Rash, urticaria	rare
Severe skin reactions (including erythema multiforme, Stevens-Johnson syndrome / Lyell's syndrome and generalized acute exanthematous pustulosis), angioedema and pruritus	indeterminate frequency
Nervous system disorders	
Dysgueusia	common

Headache, dizziness, somnolence, agitation	indeterminate frequency
Respiratory, thoracic and mediastinal disorders	
Pharyngeal hypoesthesia	common
Gastrointestinal disorders	
Oral hypoaesthesia, nausea	common
Vomiting, diarrhea, abdominal pain, dyspepsia, dry mouth	uncommon
Dry throat	rare

Sporadic cases of anaphylactic reactions including shock have been reported after marketing. If there is evidence of anaphylactic reaction (eg urticaria, angioedema, breathing difficulties, etc.), administration of the drug should be stopped without delay and medical advice is required.

4.9. Overdose

There are no specific overdose symptoms reported in humans. Based on reported cases of accidental overdose and treatment errors, the symptoms observed are the known adverse effects of Sekrol and may require symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Pharmacotherapeutic group: Preparation for cough and cold, expectorant, mucolytic.
ATC code: R05CB06.

Mechanism of action

Ambroxol hydrochloride increases secretions of the respiratory tract and the production of pulmonary surfactant and stimulates mucociliary activity. This increase induces an improvement in mucus flow and transport (mucociliary clearance).
Improved mucociliary clearance has been shown in pharmacological studies.
Increased secretions and mucociliary clearance facilitate expectoration and coughing.

Pharmacodynamic effects

The local anesthetic effect of ambroxol hydrochloride has been observed in the rabbit eye model and is probably the result of its sodium channel blocking properties: in vitro, ambroxol blocks neuronal sodium channels. The binding is reversible and depends on the concentration. This pharmacological property is consistent with the results of rapid pain relief and associated discomfort observed when ambroxol hydrochloride is inhaled in the treatment of symptoms of other upper respiratory diseases.
In vitro, ambroxol hydrochloride significantly reduced the release of cytokines by mononuclear or polymorphonuclear blood cells but also tissue-related.

Clinical efficacy and safety

In clinical studies, it was found that in patients with sore throat, pharyngeal redness and pain were significantly reduced.
Administration of ambroxol hydrochloride increases the concentration of antibiotic (amoxicillin, cefuroxime, erythromycin) in bronchopulmonary secretions and sputum.

5.2. Pharmacokinetic properties

Renal failure

In the presence of renal insufficiency or severe liver disease, Sekrol can only be used after consulting a doctor.
As with any drug with hepatic metabolism followed by renal excretion, in the presence of severe renal impairment, an accumulation of ambroxol metabolites generated in the liver can be expected.

Liver dysfunction

In patients with hepatic dysfunction removal of ambroxol hydrochloride is decreased, inducing plasma levels of approximately 1.3 to 2 times higher.

Given the high therapeutic index of ambroxol hydrochloride, a dose adjustment is not necessary.

Geriatric population

Age and sex do not have a significant effect on the pharmacokinetics of ambroxol hydrochloride and therefore there is no need to adjust the dosage.

5.3. Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Liquid sorbitol
- Glycerol
- Sodium metabisulfite,
- Hydroxyethyl cellulose,
- Tartaric acid,
- Benzoic acid,
- Aroma of cherries
- Purified water

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

Shelf life after first opening of the container: 1 month, the average use is 10-15 days.

The abbreviation "EXP." (Expiry date), included on the packaging, announces the date from which the validity of the product is no longer demonstrated (the first two digits indicate the month and the following year - the expiry date is the last day of the month indicated.

6.4. Special precautions for storage

Store at a temperature not exceeding 30 ° C in its original packaging.

6.5. Nature and contents of container

In use: Close the bottle after each use.

Bottle of 100 ml in amber glass, closed with white polyethylene screw cap.

The bottle is packed with a 2.5 - 5 ml measuring device in a cardboard box.

6.6. Special precautions for disposal and other handlings

No special requirements.

Any unused product or waste material should be disposed of in accordance with the regulations in force.

7. MARKETING AUTHORISATION HOLDER AND MANUFACURING SITE ADDRESS

7.1. Marketing Authorisation Holder

Dafra Pharma GmbH

Mühlenberg 7, 4052 Basel, Switzerland.

7.2. Manufacturer

Bilim Ilaç Sanayi ve Ticaret A.Ş (Bilim Pharmaceuticals)

GOSB, 1900 Sokak N° 1904, 41480 Gebze, Kocaeli, Turkey.

8. MARKETING AUHORISATION NUMBER

See list of MAs per country

9. DATE OF FIRST REGISTRATION

See list of MAs per country

10. DATE OF REVISION OF TEXT

January 2019