Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT (FPP)

SEKROL®

Ambroxol hydrochloride

1.1 Strength 15 mg/5ml

1.2 Pharmaceutical form Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of syrup contains 15 mg of ambroxol hydrochloride (3mg/ml).

Excipients with known effect:

Sodium metabisulphite (E223): 1 mg / 5ml
Benzoic acid (E210): 1 mg / 5ml
Sorbitol (E420): 2500 mg sorbitol 70% solution / 5ml
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup.

Clear, colourless solution with cherry odour.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Sekrol is indicated as a mucolytic in the management of acute and chronic respiratory diseases that are characterised by viscid mucoid secretions (such as bronchitis, bronchiectasis, sinusitis).

4.2. Posology and mode of administration

4.2.1. Posology

Age	Dose in mg	Volume of syrup Sekrol 15mg/5ml
0 to 2 years*	Max 7.5 mg, 2 times daily	2.5 ml, 2 times daily
2 to 5 years	7 .5 mg, 3 times daily	2.5 ml, 3 times daily

Age	Dose in mg	Volume of syrup Sekrol 15mg/5ml
5 to 12 years	10 mg, 2 to 3 times daily	5 ml, 2 to 3 times daily
12 years and older	30 to 60 mg, 2 times a day	10 to 20 ml, 2 times daily

*see section 4.2.3

At the beginning of treatment, doses can be increased by one fold.

4.2.2. Special populations

The syrup should be used very carefully in patients with kidney disease, liver disease and peptic ulcers.

Patients with hereditary fructose intolerance (HFI) must not be given this medicine unless strictly necessary.

4.2.3. Pediatric population

See dosage recommandations under 4.2.1
For children under 2 years old, the decision to use Sekrol 15mg / 5ml depends on individually specialised medical advise. Without this advice, giving the drug to a child under the age of 2 years is not recommended.

For children older than 12 years, Sekrol is available in 30 mg / 5 ml syrup.

4.2.4. Method of administration

Oral administration via dosing device.
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

4.4. Special warning and precautions for use

- Sekrol syrup contains a high amount of sorbitol. Patients with hereditary fructose intolerance must not be given this medicine. Babies and young children below the age of 2 may not yet be diagnosed with hereditary fructose intolerance.

- Cases of anaphylactic reactions and severe cutaneous adverse reactions (SCARs), including erythema multiforme, Stevens-Johnson syndrome / Lyell syndrome, and

acute generalised exanthematous pustulosis (PEAG) have been reported in patients receiving associated with ambroxol. Frequencies of these side effects are unknown. Advise your patients to stop treatment immediately if symptoms of progressive skin rash occur.

- As with all drugs metabolised by the liver and subsequently eliminated by the kidneys, severe kidney failure may produce an accumulation of metabolites generated by the liver. The syrup should be used very carefully in patients with kidney disease or liver disease.

- This medicine should be used with caution in patients with a history of, or existing peptic ulceration.

- The syrup contains sodium metabisulphite which can, in rare cases, cause hypersensitivity reactions and bronchospasm.

- The syrup contains benzoic acid which 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

Sekrol syrup should not be used in combination with antitussive medicines such as codeine, or with any secretion-reducing medicine.

4.5.2. Paediatric population

No interaction studies have been carried out in the pediatric population.

4.6. Fertility, pregnancy and lactation

4.6.1. Fertility

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

4.6.2. 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 medicines during pregnancy should be observed. Especially during the first trimester, the use of Sekrol is not recommended.

4.6.3 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.

4.7. Effects on the ability to drive and use machines

Ambroxol 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 safety 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 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	not known
Skin and subcutaneous tissue disorders	
Rash, urticaria	rare
Severe skin reactions (including erythema multiforme, Stevens-Johnson syndrome / Lyell's syndrome and generalised acute exanthematous pustulosis), angioedema and pruritus	not known
Nervous system disorders	
Dysgeusia	common
Headache, dizziness, somnolence, agitation	not known

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
Investigations	
Temporally elevation of liver enzymes	uncommon

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.

5.2. Pharmacokinetic properties

Absorption

Ambroxol hydrochloride is rapidly and completely absorbed from the gastrointestinal tract.

Distribution
When taken on an empty stomach, ambroxol reaches a maximum blood concentration within 2.5 hours. Therapeutic blood concentration is 30 ng/ml with a steady state blood concentration of 50 ng/m after multiple intakes. Ambroxol does not accumulate in the body and is for 90% bound to plasma proteins. Ambroxol passes into cerebrospinal fluid and placenta and is also detected in breast milk.

Biotransformation
About 30% of the oral dose of the substance is eliminated by first-pass-effect. The main enzyme responsible for the metabolism of ambroxol in the liver is CYP3A4. Ambroxol hydrochloride is mainly metabolised via glucuronidation in the liver with formation of metabolites (e.g. dibromoantranilic acid).

Elimination
The substance is largely metabolised and eliminated almost completely via the urine: for about 90% as glucuronides and 10% in unchanged form. Its half-life is about 9 to 10 hours. The plasma half-life of the sum of ambroxol and its metabolites is about 22 hours.

Renal failure
In patients with severe renal dysfunction, the elimination half-life of ambroxol metabolites is prolonged.

Liver failure
An accumulation of ambroxol metabolites generated in the liver can be expected. Elimination of ambroxol hydrochloride is decreased by 20-40% in patients with severe liver disease.

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

- Sorbitol solution (70%),
- Glycerol,
- Sodium metabisulfite,
- Hydroxyethyl cellulose,
- Tartaric acid,
- Benzoic acid,
- Aroma of cherries,
- Purified water

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

36 months.
Shelf life after first opening of the bottle: 1 month, the average use period is 10 days.

6.4. Special precautions for storage

Store below 30 ° C.
In use: Close the bottle well after each use.

6.5. Nature and contents of container

Bottle in amber coloured glass, containing 100 ml of syrup, closed with white polyethylene screw-cap.
Box with one bottle , a 2.5 - 5 ml measuring device and patient leaflet.

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 local requirements.

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

May 2021