

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Etrilect 0.5 mg/ml + 1 mg/ml oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of oral solution contains:
0.533 mg bromhexine hydrochloride
1.0 mg ephedrine hydrochloride

Excipient with known effect:

1 ml of oral solution contains 30.26 mg ethanol. See section 4.4.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution
Clear, colourless to light-yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cough with viscous mucus with a concurrent need for bronchodilator effect.

4.2 Posology and method of administration

Posology

<i>Adults and children 15 years and over:</i>	15 ml, 3 to 4 times daily
<i>Children 11 to 14 years:</i>	10–15 ml, 3 times daily
<i>Children 6 to 10 years:</i>	10 ml, 3 times daily
<i>Children 2 to 5 years:</i>	5 ml, 3 times daily
<i>Children over 6 months:</i>	2.5 ml, 3 times daily

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Caution is advised when treating patients with cardiovascular diseases, hypertension, hyperthyroidism, prostatic hypertrophy, closure glaucoma, angle, diabetes mellitus.

Cardiovascular effects may be seen with sympathomimetic drugs, including ephedrine. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with beta agonists. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving Etrilect should be warned to seek

medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

Caution is advised when treating patients with gastric ulcers.

Caution is advised when treating patients with haemoptysis because the constituent ingredient bromhexine can lead to rejection of fibrin clots and result in new bleeding.

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

There is some risk for the development of dependence at high doses and with prolonged use.

Excipients (s)

Ethanol

This medicine contains 30.26 mg of alcohol (ethanol) per ml.

The amount in 5 ml of this medicine is equivalent to less than 4 ml beer or 2 ml wine.

The small amount of alcohol in this medicine will not have any noticeable effects.

Sodium

This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially 'sodium-free'.

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

Products containing ephedrine should not be combined with the selective reversible MAO inhibitor moclobemide, or with non-selective irreversible MAO inhibitors (e.g. selegiline), or with older irreversible MAO inhibitor antidepressants. There have been case reports describing severe headache, severe rise in blood pressure and occasional cases of subarachnoid haemorrhage. The cause is ephedrine's indirect effect on the central nervous system's release of adrenergic neurotransmitters.

Since ephedrine has both alpha- and beta-agonist properties it should be avoided or used with care in patients undergoing anaesthesia with cyclopropane, halothane, or other volatile anaesthetics.

An increased risk of arrhythmias may occur if given to patients receiving cardiac glycosides, quinidine, or tricyclic antidepressants.

There is an increased risk of vasoconstrictor or pressor effects in patients receiving ergot alkaloids or oxytocin.

Patients treated with several different antihypertensive medications have impaired vasomotor control and are therefore more sensitive to substances with vasoconstrictive properties, such as ephedrine.

In one small study, ephedrine was shown to reduce the effect of dexamethasone in patients with asthma. It is unknown how this relates to other corticosteroids.

4.6. Fertility, pregnancy and lactation

Pregnancy

Available preclinical studies, as well as clinical experience, have not produced any evidence of undesirable effects during pregnancy. However, normal caution must be observed when using medicinal products during pregnancy, especially during the first trimester.

Breastfeeding*Bromhexine*

Bromhexine is probably excreted into breast milk and should be avoided during breastfeeding.

Ephedrine

There is insufficient information on whether ephedrine is excreted into human milk.

4.7. Effects on ability to drive and use machines

No studies have been conducted.

Dizziness can occur during treatment with Etrilect. This should be considered when full alertness is required, for example when driving.

In a study of pseudoephedrine (a related substance to ephedrine) in combination with an antihistamine, there was no impact on driving.

4.8. Undesirable effects

10 to 15% of treated patients can be expected to experience undesirable effects.

The undesirable effects are classified by system organ system and frequency.

The frequency is classified as follows: Very common ($\geq 1/10$), Common ($\geq 1/100$ to $< 1/10$),

Uncommon ($\geq 1/1,000$ to $< 1/100$), Rare ($\geq 1/10,000$ to $< 1/1,000$), Very rare ($< 1/10,000$), not known (cannot be estimated from the available data)

Frequency/ System Organ Class	Common	Uncommon	Rare	Not known
Immune system disorders			Hypersensitivity reactions	Anaphylactic reactions including anaphylactic shock, angioedema and pruritus
Psychiatric disorders	Anxiety	Insomnia	Hallucinations, confusion, aggressiveness	
Nervous system disorders	Tremor			
Cardiac disorders	Palpitations			
Respiratory, thoracic and mediastinal disorders			Bronchospasm	
Gastrointestinal disorders		Nausea, diarrhoea and vomiting	Dry mouth	Reduced appetite
Skin and subcutaneous tissue disorders	Urticaria, rash			Severe cutaneous adverse reactions (including erythema multiforme, Stevens-Johnson syndrome / toxic epidermal necrolysis and acute generalized exanthematous pustulosis)

Renal and urinary disorders	Difficulty in micturition, urinary retention			
General disorders and administration site conditions	Dizziness, headache			
Investigations			Transaminase increase	

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 [the national reporting system listed in Appendix V](#).

4.9. Overdose

Bromhexine + ephedrine 0.5 mg/ml + 1 mg/ml oral solution

10 ml to an 8-month old infant caused mild to moderate intoxication;
30–50 ml to 2–3 year-olds resulted in mild intoxication (after charcoal administration);
75–100 ml to 2–3 year-olds caused mild to moderate intoxication;
250 ml to a 4-year-old resulted in severe intoxication.

Bromhexine

Toxicity: 80 mg to a 2-year-old resulted in no symptoms.

Symptoms: Nausea, vomiting at high doses.

Treatment: If justifiable, stomach pumping, charcoal. Symptomatic treatment.

Ephedrine

Toxicity: Individually, there is highly variable sensitivity (thyrotoxic cases are particularly sensitive). 10 mg to an 8-month infant caused mild to moderate intoxication. 15–40 mg caused mild, 50–75 mg mild to moderate, 100–150 mg moderate, and 150–250 mg moderate to severe intoxication in children over 2 years.

Symptoms: Fatigue, slurred speech, tremors, headache, anxiety, irritability, tachycardia, palpitations. Nausea, vomiting. At high doses, symptoms also include somnolence, mydriasis, excitation, hallucinations, seizures, hyperthermia, blood pressure (possibly later hypotension), arrhythmia. Hypokalemia. Urinary retention. In severe cases, there may possibly be a risk of rhabdomyolysis and renal failure.

Treatment: If justifiable, stomach pumping, charcoal and maybe laxatives. Monitoring of consciousness and circulation. In severe cases, continuous ECG monitoring. In the case of convulsions, diazepam 5–10 mg for adults (0.1–0.2 mg/kg for children). For symptomatic tachycardia: metoprolol or atenolol. In cases of hypertension requiring treatment, alpha blockers such as phentolamine should be administered. Alternatively, labetalol can be tried. Symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mucolytics, combinations, ATC code: R05CB10

The active substances in Etrilect are bromhexine hydrochloride and ephedrine hydrochloride. Bromhexine hydrochloride is considered to have an expectorant and mucolytic effect that dissolves sticky secretions. This may facilitate the expectoration of mucus. Ephedrine hydrochloride acts as a bronchodilator and decongestant.

5.2. Pharmacokinetic properties

Ephedrine is rapidly and completely absorbed. Elimination is mainly via the kidneys, but a small portion is metabolised before being eliminated. The half-life is approximately 3–6 hours depending on the pH of the urine, with a low pH accelerating elimination.

Bromhexine hydrochloride is rapidly absorbed, and the maximum plasma concentration is reached after about an hour. Bromhexine hydrochloride undergoes extensive first-pass metabolism, and the oral bioavailability is approximately 20%. There is a high degree of protein binding. 85–90% of bromhexine hydrochloride is eliminated as metabolites in urine, with a terminal half-life of up to 12 hours. Only a small fraction is eliminated unchanged in the urine, with a half-life of 6.5 hours.

5.3. Preclinical safety data

There is no relevant preclinical data for evaluation of safety beyond that already stated in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol
Polysorbate 20
Citric acid monohydrate
Ethanol (96%)
Levomenthol
Peppermint flavour
Blood orange flavour
Sodium hydroxide (E524) (for pH adjustment)
Water, purified

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

18 months

6.4. Special precautions for storage

Store in the original package in order to protect from light.
Do not store above 25 °C.

6.5. Nature and contents of container

Amber glass bottle with a child-resistant screw cap (HDPE/PP).
Amber glass bottle with a pouring ring (PE) and a temper-evident screw cap (PP/PE).
Each pack contains a measuring device (plastic cup).

Pack sizes: 300 ml and 500 ml oral solution.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special instructions.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}

Date of latest renewal: {DD month YYYY}

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

{DD/MM/YYYY}

{DD month YYYY}

[To be completed nationally]

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