

Trachisan® Lozenges

Drug Substance: Tyrothricin, Lidocaine hydrochloride, Chlorhexidine digluconate

Page 1 of 7

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Trachisan® Lozenges, lozenges

2. QUALITATIVE AND QUANTITATIVE COMPOSITION (Active ingredients)

Each lozenge contains:

Tyrothricin	0.5 mg
Lidocaine hydrochloride 1 H ₂ O	1.0 mg
Chlorhexidine digluconate	1.0 mg

Excipients see under point 6.1.

3. PHARMACEUTICAL FORM

Lozenges.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Inflammatory and infectious diseases of the oral cavity and pharynx, such as stomatitis, gingivitis, periodontitis, glossitis, tonsillitis and pharyngitis; dysphagia and other conditions involving a violation of swallowing. For the prevention of infections before and after surgical intervention in areas of the oral cavity and pharynx (tooth extraction, surgical treatment of the gingiva, tonsillectomy).

4.2 Posology and method of administration

Let 1 tablet dissolve in the mouth every 2 hours. Daily dose for adults and children over 12 years old – 8 tablets; for children from 4 to 12 years old – 6 tablets. As a rule, the symptoms of the disease disappear after a few days, but to achieve a stable therapeutic effect, it is recommended to continue therapy for another 2 to 3 days. If the patient's condition does not improve after 5 days of use, consultation with a physician is necessary.

Trachisan® Lozenges should not be used for more than 2 weeks without interruption, unless otherwise prescribed by a doctor or dentist.

4.3 Contraindications

Should not be used by fructose intolerance and by known hypersensitivity to any ingredient of the drug, non-bleeding desquamation of the oral mucosa (erosive and desquamative changes), larger fresh wounds in the oral and pharyngeal cavities.



Trachisan® Lozenges

Drug Substance: Tyrothricin, Lidocaine hydrochloride, Chlorhexidine digluconate

Page 2 of 7

4.4 Special warnings and special precautions for use

It is not recommended to give Trachisan® Lozenges to children under 4 years, as the preparation should be sucked.

By analogy with all other pharmaceutical preparations, it is possible to take Trachisan during pregnancy and lactation only after prior consultation with a doctor.

Trachisan® Lozenges contain lidocaine. Cross-allergy to lidocaine hydrochloride is expected in patients with a history of known allergy to other local amide type anaesthetics.

4.5 Interaction with other medicinal products and other forms of interaction

Adverse effects associated with the concomitant use of other drugs in conjunction with Trachisan® Lozenges have so far not become known.

4.6 Pregnancy and lactation

Although the active constituent combination contained in Trachisan® Lozenges is safe in therapeutic doses due to its pharmacological properties, the product should basically be used during pregnancy and lactation only after consulting a doctor.

4.7 Effects on ability to drive and use machines

No special precautions need be taken by patients taking Trachisan® Lozenges when driving or operating machines.

4.8 Undesirable effects

In rare cases hypersensitivity reactions such as local irritation, oropharyngeal swelling, skin reactions or shortness of breath may occur. Severe or generalized courses cannot be excluded. Local undesirable effects, such as bleeding of the gums (rare), increased formation of dental calculus (rare), irritation or reversible desquamation of the oral mucosa (very rare) may occur. Trachisan is usually well tolerated. However, the product may lead to short-term changes in taste, temporary numbness of the tongue. With prolonged use in isolated cases, there may be a slight discoloration to yellow or light brown color of teeth, dental fillings and prostheses or the tongue, in such cases it is necessary to adhere to careful oral hygiene. Color disappears on its own after discontinuation of the drug.

4.9 Overdose

Due to the pharmacological properties of the contents, no toxic effects are to be expected even after accidental ingestion of large amounts of Trachisan® Lozenges.



Trachisan® Lozenges

Drug Substance: Tyrothricin, Lidocaine hydrochloride, Chlorhexidine digluconate

Page 3 of 7

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mouth and throat therapeutic agent.

ATC code: R02A

Trachisan® Lozenges are used to treat inflammation in the oral cavity and throat. They contain an active substance combination whose constituents exhibit analgesic and antimicrobial properties.

Tyrothricin is a combination of different cyclic and linear polypeptides that have an anti-bacterial effect and which are formed by the anaerobic, sporiferous *Bacillus brevis*. The combination comprises 70-80% tyrocidins - basic, cyclic decapeptides - and 20-30% gramicidins - neutral, linear pentadecapeptides.

The spectrum of effect principally covers gram-positive cocci and bacteria and various forms of fungi, such as *Candida albicans*.

Tyrothricin gives rise to the release of substances containing nitrogen and phosphate from within the bacteria cells which, analogous to the cationic detergents, destroy the osmotic barrier of the bacterial cell membrane. Due to the direct attack on the bacterial cell wall, the effect is not confined to growing or dividing bacteria, which explains the bactericidal effect of the quantity of tyrocidin.

Gramicidins, on the other hand, form cation-conducting canals in the bacterial cell membrane, which, particularly owing to a loss of potassium, leads to changes in the intracellular cation concentration and finally to cytolysis. Furthermore, the gramicidin components lead to a decoupling of the respiratory chain phosphorylation.

Due to the particular mode of action of tyrothricin, which is not known in systemically used antibiotics, cross-resistances have not been observed.

Chlorhexidine is a base and therefore most stabile as a salt-form.

The free base consisting of diacetate and dihydrochloride, is only minimally soluble in water (0.08g, 1.0g and 0.06g/100ml), whereby digluconate is very soluble (> 50g/100ml).

For this reason, mainly digluconate is used for various indications.

Chlorhexidine and its salts boast a wide antimicrobial effect against gram-positive and gram-negative bacteria.

The effect against some gram-negative bacteria (*Pseudomonas* and *Proteus* strains) and against yeasts, Dermatophytes and *Mycobacteria* is minimal.

It is ineffective against bacterial spores, fungus spores, viruses and saprogenic fungi.

The mean inhibitory concentrations are (µg/ml):

bacteria:

<i>Escherichia coli</i>	0.93
<i>Enterobacter</i>	8.33
<i>Serratia marcescens</i>	26.6
<i>Pseudomonas aeruginosa</i>	> 73
β-haemolytic <i>Streptococci</i>	0.29



Trachisan® Lozenges

Drug Substance: Tyrothricin, Lidocaine hydrochloride, Chlorhexidine digluconate

Page 4 of 7

Streptococcus faecalis	0.97
Salmonella sp.	4.65
Klebsiella sp.	8.97
Proteus spec.	> 67
Streptococcus mutans	0.19
Staphylococcus aureus	1.17

yeasts, Dermatophytes and moulds:

Candida albicans	11.0
Microsporum canis	18.0
Aspergillus versicolor	75.0

Chlorhexidine is more effective in ranges with neutral and faintly alkaline pH values. In acidic ranges, its efficacy is reduced.

The efficacy of chlorhexidine is also reduced in the presence of soap, blood or pus (cell fragments) (100-1000 x higher inhibitory concentrations required).

Mouth washes containing 10 ml of a 0.2% chlorhexidine solution lead to a great reduction in the amount of salivary bacteria, which can be detected for up to 12 hours. This also correlates with a reduction in the rate of plaque formation.

When used over months, the effect diminishes through reversible displacement in the bacterial spectrum of oral flora and plaque. No tests are known with regard to the consequences of displacement of the oral germ spectrum.

The mechanism of effect of chlorhexidine is based on its affinity for microbial cell walls, the surface properties of which are altered on contact with the active constituent.

The lipophilic groups lead to disorientation of the lipoprotein membrane of the cell wall, and adsorption of chlorhexidine leads to disturbance of the osmotic equilibrium with subsequent breakdown of the cytoplasmatic membrane of the pathogen cell.

Lidocaine hydrochloride is a local anaesthetic of the amide type. It produces a blockade of the sodium channels of nerve fibres, so that the nerve membrane can no longer be depolarized by the action potential. The transmission of stimuli in pain-conducting nerve fibres is thereby blocked.

5.2 Pharmacokinetic properties

Tyrothricin

When administered locally, measurable resorption takes place neither through the damaged skin nor through the mucosa. Moreover, since tyrothricin is completely destroyed as a peptide by gastric juice, pharmacologically relevant serum concentrations are not to be expected when used accordingly.

Chlorhexidine

High activity in the alimentary tract was determined after oral application of chlorhexidine to rats and mice. Resorption occurs only slowly.

After using mouth washes, chlorhexidine is adsorbed by the tooth enamel, dentin, cement, tooth pellicle, mucosae and dentures, crowns, fillings etc. Chlorhexidine can be detected in saliva for up to 8 hours (depot effect), due to slow resorption.

Resorption of chlorhexidine over an intact oral mucosa is not known.



Trachisan® Lozenges

Drug Substance: Tyrothricin, Lidocaine hydrochloride, Chlorhexidine digluconate

Page 5 of 7

Excretion of chlorhexidine in various experimental animals takes place mainly via the faeces (90%). In human experiments, the elimination half-life was 4 days.

Lidocaine hydrochloride

is indeed absorbed after oral administration but is 50% inactivated after the first pass through the liver. The small amount of active constituent contained in Trachisan® Lozenges practically excludes a systemic effect.

5.3 Preclinical safety data

Tyrothricin

Tyrothricin is a particularly well tolerated local antibiotic which leads neither to histological lesions nor to irritations of the mucosae or skin when administered accordingly.

When administered intravenously, the LD50 of tyrothricin lies by 3.7 mg/kg BW in the mouse and by intraperitoneal application by 20-45 mg/kg KG BW. When orally administered, tyrothricin is tolerated without reaction.

Mutagenic, cancerogenic or teratogenic effects of tyrothricin have not been observed up to the present.

Chlorhexidine and its salts have a slight acute and chronic toxicity (oral LD50 1.8-3.0 g/kg BW in the rat and 2.5 g/kg BW in the mouse).

The toxicity of the free base and salts is more or less similar.

Due to its solubility in watery solutions, acute toxic amounts can only be administered together with digluconate.

The acid residues, which are set free after systemic ingestion and metabolism, are only slightly toxic.

Bleeding of the gingiva can be promoted, when chlorhexidine is permanently used as a mouth wash without brushing the teeth.

In studies carried out on animals, histological lesions were observed in open bone wounds or wounds with necrotic or ulcerous tissue.

Administration of chlorhexidine 0.2 and 0.02% to drinking water over a period of 14 days led to reversible dysplasia and leucoplasia (pre-malignant alterations) of the epithelium of the tongue in rats.

Mutagenicity:

Chlorhexidine showed mutagenic effects in both Ames and DNA-repair tests.

However, negative results were obtained in chromosome mutation tests on mammalian soma cells.

Reproduction toxicity:

After oral administration of chlorhexidine to pregnant rats, neither deviations from the norm, embryonic or foetal deformities, nor reduced fertility were observed.

These tests, however, cannot exclude such eventual effects on humans.

Lidocaine: The amount of active constituent contained in Trachisan® Lozenges for the purpose of local anaesthesia is so small that systemic and/or toxic actions can be practically excluded.



Trachisan® Lozenges

Drug Substance: Tyrothricin, Lidocaine hydrochloride, Chlorhexidine digluconate

Page 6 of 7

Mutagenic and tumorigenic potential:

There are references that a product of metabolism in rats and also possibly in humans, namely 2.6-xylidine, which results from lidocaine/etidocaine, could have mutagenic effects. These references result from in-vitro tests, where this metabolite was used in very high, almost toxic concentrations. There are presently no grounds for having to say that the parent substances, lidocaine and etidocaine, are themselves mutagenic.

In a cancerogenicity study with transplacental exposure and postnatal treatment over 2 years with 2.6-xylidine on rats, malignant and benign tumours, particularly in the nasal cavity (ethmoturbinalia), were observed in a highly sensitive test system (transplacental exposure and postnatal treatment over 2 years with very high doses). That these findings are of relevance for humans is not improbable. Therefore, the preparation should not be administered in high doses over a long period of time.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (E420), magnesium stearate, peppermint oil
Each tablet contains 0.69 g sorbitol, corresp. to 0.057 BU.

6.2 Incompatibilities

None known to date.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at a temperature not exceeding 25° C in a place protected from moisture, out of reach of children.

6.5 Nature and contents of container

Boxes of 20 tablets (2 blisters of 10 tablets).

6.6 Special precautions for disposal and other handling

No special instructions.



Trachisan® Lozenges

Drug Substance: Tyrothricin, Lidocaine hydrochloride, Chlorhexidine digluconate

Page 7 of 7

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

September 2024

11. CLASSIFICATION

Pharmacy only medicine

