

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE HUMAN MEDICINAL PRODUCT

ANDOREX Gargle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

200 ml solution;

Active substance:

One diameter (15 ml) contains 22.5 mg benzydamine hydrochloride and 18 mg chlorhexidine gluconate.

Excipient(s):

15 ml of solution contains:

Sorbitol (70%)	2.40 g
Ethanol	1.5 ml
Tartrazine	0.00009 g

For excipients refer to Section 6.1.

3. PHARMACEUTICAL form

Solution.

Green and clear solution with mint taste and scent.

4. CLINICAL FEATURES

4.1. Therapeutic Indications

- Gingivitis and stomatitis with inflammation and pain in the mouth and throat mucosa, pharyngitis, tonsillitis and aphthous lesions,
- Mouth and throat antiseptics, relieving the swallowing function of the patient and relieving symptomatic gum disorders
- Before and after periodontal interventions,
- Mucositis after radiotherapy and chemotherapy or other reasons,
- Prevention of dental plaques

ANDOREX is used.

4.2. Posology and mode of administration

Posology/frequency and duration of administration:

Adult dose for ANDOREX is 15 ml. It is administered with 1.5-3-hour intervals throughout the day.

Method of administration:

ANDOREX is used to rinse mouth and gargle.

ANDOREX is used undiluted.

It is kept in the mouth for at least 30 seconds.

It is expurged from mouth after use.

Chlorhexidine contained in the ANDOREX reduces plaque and gingivitis during the course of the treatment. If ANDOREX is used as an alternative to hygiene procedures, the mouth should be rinsed with ANDOREX for at least 1 minute. In order to minimize coloration caused by chlorhexidine in ANDOREX it is advised to brush your teeth before administration.

Additional information regarding special populations:

Renal/Liver failure:

As benzydamine absorbed is highly metabolized in the liver, systemic effect should be taken into consideration for patients with severe liver disorder. As benzydamine and metabolites absorbed are eliminated from the body with urine, systemic effect should be taken into consideration for patients with renal disorder.

Pediatric population

Gargle for 30 seconds every 1.5-3 hours with 5-15 ml ANDOREX for children over 12 years old.

It should not be continuously used for more than 7 days.

Gargle should be diluted with water in case of burning and stinging sensation.

Geriatric population:

No dose change is required for elder people.

4.3. Contraindications

- It is contraindicated for people with known hypersensitivity to benzydamine and chlorhexidine.
It should not be used for people with hypersensitivity to any of the substances contained in the formulation.
- ANDOREX should be not used during pregnancy and breast feeding period.

4.4. Special warnings and special precautions of use

Used externally.

Due to the absence of sufficient number of clinical studies ANDOREX is not recommended for children under 12 years old.

It is for oral use only; avoid contact with eyes and ears.

It may lead to reversible color change in the mouth, on the tongue and teeth.

ANDOREX should not be swallowed and expurged through expuition. It is used undiluted.

If sore throat is due to bacterial infection or accompanied by an infection, anti-bacterial treatment may be considered in addition to ANDOREX use.

Impaired renal function: As benzydamine and metabolites absorbed are eliminated from the body with urine, systemic effect should be taken into consideration for patients with renal disorder.

Impaired liver function: As benzydamine absorbed is highly metabolized in the liver, systemic effect should be taken into consideration for patients with severe liver disorder.

As this medical product contains sorbitol, patients with rare genetic fructose intolerance disorder should not use this medication.

This medicinal product contains small amounts - less than 100 mg (1.5 ml) per dose - ethanol (alcohol).

Tartrazine contained in this medicinal product may cause an allergic reaction.

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

Chlorhexidine;

Chlorhexidine salts are incompatible with soap and other anionic compounds.

Chlorhexidine salts are compatible with cationic and nonionic surfactants; however when used in high concentrations, activity of chlorhexidine may be reduced due to micelle bonding.

Solubility may be increased with surfactants including cetrimide and lissapol NX.

Is incompatible with anionic polyelectrolytes including acacia gum, sodium alginate and sodium carboxymethyl cellulose, and starch and gummi tragacanthae; the effects are also reduced with these substances.

Is also incompatible with other substances including brilliant green, chloramphenicol, copper sulphate, fluorescein sodium, formaldehyde, silver nitrate and zinc sulphate.

When diluted with hard waters, it may precipitate as undissolved salts due to interference with Ca^{+2} and Mg^{+2} cations.

If the solutions of chlorhexidine salts combined with benzoates, bicarbonates, carbonates, borates, nitrates, phosphates and sulphates is concentrated higher than 0.05 %, they precipitate as the number of salts formed is low. As cetrimide increase the solubility of these salts, no precipitation is available when combined with cetrimide.

Chlorhexidine is compatible with gluconate, cetrimide and benzalkonium chloride. These synergistically increase the bactericide effect. Cetrimide prevents precipitation of chlorhexidine with hard waters. Except for chlorhexidine gluconate, chlorhexidine and its salts dissolve better in alcohol than water. Chlorhexidine gluconate solution may precipitate when added to alcohol. The presence of ethanol in the formulation makes the solution more effective against Gram-negative microorganisms. They can be adsorbed while filtered through cellulosic filters.

No drug interaction with benzydamine is reported.

4.6. Pregnancy and lactation

General recommendation

Pregnancy category: C

Women with childbearing potential/Birth control (contraception)

ANDOREX has no effect on contraception, but women with childbearing potential should use it carefully, since ANDOREX contains alcohol.

Pregnancy period:

The administration of ANDOREX during pregnancy period is contraindicated.

Animal studies are limited in terms of effects on pregnancy and/or embryo-fetal development and/or birth and/or postnatal development. Potential risk on human is unknown.

Lactation period:

No data is available whether benzydamine or chlorhexidine digluconate is eliminated from body with human or animal milk. For this reason, possible risk for breast-fed child cannot be avoided. The use of ANDOREX during pregnancy period is contraindicated.

Reproductivity/Fertility:

There are studies on reproductivity and fertility with chlorhexidine gluconate. No dangerous effect is seen on fertility of rats, and no dangerous effect is seen on fetus of rats and rabbits. No sufficient study is available on animals with benzydamine.

4.7. Effects on ability to drive and use machines

No effect on the ability to drive vehicles and use machines.

4.8. Undesirable effects

Reported undesirable effects are listed below according to their frequency. Very common ($\geq 1/10$); common ($\geq 1/100$ to $<1/10$); uncommon ($\geq 1/1000$ to $<1/100$); rare ($\geq 1/10,000$, $<1/1000$); very rare ($<1/10,000$); unknown (can not be estimated from the available data).

Immune system disorders

Very rare: Allergic reaction, hypersensitivity and anaphylaxis

Nervous system disorders

Very common: Temporary decreased sensation in the mouth

Common: stinging and burning sensation in the mouth

Unknown: Dizziness, headache, somnolence

Respiratory, thoracic and mediastinal disorders

Very rare: Laryngospasm, bronchospasm.

Unknown: Pharyngeal irritation, cough

Gastrointestinal disorders

Common: Oral numbness, nausea, vomiting, retching

Unknown: dry mouth

Skin and subcutaneous tissue diseases:

Very rare: Irritation-related skin reactions, pruritus with rash, urticaria, photodermatitis, oral desquamation.

General disorders and administration site conditions

Common: Change in taste, staining on teeth and other oral surfaces, increase in calculus (tartar) formation

Staining on the teeth is harmless and it can be minimized by brushing.

Very rare: Local dryness, thirst, tingling, freshness sensation in the mouth

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continuous monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to

Turkish Pharmacovigilance Center (TÜFAM) (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; tel: 0 800 314 00 08; Fax: 0 312 218 35 99)

4.9. Overdose and treatment

If ANDOREX is drunk by mistake, symptomatic and supportive treatment should be provided. No specific antidote is available.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic Group: Antiseptic (topical pharyngeal), topical oral anti-inflammatory
ATC code: A01AD11

Benzydamine is an anti-inflammatory analgesic agent which is not related to steroid group. As benzydamine is a base, it is different from other non-steroid anti-inflammatory agents.

Benzydamine results in local anesthetic effect in concentrations used in topical treatment. Reported analgesic activity of benzydamine is higher than non-inflammatory pain in models with experimental inflammation.

Chlorhexidine is a biguanide antiseptic and when general oral hygiene is discontinued, it helps to minimize plaque and gingivitis formation. It has affinity to tooth enamel hydroxyapatite, tooth surface and oral structures containing bacteria and saliva proteins. Chlorhexidine reduces dental plaque deposition as well as redness on gingiva, swelling or gingivitis characterized by bleeding. It reduces the frequency of aphthous ulcers formation and increases healing rate after periodontal surgery.

Anti-inflammatory mechanism of activity of benzydamine is not related to adrenal axis secretion. As other non-steroidal anti-inflammatory agents, benzydamine inhibits prostaglandin biosynthesis under certain conditions. However this feature is not completely explained. Stabilizer effects on cellular membranes may be related to mechanism of action.

Upon normal topical administration of the drug, chlorhexidine shows bactericidal effect after extended bacteriostatic effect. Chlorhexidine is effective on many gram(+) and gram (-) bacteria, ferment, some fungus types and viruses. Chlorhexidine delays bacterial formation through its delayed skin effect. It is absorbed through microbial cell wall and results in membrane leakage.

5.2. Pharmacokinetic properties

Absorption:

It is seen that systemic absorption is not available following the administration of chlorhexidine gluconate topical oral solution as mouthwash. When used as prescribed 4% of the oral gargle is swallowed and some of it is absorbed. 90% of the swallowed chlorhexidine is not absorbed and eliminated through feces directly.

When chlorhexidine gluconate 0.12% topical oral solution is used as mouthwash, 30% of the drug remains in the mouth cavity. Chlorhexidine gluconate is released gradually within 24 hours.

Following the topical administration of benzydamine hydrochloride, benzydamine is absorbed by the inflammatory oral mucosa and shows anti-inflammatory and local anesthetic effect on the application area. The level of plasma benzydamine acquired upon oral use is low and directly proportional to actual intake rate.

Distribution:

ANDOREX is a local effective drug. For this reason, it should not be swallowed during prescribed use. Thus systemic absorption and distribution is not expected. In addition absorption of both compounds from gastrointestinal mucosa is low.

Biotransformation:

As the absorption rate of chlorhexidine is minimal, it cannot be measured from plasma. Benzydamine is generally metabolized through oxidation and conjugation.

Elimination:

Chlorhexidine does not accumulate in the body and only a small amount of it is metabolized. About 10% of chlorhexidine swallowed is eliminated via kidney upon absorption and 90% of the drug which is not absorbed is eliminated with feces.

Benzydamine and its metabolites in systemic circulation is mostly eliminated with urine.

5.3. Pre-clinical safety data

Oral LD50 of clorhexidine gluconate exceeds 3 mg/kg in male and female rats; 2.5 mg/kg in male mice, 2.6 mg/kg in female mice; IV LD50 of it is 21 mg/kg in male rat, 23 mg/kg in female rats, 25 mg/kg in male mice, 24 mg/kg in female mice; subcutaneous LD50 is more than 1 g/kg in male and female rats, 637 mg/kg in male mice and 632 mg/kg in female mice. Oral LD50 of clorhexidine gluconate in human is about 2 g/kg. Lethal dose of benzydamine is highly above the treatment dose in acute studies. Therapeutic dose is 0.7-1.0 mg/kg in human. LD50 values (mg/kg) for mice are detected as 33 i.v.; 110 i.p.; 218 s.c. and 515 p.o; 100 i.p. and 1050 p.o. in rats.

6. PHARMACEUTICAL PROPERTIES

6.1. List of excipients

Peppermint essence
Sorbitol (E420)
Patent blue V
Glycerol
Polysorbate 20
Tartrazine (E102)
Ethanol
Purified water

6.2. Incompatibilities

Chlorhexidine gluconate solution may precipitate when added to alcohol. Is incompatible with anionic polyelectrolytes including acacia gum, sodium alginate and sodium carboxymethyle cellulose, and starch and gummi tragacanthae. Chlorhexidine salts are incompatible with soap and other anionic compounds. Is also incompatible with other substances including brillant green, chloramphenicol, copper sulphate, fluorescein sodium, formaldehyde, silver nitrate and zinc sulphate.

6.3. Shelf-life

36 months

6.4. Special precautions for storage

Store at room temperature below 25 °C.

6.5. Nature and contents of container

In 200 ml Amber coloured PET bottles together with 15 ml measuring cup, in cardboard box.

6.6. Disposal of the residual substances of human medicinal product and other special precautions

Unused products and waste materials should be disposed of in accordance with “Medicinal Products Waste Management Directive” and “Packaging and Packaging Waste Management Directive”.

7. AUTHORIZATION HOLDER

Humanis Saglik A.S.

Mahmutbey Mahallesi, Tasocagi Yolu

Caddesi, Solen Residence Apt. No:19/1/11

Bagcilar/Istanbul/TURKEY

8. MARKETING AUTHORIZATION NUMBER(S)

201/86

9. DATE OF FIRST AUTHORIZATION/AUTHORIZATION RENEWAL DATE

Date of first authorization: 24.01.2003

Date of authorization renewal:

10. DATE OF REVISION OF THE TEXT

25.10.2021