NEW ZEALAND DATA SHEET

1. PRODUCT NAME

DEVATIS SORE THROAT RELIEF GARGLE

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:
DEVATIS SORE THROAT RELIEF GARGLE contains benzydamine hydrochloride and chlorhexidine gluconate.
Each 15 ml dose contains 22.5 mg benzydamine hydrochloride (0.15% w/v) and 18 mg chlorhexidine gluconate (0.12% w/v).

Excipient with known effect:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gargle.
DEVATIS SORE THROAT RELIEF GARGLE is a clear, colorless to yellowish colored solution with peppermint odor.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
It is used for mouth and throat antisepsis, for relief of patient's swallowing function and as symptom reliever in gingival diseases. It can be used for prophylaxis before dental procedures.

4.2 Posology and method of administration
Adult dose of DEVATIS SORE THROAT RELIEF is 15 ml. It is administered at 1.5-3-hour intervals during a day.

Method of administration:
DEVATIS SORE THROAT RELIEF is for mouth rinse or gargle.
DEVATIS SORE THROAT RELIEF is used without dilution.
It is kept in mouth for 30 seconds at minimum.
It is expectorated after each use.

Chlorhexidine in DEVATIS SORE THROAT RELIEF reduces plaque and gingivitis during treatment. If DEVATIS SORE THROAT RELIEF is used as an alternative to oral hygiene procedures, DEVATIS SORE THROAT RELIEF should be hold in the mouth for at least 1 minute. Teeth should be brushed before use in order to minimize the discoloration induced by chlorhexidine in DEVATIS SORE THROAT RELIEF.

Additional information on special population

Renal/Hepatic impairment
As absorbed benzydamine is highly metabolized in the liver, the possibility of systemic effect should be taken into consideration in patients with severe hepatic impairment.
As absorbed benzydamine and its metabolites are excreted in the urine, the possibility of systemic effect should be taken into consideration in patients with severe renal impairment.

Adolescents (12 years of age and above)
Gargle with 5-15 ml DEVATIS SORE THROAT RELIEF for 30 seconds every 1.5-3 hours.
It should not be used for more than 7 days continuously.
In case of burning and stinging sensation, gargle should be diluted with water.
Due to insufficient number of clinical studies, DEVATIS SORE THROAT RELIEF is not recommended for children under 12 years of age.

Geriatric population
The same dose as adults can be applied to geriatric patients.

4.3 Contraindications
It is contraindicated in patients with hypersensitivity to benzydamine and chlorhexidine and any of the ingredients in DEVATIS SORE THROAT RELIEF.
It should not be used during pregnancy and lactation.

4.4 Special warnings and precautions for use
- For external use.
- Due to insufficient number of clinical studies, DEVATIS SORE THROAT RELIEF is not recommended for children under 12 years of age.
- It is used only in the mouth; its contact with eyes and ears should be avoided. If it contacts with eyes, eyes should be well-rinsed with plenty of water.
- It may cause reversible color change in mouth, on tongue and teeth. Teeth should be brushed before use in order to minimize the discoloration.
- DEVATIS SORE THROAT RELIEF should not be swallowed and should be expectorated after each use. It is used without dilution.
- If sore throat is caused by bacterial infection or accompanied by infection, antibacterial treatment can be considered in addition to DEVATIS SORE THROAT RELIEF use.
- As absorbed benzydamine and its metabolites are excreted in urine, possibility of systemic effect should be taken into consideration in patients with severe renal impairment.
- As absorbed benzydamine is metabolized highly in liver, possibility of systemic effect should be taken into consideration in patients with severe hepatic impairment.
- This medicinal product contains ethanol (alcohol) in small amount – less than 100 mg for each dose.

4.5 Interaction with other medicines and other forms of interaction
DEVATIS SORE THROAT RELIEF does not have any known significant drug interaction. Chlorhexidine, one of the drug substances it contains, is incompatible with some agents:
- Chlorhexidine salts are incompatible with soap and other anionic compounds.
- Chlorhexidine salts are compatible with cationic and nonionic surface active agents; however, when they are co-administered at high concentrations, micelle may reduce chlorhexidine activity due to binding.
- Solubility of chlorhexidine salts can be increased with surfactants such as cetrimide and lissapol NX.
- It is incompatible with anionic poly-electrodes such as gum arabic, sodium alginate, sodium carboxy methyl cellulose and it is incompatible with starch and gummi tragacanthae; their effects are also reduced with these agents.
- Chlorhexidine is also incompatible with substances such as brilliant green, chloramphenicol, copper sulphate, fluorescein sodium, formaldehyde, silver nitrate and zinc sulphate.
- As chlorhexidine interacts with Ca and Mg cations when diluted with hard water, it may precipitate as insoluble salts.
- If solutions of chlorhexidine salts combined with benzoates, bicarbonates, carbonates, borates, nitrates, phosphates and sulphates are more concentrated than 0.05%, its solubility precipitates as it will form salts with less solubility. As cetrimide enhances solubility of these salts, these precipitations do not occur when they are combined with cetrimide.

- Chlorhexidine gluconate is compatible with cetrimide and benzalkonium chloride. These synergistically enhance 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 it is added over alcohol. Ethanol in formulation renders the solution more effective against gram negative microorganisms. They can be adsorbed during filtration through cellulosic filters.

Drug interactions with benzydamine have not been reported.

4.6 Fertility, pregnancy and lactation

General recommendation
Pregnancy category is C.

Women of child-bearing potential/Contraception
DEVATIS SORE THROAT RELIEF does not have any effect on contraception; however, as DEVATIS SORE THROAT RELIEF contains alcohol, women of child-bearing potential should use it cautiously.

Pregnancy
DEVATIS SORE THROAT RELIEF is contraindicated during pregnancy.
Animal studies do not indicate effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development. Potential risk to humans is unknown.

Breast-feeding
Data is not available for breastfeeding women. Therefore, it is contraindicated in breastfeeding women.

Fertility
Reproduction and fertility studies with chlorhexidine gluconate have been conducted. No evidence of impaired fertility was observed in rats, and no evidence of harm to the fetus was observed in rats and rabbits.
There is not sufficient study conducted on animals for benzydamine.

4.7 Effects on ability to drive and use machines
No effects on the ability to drive or operate machinery have been observed.

4.8 Undesirable effects
Reported undesirable effects are listed according to the following frequency. Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10000 to <1/1000), very rare (<1/10000) and unknown (cannot be estimated based on available data).

DEVATIS SORE THROAT RELIEF is generally well-tolerated and its side effects are minor.
There is not any serious side effect and adverse effect reported at the end of clinical studies.
Mostly, local side effects are observed. Systemic side effects, generally, are not observed and not serious.

Central nervous system disorders
Very rare: Dizziness, headache and numbness

Gastrointestinal diseases
Common: Oral numbness
Very rare: Nausea, vomiting, gag reflex, gastrointestinal diseases

General disorders and administration site diseases
Common: Altered taste, staining of teeth and other oral surfaces, increase in calculus (tartar) formation
Tooth staining is harmless and can be minimized through tooth-brushing before administration.

Rare: Burning and stinging sensation
Very rare: Local dryness, thirstiness, tingling, and feeling of coolness in the mouth

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose
Intoxication is not possible considering method of administration of the drug substance.
However, if DEVATIS SORE THROAT RELIEF is accidentally swallowed, symptomatic treatment should be instituted. There is no specific antidote.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic Group: Antiseptic (Topical Pharyngeal), Topical oral anti-inflammatory
ATC code: A01AD02

Benzydamine is an anti-inflammatory analgesic agent structurally unrelated to the steroid group. Benzydamine differs from other non steroid anti-inflammatory agents in that it is a base.
At concentrations used for topical treatment, benzydamine exerts local anesthetic effect. The analgesic activity of benzydamine was more reported in models involving experimental inflammation rather than non-inflammatory pain.

The mechanism of anti-inflammatory action of benzydamine is not related to stimulation of the pituitary-adrenal axis. Like other non steroidal anti-inflammatory agents, benzydamine inhibits the biosynthesis of prostaglandins under certain conditions, but its properties in this respect have not been fully explained. The stabilizing effect on cellular membranes may be involved in the mechanism of action.

Following normal topical application of the medicine, chlorhexidine produces bactericidal effect, followed by a prolonged bacteriostatic action.

Chlorhexidine is a biguanide antiseptic that helps to reduce the development of plaque and gingivitis when usual oral hygiene measures are interrupted. It is a strong base with affinity for oral structures including hydroxyapatite of tooth enamel, pellicle of tooth surface, bacteria and salivary proteins. Chlorhexidine reduces dental plaque deposition and associated gingivitis as characterized by redness, swelling or bleeding of the gingiva. It reduces frequency of aphthous ulcer formation and increases the rate of healing following periodontal surgery.

Chlorhexidine is active against a wide range of microorganisms including gram-positive, gram-negative bacteria, yeast and some fungi and viruses. Chlorhexidine appears to delay bacterial growth by a delayed surface action. It is absorbed onto microbial cell walls and causes membrane leakage.

5.2 Pharmacokinetic properties

General characteristics
Absorption:
Systemic absorption does not appear to occur following administration of chlorhexidine gluconate topical oral solution as mouth gargle. When it is administered as described, 4% of mouth gargle dose is ingested and

some part is absorbed. 90% of the ingested chlorhexidine dose is not absorbed and excreted directly in feces. Following topical administration of benzydamine hydrochloride, benzydamine is well absorbed into the inflamed oral mucosa where it exerts anti-inflammatory and local anesthetic effect on administration site. Plasma benzydamine level following use of benzydamine is low and parallel the amount actually ingested.

Distribution:
Following administration of chlorhexidine gluconate 0.12% topical oral solution as a mouth gargle, approximately 30% of the medicine is retained in the oral cavity. Chlorhexidine is gradually released for up to 24 hours.

Biotransformation:
As Chlorhexidine gluconate is poorly absorbed, no detectable blood levels have been found. Benzydamine is metabolized generally by oxidation and conjugation.

Elimination:
Chlorhexidine is not accumulated in body and only small amount of it is metabolized. Approximately 10% of the ingested chlorhexidine is excreted via kidneys following absorption; 90% unabsorbed is excreted in feces.
Benzydamine and its metabolites entering in the systemic circulation are excreted largely in the urine.

5.3 Preclinical safety data
Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
The other ingredients are saccharin sodium, glycerin, polysorbate 20, ethanol, purified water, peppermint flavor, sodium hydrogen carbonate/HCl (used as pH adjusting agent, if needed).

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store at or below 25°C and protect from light.

6.5 Nature and contents of container
DEVATIS SORE THROAT RELIEF GARGLE is presented in a 200 ml, amber colored glass bottle closed with polypropylene cap.

6.6. Special precautions for disposal
No special requirements for disposal.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Pharmacy Medicine.

8. SPONSOR

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9. DATE OF FIRST APPROVAL

Date of first authorization: 17.08.2017
Date of latest renewal:

10. DATE OF REVISION OF THE TEXT

June 2018