

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ledermix for Dental Use

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1. Ledermix 30 mg/g + 10 mg/g Dental Paste. Each gram contains: Demeclocycline calcium equivalent to Demeclocycline hydrochloride 30mg. Triamcinolone acetonide 10mg.
2. Ledermix 20 mg/g + 6.7 mg/g Dental Cement Powder. Each gram contains: Demeclocycline hydrochloride 20mg. Triamcinolone acetonide 6.7mg. For use with Ledermix Hardener 'F' Dental Liquid and Ledermix Hardener 'S' Dental Liquid.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Ledermix for Dental Use is a combination pack consisting of 4 separate unit containers as follows:

1. Ledermix Dental Paste is a greyish yellow smooth paste, free from gritty particles.
2. Ledermix Dental Cement Powder is a fine cream coloured powder.
3. Ledermix Hardener 'F' Dental Liquid is a clear colourless to yellow liquid with an odour of oil of cloves.
4. Ledermix Hardener 'S' Dental Liquid is a clear colourless to yellow liquid with an odour of oil of cloves.

Each of the units is also supplied separately.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

A topical dental preparation with antibiotic and corticosteroid properties. LEDERMIX is indicated in pulpitis (except total purulent pulpitis) and periodontitis.

4.2 Posology and method of administration

Adults:

Pulpitis: LEDERMIX Dental Paste is applied with a small cotton pledget to the dentine adjacent to the pulp or to the exposed pulp. The cavity is then closed with a temporary dressing. Approximately three to six days later the vitality of the tooth is determined, the cavity is re-opened and the cotton pledget is removed. The dentine close to the pulp, or the wound in the pulp, is covered with LEDERMIX Dental Cement prepared in the following manner: To one drop of the Hardener (no more) add sufficient LEDERMIX Dental Cement Powder to obtain an homogeneous mixture of cream-like consistency. This Cement, which hardens rapidly, may be applied with an amalgam plugger or blunt probe.

In small cavities with small areas of pulp exposure, LEDERMIX Dental Cement suffices as a base. In larger cavities or more extensive pulp exposure, it is advisable to use LEDERMIX Dental Cement as a lining cement only and then to cover it with a structural layer of zinc phosphate or zinc oxide-eugenol cement before inserting the permanent restoration. Occasionally, the use of LEDERMIX Dental Paste may be eliminated and LEDERMIX Dental Cement Powder (mixed with Hardener) applied in the first treatment period.

However, as a general rule, and particularly in acute pulpitis and in teeth where the pulp is exposed, the prepared LEDERMIX Dental Cement should NOT be applied without previous treatment with LEDERMIX Dental Paste.

Pulp vitality should be monitored regularly.

Periodontitis: In acute periodontitis, the canal may be prepared to the apex at the first sitting. After irrigation, the canal may be filled completely with LEDERMIX Dental Paste and sealed. This treatment can be repeated if necessary on the follow-up visit about one week later, or the canal may be irrigated to remove the Paste and further treatment carried out according to one of the generally accepted methods. If an alveolar abscess is present, drainage should be effective before beginning treatment with LEDERMIX.

Pulp vitality should be monitored regularly.

Children:

The use of tetracyclines during tooth development in children under the age of 12 years may cause permanent discolouration. Enamel hypoplasia has also been reported. LEDERMIX is therefore contraindicated in children of this age group.

There is no data to support the use of LEDERMIX in children over 12 years of age and therefore its use cannot be recommended.

4.3 Contraindications

LEDERMIX is contra-indicated in

- instances of total purulent pulpitis
- patients hypersensitive to any of the ingredients of LEDERMIX.
- children under the age of 12 years.

4.4 Special warnings and precautions for use

Precautions: The suppression of the inflammatory process by the use of a corticosteroid may result in a temporary reduction of the resistance of the pulp to infection and a reduced healing capacity. Therefore, LEDERMIX Dental Paste should not be in contact with the exposed pulp for too long. If the application of this water-soluble preparation is uncontrolled, or if the temporary dressing fits loosely, the danger exists that the pulp may not survive. The tip of the LEDERMIX Dental Paste tube should always be kept clean and tightly closed after use.

Prolonged or repeated use of any anti-infective may result in super infection or the development of resistant micro- organisms.

The LEDERMIX Cement Vial must be kept tightly closed after use.

If severe reactions or idiosyncrasies are encountered, the restorations should be removed and appropriate measures instituted.

Prescribers should be aware of the possible role of corticosteroids in cataract development.

Tooth discolouration has been reported during *in vitro* studies in animal or human teeth filled with Ledermix. This may be exacerbated by exposure to light and prolonged tooth contact with Ledermix. Darkening/grey brown discolouration has also been reported in a study in humans after Ledermix use following avulsion and replantation of teeth. This should be taken into consideration when treating visible teeth.

In vitro studies have shown that the active ingredients demeclocycline and triamcinolone are degraded by admixture with calcium hydroxide powder and calcium hydroxide 40% paste in a 50:50 ratio by weight. Ledermix paste should not be mixed with calcium hydroxide prior to application.

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 Interaction with other medicinal products and other forms of interactions

None known.

4.6 Fertility, pregnancy and lactation

Use in pregnancy

There are no specific data available on the use of LEDERMIX in pregnancy.

Results of animal studies indicate that tetracyclines cross the placenta, are found in foetal tissues and can have toxic effects on the developing foetus (often related to retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intra-uterine growth retardation.

The use of drugs of the tetracycline class during tooth development (last half of pregnancy) may cause permanent discolouration of the teeth (yellow-grey-brown). This adverse reaction is more common during long term use of the drug but has been observed following repeated short term courses. Enamel hypoplasia has also been reported.

The constituents of LEDERMIX are leached from the site of application in minute quantities over a long period of time. The relevance of findings relating to human and animal exposure to systemic tetracyclines or corticosteroids to the intra-cavity application of LEDERMIX is unclear. LEDERMIX is not recommended for use in pregnancy unless considered essential.

Use in Lactation

There are no specific data on concentrations of triamcinolone and demeclocycline in breast milk after intra-cavity administration of LEDERMIX. Very small amounts of the active ingredients may leach from the site of application into the maternal circulation over a prolonged period. There is a theoretical risk of permanent tooth discolouration and enamel hypoplasia in the infant.

LEDERMIX should therefore not be used during lactation unless considered essential.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Modern clinical data required to determine the frequency of undesirable effects are lacking for LEDERMIX. LEDERMIX is administered locally into the tooth cavity. However the various constituents are leached from the site of application in minute quantities over a long period of time. There is therefore the potential for systemic side effects.

System Organ Class	Frequency unknown (cannot be determined from available information)
<i>Immune system disorders</i>	Hypersensitivity, anaphylactic reaction, urticaria, rash, pruritus
<i>Gastrointestinal disorders</i>	Dental necrosis, tooth discolouration
<i>Eye disorders</i>	Vision, blurred (Also see section 4.4)

It has been suggested that in certain situations pulpal necrosis may occur. It is therefore advisable to monitor pulp vitality regularly and carry out endodontic treatment as appropriate.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

None known.

5 PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties**

ATC Code: A01A Stomatological preparations.

Demeclocycline hydrochloride has the antimicrobial activity and uses described for tetracycline hydrochloride. It is excreted more slowly and effective blood concentrations are maintained for a longer period.

An antimicrobial substance produced by the growth of certain strains of *Streptomyces aureofaciens* or by any other means. It occurs as a yellow, odourless, crystalline powder. The BP specifies not less than 900µg per mg, both calculated on the anhydrous basis.

Soluble 1 in 30 to 60 of water and 1 in 50 of methyl alcohol; slightly soluble in alcohol; practically insoluble in acetone, chloroform and ether; soluble in aqueous solutions of alkali hydroxides and carbonates.

Triamcinolone acetonide is a potent fluorinated corticosteroid with anti-inflammatory, antipruritic and anti-allergic actions.

5.2 Pharmacokinetic properties

Peak plasma concentrations of about 24µg per ml have been reported 3 to 6 hours after an oral dose of 500mg demeclocycline hydrochloride and persist for longer than after a similar dose of tetracycline, only falling to about 1µg per ml after 24 hours. Its biological half-life is about 12 hours. The renal clearance of demeclocycline is about half that of tetracycline.

5.3 Preclinical safety data

None stated.

No further information of use to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ledermix Dental Cement Powder:

Zinc oxide
Canada balsam
Resin
Calcium hydroxide

Ledermix Dental Paste:

Calcium chloride
Zinc oxide
Sodium sulphite anhydrous (E221)
Trolamine
Macrogol 3000
Macrogol 400
Sodium calcium edetate
Silica colloidal anhydrous
Purified water

Ledermix Hardener 'F' Dental Liquid:

Eugenol
Turpentine Oil, Pinus Pinaster Type

Ledermix Hardener 'S' Dental Liquid:

Eugenol
Turpentine Oil, Pinus Pinaster Type
Macrogol 4000

6.2 Incompatibilities

Calcium hydroxide inactivates the antibiotic and steroid components of Ledermix Dental Paste. Ledermix paste should not be mixed with calcium hydroxide prior to application. See section 4.4.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container.

Do not refrigerate.

For Ledermix Dental Paste / Cement Powder: Keep tube/bottle tightly closed to protect from moisture.

6.5 Nature and contents of container

Ledermix for Dental Use - Combination Kit:

2g Ledermix Dental Cement Powder.

5ml Hardener 'F' with separate glass dropper.

5ml Hardener 'S' with separate glass dropper.

3g Ledermix Dental Paste.

Ledermix for Dental Use Refill Kit No. 2:

5g Ledermix Dental Paste.

Ledermix for Dental Use Refill Kit No. 3:

3g Ledermix Dental Cement Powder.

Ledermix for Dental Use Refill Kit No. 4:

5ml Hardener 'F' with separate glass dropper.

Ledermix for Dental Use Refill Kit No. 5:

5ml Hardener 'S' with separate glass dropper.

Ledermix Dental Cement Powder, Hardener 'F' and Hardener 'S' are presented in Type III amber glass bottles with plastic screw caps. Ledermix Dental Paste is presented in an aluminium tube with plastic screw cap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Henry Schein UK Holdings Limited
Medcare House
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Gillingham Kent
ME8 0SB
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8 MARKETING AUTHORISATION NUMBER

PA1321/002/001

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