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.

Excipients with known effect
Ledermix Dental Paste contains sodium sulphite anhydrous (E211) 0.30% w/w and sodium calcium edetate 0.05% w/w.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

LEDERMIX is a dental treatment for topical application. It is supplied as a kit containing LEDERMIX Dental Paste, LEDERMIX Dental Cement Powder, Ledermix Hardener ‘F’ Dental Liquid (fast setting time) and Ledermix Hardener `S' Dental Liquid (slow setting time).

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Ledermix is a dental treatment which combines the antibiotic action of demeclocycline with the anti-inflammatory action of triamcinolone acetonide.

Ledermix is indicated in pulpitis, periapical periodontitis, and hypersensitive dentine.

4.2. Posology and method of administration

Adults:
Pulpitis: In all instances of exposed pulp and in acute pulpitis (except total purulent pulpitis), Ledermix 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 such as zinc oxide-eugenol.

Approximately three to six days later, the vitality of the tooth is determined, the cavity is reopened and the cotton pledget is removed. The dentine close to the pulp, or the wound in the pulp, is covered with Ledermix Cement prepared in the following manner. To one drop of the hardener (no more), add sufficient Ledermix Cement Powder to obtain a homogenous 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 Cement suffices as a base. In larger cavities or more extensive pulp exposure, it is advisable to use Ledermix 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. In certain instances of hyperaemia and partial serious pulpitis with closed pulp cavity, the use of Ledermix Paste may be eliminated with Ledermix Cement mixed with the 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 Cement should not be applied without previous treatment with Ledermix Paste. Pulp vitality should be monitored regularly.

Periapical periodonitis:
In primary acute periapical periodontitis and acute exacerbations of chronic periapical periodonitis, the canal may be prepared to the apex at the first sitting. After irrigation, the canal may be filled completely with Ledermix 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.

Hypersensitive dentine following cavity or crown preparations:
In instances of hypersensitive dentine following cavity or crown preparations, Ledermix Cement plus hardener may be used as sublining for deep cavities. 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.

Preparation of the cement:

Ledermix Cement belongs to the class of zinc oxide-eugenol dental cements. The setting time of all such cements is greatly affected by temperature and humidity conditions and by the technique of the individual operator. Vigorous and prolonged mixing, or spreading the mix thinly over the slab leads to accelerated setting, whilst lowering the temperature of the mixing slab will prolong the setting time. Under any given set conditions, however, the operator may obtain a faster or slower setting of the paste using the appropriate hardener. In general it will be found that the time required for the mixture to set obtained by the use of Hardener `S' will be approximately three to four times that obtained with hardener `F'.

Under conditions of high temperature and humidity, care should be taken to blend rapidly a small amount of Ledermix Cement Powder (taking no more than 10 to 15 seconds) into one drop of Hardener with two to three strokes of the spatula. All of the resultant mix should then be taken up at once on the spatula blade.

4.3. Contraindications

Ledermix is contraindicated 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 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 Paste tube should always be kept clean and tightly closed after use. Store in a cool place.

The Ledermix Cement vial must be kept tightly closed after use.

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

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. Interactions with other medicinal products and other forms of interaction

None known.

4.6. Fertility, Pregnancy and lactation

Use in pregnancy
There are no data from the use of LEDERMIX in pregnant women.

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 during pregnancy and in women of child-bearing potential not using contraception.

Use in Lactation
There is insufficient information on the excretion 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.

A risk to the suckling child cannot be excluded. LEDERMIX should therefore not be used during breast-feeding.

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
Immune system disorders	Hypersensitivity, anaphylactic reaction, urticaria, rash, pruritus
Gastrointestinal disorders	Dental necrosis, tooth discolouration
Eye disorders	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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 *Steptomyces aureofaciens* or by any other means. It occurs as a yellow, odourless, crystalline powder. The BP specifies not less than 900-ig 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 24pg per ml have been reported 3 to 6 hours after an oral dose of 500mg of demeclocycline hydrochloride and persist for longer than after a similar dose of tetracycline, only falling to about 1 jig 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. Pre-clinical safety data

None stated.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Ledermix Dental Cement Powder:
Zinc oxide
Canada balsam neutral solidified
Resin
Calcium hydroxide

Ledermix Dental Paste:
Calcium chloride
Zinc oxide
Sodium sulphite anhydrous (E221)
Trolamine
Macrogol 3000
Macrogol 400
Sodium calcium edetate
Colloidal anhydrous silica
Purified water

Ledermix Hardener F Dental Liquid:
Eugenol
Turpentine oil, pinus pinaster type

Ledermix Hardener S Dental Liquid:
Eugenol
Macrogol 4000
Turpentine oil, pinus pinaster type

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

24 months.

6.4. Special precautions for storage

LEDERMIX* should not be stored above 25°C.
Store LEDERMIX* in the original pack.

Do not refrigerate.

6.5. Nature and contents of container

LEDERMIX for Dental Use - Combination Kit:
2 g LEDERMIX Dental Cement Powder.
5 ml Hardener `F' with separate glass dropper.
5 ml Hardener `S' with separate glass dropper.
3 g LEDERMIX Dental Paste.

LEDERMIX for Dental Use Refill Kit No.2:
5 g LEDERMIX Dental Paste

LEDERMIX for Dental Use Refill Kit No.3:
3 g e[1] LEDERMIX Dental Cement Powder

LEDERMIX for Dental Use Refill Kit No. 4:
5 m1 Hardener `F'

LEDERMIX for Dental Use Refill Kit No. 5:
5 m1 Hardener `S'

LEDERMIX for Dental Use Refill Kit No. 6:
2.5 ml e[1] Hardener 'S

LEDERMIX for Dental Use Refill Kit No. 7:
2.5 ml e[1] Hardener 'F'

6.6. Special precautions for disposal

None.

7. MARKETING AUTHORISATION HOLDER

Henry Schein UK Holdings Limited
Medcare House,
Centurion Close
Gillingham Business Park
Gillingham
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ME8 0SB
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

PL 50837/0002

[1] e = nominal weight

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/03/2007

10. DATE OF REVISION OF THE TEXT

30/04/2019