SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Oracort E

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Triamcinolone acetonide 1 mg
Lidocaine hydrochloride monohydrate 30 mg

3. PHARMACEUTICAL FORM

Topical oral paste.
Yellow, viscous, grainy paste.

4. INDICATIONS AND USAGE

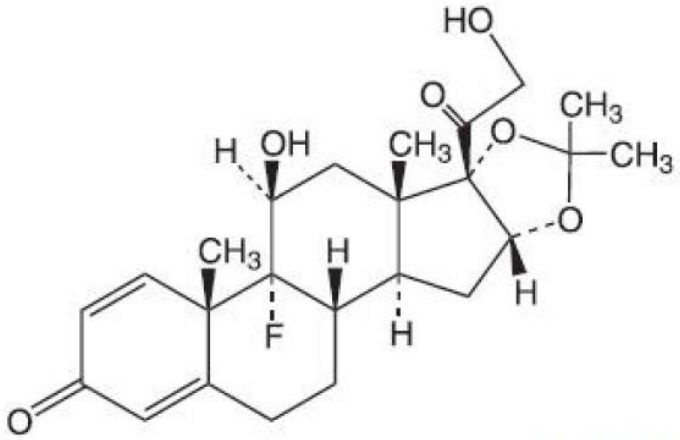
Oracort E is indicated for adjunctive treatment and temporary relief of pain and symptoms associated with oral inflammatory and ulcerative lesions.

5. DOSAGE AND ADMINISTRATION

Press a small dab to the lesion until a thin film develops. A larger quantity may be required for coverage of some lesions. For optimal results use only enough to coat the lesion with a thin film. Do not rub in. Attempting to spread this preparation may result in granular, gritty sensation and cause it to crumble. After application, however, a smooth, slippery film develops.
The preparation should be applied at bedtime to permit steroid contact with the lesion throughout the night. Depending on the severity of symptoms, it may be necessary to apply the preparation two or three times a day, preferably after meals. If significant repair or regeneration has not occurred in seven days, further investigation is advisable.

6. DESCRIPTION

Oracort E contains the corticosteroid triamcinolone acetonide in an adhesive vehicle suitable for application to oral tissues. Triamcinolone acetonide is designated chemically as 9-fluoro-11β, 16α, 17, 21-tetrahydroxypregna-1, 4-diene-3, 20- dione cyclic 16, 17-acetal with acetone. The structural formula of triamcinolone acetonide is as follows:



$C_{24}H_{31}FO_6$ MW 434.50

Each gram of Oracort E contains 1 mg triamcinolone acetonide and 30 mg lidocaine hydrochloride monohydrate in an emollient dental paste.

Excipients:
Paraffin liquid, gelatin, pectin, sodium carboxymethylcellulose, polyethylene A-6.

7. CLINICAL PHARMACOLOGY

Pharmacodynamic properties of triamcinolone

Pharmacotherapeutic group: Corticosteroids for local oral treatment.

ATC code: A01AC

Like other topical corticosteroids, triamcinolone acetonide has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A_2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A_2.

Pharmacodynamic properties of lidocaine

Pharmacotherapeutic group: Other agents for local oral treatment.

ATC code: A01AD11

Lidocaine reversibly prevents the opening of the Na+ channels and thus the development of action potential. The active substance binds to a specific

receptor on the Na+ channel of the nerve and thereby prevents the transport of ions through the pores and thus the development of an action potential. This locally suppresses stimulus conduction.

The pain sensation is suppressed, with thin non-myelinated nerve fibers being blocked more quickly than thicker motor nerves. The sensations are blocked in the following order: pain, cold/heat, touch and pressure.

Pharmacokinetics
The extent of absorption through the oral mucosa is determined by multiple factors including the vehicle, the integrity of the mucosal barrier, the duration of therapy, and the presence of inflammation and/or other disease processes. Once absorbed through the mucous membranes, the disposition of corticosteroids is similar to that of systemically administered corticosteroids. Corticosteroids are bound to the plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys; some corticosteroids and their metabolites are also excreted into the bile.

The active substance lidocaine is absorbed very quickly, within a few seconds to minutes, due to the special morphological conditions that distinguish the oral mucosa from the “normal” skin (no *stratum corneum*, blood vessels are more dense on the surface), and the effect lasts for about 1 hour.
Lidocaine is metabolised through extensive first-pass metabolism in the liver. 90-95% is metabolised (separation of the alkyl groups at the amino nitrogen, hydroxylation at the ring, hydrolytic cleavage of the acid-amide bond). Approximately 5-10% of the dose is excreted unchanged via the kidneys. The metabolic rate may be considerably reducedin hepatic impairment.

8. PRECLINICAL SAFETY DATA

Due to the rapid metabolism of lidocaine, a systemic or even a toxic effect of Oracort E is not to be expected with application at the recommended frequency in the recommended amount.

Chronic toxicity

Studies lasting 6 months have been conducted in rats and dogs. The studies in rats did not reveal any pathological changes caused by lidocaine. The studies in dogs showed changes in the liver (fatty degeneration) after subcutaneous administration of 30 mg/kg and after oral administration of 50-60 mg/kg.

Reproductive toxicity

No teratogenic effects were found in embryonic/foetal development studies in which rats or rabbits were treated with lidocaine during organogenesis. Embryotoxicity was observed in rabbits at maternally toxic doses. In rats, a reduced survival rate of the offspring was observed in mothers treated with lidocaine in late pregnancy and during lactation at a maternally toxic dose that affected the duration of gestation.

Genotoxicity and carcinogenicity
Genotoxicity studies on lidocaine yielded negative results. However, genotoxicity studies with 2,6-xylidine *in vitro* revealed a genotoxic potential of this lidocaine metabolite. Tumours in the nasal cavity, subcutaneous tissue and liver were observed in a carcinogenicity study in rats with in-utero and lifelong postnatal exposures to 2,6-xylidine.

Local tolerability studies

Local tolerability was studied in hamsters over a 4-week period (hamster cheeks). The observed reactions were non-specific. There were no clinically relevant changes after administration of lidocaine.

Study of the potential for sensitisation

The sensitising potential of lidocaine was studied in guinea pigs using the Magnusson and Kligman method. Under the chosen experimental conditions, the product showed only a minor sensitising capacity at 24 hours.

9. CONTRAINDICATIONS

- Hypersensitivity to the active substances or to other amide local anaesthetics or to any of the excipients listed in section 6.
- In the presence of fungal, viral, or bacterial infections of the mouth or throat.

10. PRECAUTIONS

General
Oracort E may cause local adverse reactions. If irritation develops, Oracort E should be discontinued and appropriate therapy instituted. Allergic contact sensitization with corticosteroids is usually diagnosed by observing failure to heal rather than noting a clinical exacerbation as with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic patch testing.

If concomitant mucosal infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favorable response does not occur promptly, use of Oracort E should be discontinued until the infection has been adequately controlled. If significant regeneration or repair of oral tissues has not occurred in seven days, additional investigation into the etiology of the oral lesion is advised.
Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, glucosuria, and other adverse effects known to occur with parenterally-administered steroid preparations; therefore, it may be advisable to periodically evaluate patients on prolonged therapy with corticosteroid-containing dental pastes for evidence of HPA axis suppression (see **PRECAUTIONS, Laboratory Tests**). If HPA axis suppression is noted, an attempt should be made to withdraw the drug or to reduce the frequency of

application. Recovery of HPA axis function is generally prompt and complete upon discontinuation of therapy.

Caution in patients with wounds or traumatized mucosa near the intended site of use. Destruction of mucosa results in increased systemic absorption. Swallowing may be impeded, and the risk of aspiration may be increased. Numbness of the tongue or oral mucosa may increase the risk of injury from the user biting their own tongue, cheek, etc.

Although the absorbed quantities of lidocaine after local administration are significantly lower than after infiltration or line anaesthesia, systemic effects cannot be completely ruled out under very unfavorable absorption conditions (severely damaged mucosa). Oracort E should therefore only be used with caution in patients with severe disorders of the cardiac conduction system, acute decompensated heart failure and severe kidney or liver disease.
In this case, administration to large areas should be avoided.

Interaction with other medicinal products and other forms of interaction
Clinically relevant interactions are very unlikely due to local administration and the amount administered. It is possible, however, that the pain-inhibiting effect of other local anaesthetics could be potentiated.
The interactions with other medicinal products known for lidocaine (antiarrhythmics, beta blockers) are not significant in the local administration of Oracort E on the oral mucosa.

Laboratory Tests
A urinary free cortisol test and ACTH stimulation test may be helpful in evaluating HPA axis suppression.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Animal studies have not been performed to evaluate triamcinolone acetonide for potential to induce carcinogenesis, mutagenesis, or impairment of fertility.

Pregnancy and breastfeeding

Teratogenic effects
Triamcinolone acetonide has been shown to induce teratogenic effects in several species. In mice and rabbits, triamcinolone acetonide induced an increased incidence of cleft palate at dosages of approximately 120 µg/kg/day and 24 µg/kg/day, respectively (approximately 12 times and 10 times the amount in a typical daily human dose of Oracort E when compared following normalization of the data on the basis of body surface area estimates, respectively). In monkeys, triamcinolone acetonide induced cranial skeletal malformations at the lowest dosage studied (500µg/kg/day), which was approximately 200 times the amount in a typical daily human dose of Oracort E when compared following normalization of the data on the basis of body surface area estimates.

There are no adequate and well controlled studies in pregnant women. However, a retrospective analysis of birth defects among children born to mothers that used drugs of the same class as Oracort E (corticosteroids) during pregnancy found an approximately 3 times increased incidence of cleft palate.

There is insufficient data from the use of lidocaine in pregnant women. Lidocaine crosses the placenta and can be absorbed by fetal tissue. The potential risk for humans is not known.
Oracort E should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether oral application of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Caution should be exercised when corticosteroid containing dental pastes are prescribed for a nursing woman.

Lidocaine passed into breast milk in small amounts.

Oracort E should not be used during breastfeeding unless it is clearly necessary.

Pediatric Use
The safety and efficacy of Oracort E in children is unknown. Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's Syndrome than mature patients because of a larger skin surface area to body weight ratio. Administration of corticosteroid-containing dental pastes to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

Geriatric Use
Clinical studies of Oracort E did not include sufficient numbers of subjects age 65 and older to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

Effects on ability to drive and use machines

Oracort E is not known to have adverse effects on ability to drive and use machines.

11. ADVERSE REACTIONS

The following local adverse reactions may occur with corticosteroid-containing dental pastes: burning, itching, irritation, dryness, blistering or peeling not present prior to therapy, perioral dermatitis, allergic contact dermatitis, maceration of the oral mucosa, secondary infection, and atrophy of the oral mucosa.

Also, see **PRECAUTIONS** for potential effects of systemic absorption.

The following adverse reactions may occur with lidocaine-containing dental pastes:
Very rare (<1/10,000)

Immune system disorders
Hypersensitivity such as urticaria (local), contact dermatitis
Anaphylactic reaction
Anaphylactic shock

Nervous system disorders
Taste disorder

General disorders and administration site conditions
Local reactions such as mucosal burning, local swelling, erythema at the site of application

Skin and subcutaneous tissue disorders
Pruritus
Skin redness

Injury, poisoning and procedural complications
Pain at the site of application
Numbness at the site of application

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:
http://sideeffects.health.gov.il

12. OVERDOSE

To date, there are no known cases of intoxication after the use of Oracort E.

If a systemic adverse reaction occurs, the following are recommended as emergency measures/antidotes: Keep the airway clear, monitor blood pressure, pulse and pupil size; position the patient lying flat with raised legs if there is an acute and dangerous drop fall in blood pressure, administer a beta-sympathomimetic (e.g. isoprenaline); if seizures occur give diazepam; if there is increased vagal activity (bradycardia) give atropine; if necessary, administer oxygen, IV volume replacement and resuscitation.

13. HOW SUPPLIED

Oracort E is supplied in tubes containing 5 g of dental paste.

14. STORAGE

Store below 25° in a cool dark place.

15. SHELF LIFE

The expiry date of the products is printed on the package materials.

Shelf-life after first opening: 3 months

16. MARKETING AUTHORISATION HOLDER AND MANUFACTURER

Taro Pharmaceutical Industries Ltd.
14 Hakitor St., Haifa Bay 2624761
Israel

17. MARKETING AUTHORISATION NUMBER

037-10-22812-00

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