SUMMARY OF PRODUCT CHARACTERISTICS

NAME OF THE MEDICINAL PRODUCT

Oracort E

QUALITATIVE AND QUANTITATIVE COMPOSITION

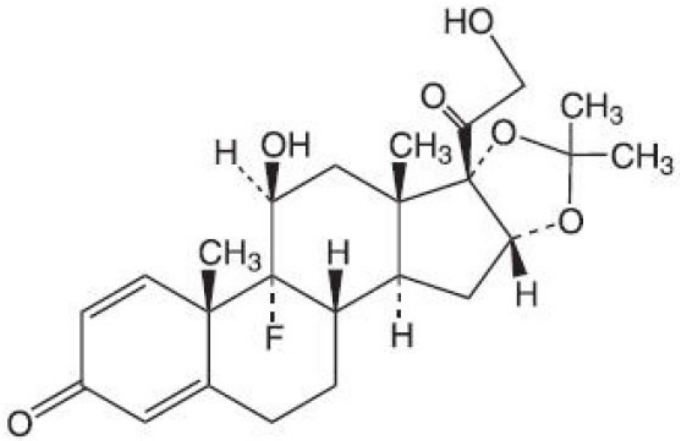
Triamcinolone Acetonide 1 mg
Lidocaine Hydrochloride monohydrate 30 mg

Topical Oral Paste

Excipients:
Paraffin liquid, gelatin, pectin, sodium carboxymethylcellulose, polyethylene.

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

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.

CLINICAL PHARMACOLOGY

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 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.

Lidocaine reversibly prevents opening of Na+ channels and thus the development of an action potential. The active substance binds to a specific receptor on the Na+ channel of the nerve, thereby preventing the transport of ions through the pores and thus the development of an action potential.
This leads to suppression of conduction locally.

Pain perception is suppressed, with thin unmyelinated nerve fibres more rapidly inactivated than thicker motor nerves. The sensations are inactivated in the following sequence: 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.

Given the special morphological conditions that distinguish the oral mucosa from “normal” skin (no horny layer, blood vessels lie closer to the surface), the active substance lidocaine is very rapidly absorbed within a few seconds to minutes and the effect lasts for about 1 hour.
Lidocaine is metabolised through extensive first-pass metabolism in the liver. 90-95% is metabolised (cleavage of the alkyl residues on the amino nitrogen, ring hydroxylation, hydrolytic cleavage of the amino-amide bond). Approximately 5-10% of the dose is excreted unchanged via the kidneys. The rate of metabolism may be greatly diminished in hepatic impairment.

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 if the recommended frequency of administration and quantity are used.

Acute toxicity

The acute toxicity of lidocaine has been tested in several species and using different methods of administration (see Table).

Species	Intravenous administration (mg/kg)	Oral administration (mg/kg)	Subcutaneous administration (mg/kg)
Mouse	15	220	163
Rat	21	--	570
Rabbit	25.6	--	--
Guinea pig	24.5	--	--

The first toxic effects on the central nervous system were seen after intravenous doses of 3-5 mg/kg and subcutaneous doses of 30-50 mg/kg. The limit dose below which administration of lidocaine is considered safe is 4 mg/kg body weight with IM injection.

Chronic toxicity

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

Reproductive toxicity

Studies on embryonic/fetal development, in which rats or rabbits were treated with lidocaine during the period of organogenesis, did not show any teratogenic effects. Embryotoxicity was observed in rabbits at maternally toxic doses. In rat dams treated with lidocaine during the late stage of gestation and during lactation using a maternally toxic dose that affected the length of gestation, a reduced survival rate of the progeny was observed.

Studies on local tolerability

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.

CONTRAINDICATIONS

Oracort E is contraindicated in those patients with a history of hypersensitivity to the active substance or to any of the excipients; it is also contraindicated in the presence of fungal, viral, or bacterial infections of the mouth or throat.
Oracort E is contraindicated in those patients with a history of hypersensitivity to any other local anaesthetics of the amino amide type.

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.

Although the absorbed quantity of lidocaine after local use is much lower than after infiltration or regional anaesthesia, systemic effects cannot be completely ruled out if the absorption conditions are very unfavourable (severely damaged mucosa). Oracort E should therefore only be used with special care in patients with severe disorders of the pacemaker/conduction

system of the heart, acute decompensated heart failure and severe renal or hepatic disorders.

Information for the Patient
Patients using topical corticosteroids should receive the following information and instructions:
1. This medication is to be used as directed by the physician or dentist. It is for oral use only; it is not intended for ophthalmic or dermatological use.
2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
3. Patients should report any signs of adverse reactions.
4. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician or dentist.

Interaction with other medicinal products and other forms of interaction
Given the local administration and quantity administered, clinically relevant interactions are very unlikely. It is possible, however, that the analgesic effect of other local anaesthetics could be potentiated. The interactions with other medicinal products (antiarrhythmics, beta blockers) that are otherwise known to occur with lidocaine are unimportant with 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.

Studies on the genotoxicity of lidocaine were negative. However, in vitro genotoxicity studies with 2,6-xylidine showed this lidocaine metabolite to have a genotoxic potential. As part of a carcinogenicity study in rats with in utero and life-long postnatal exposure to 2,6-xylidine, tumours in the nasal cavity, subcutaneous tissue and liver were observed.

Pregnancy Category C

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. Oracort E should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

There is insufficient data from the use of lidocaine in pregnant women. Lidocaine can cross the placenta and may be absorbed by fetal tissue. The potential risk for humans is not known. Lidocaine is excreted in breast milk in low quantities.
Oracort E should not be used during pregnancy or lactation unless it is clearly necessary.

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 is excreted in breast milk in low quantities.
Oracort E should not be used during pregnancy or lactation 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.

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.

The following adverse reactions may occur with lidocaine-containing dental pastes:

The frequencies for adverse reactions are based on the following categories:
Very common (1/10≤)
Common (≥10/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (1/10,000>)
Not known (cannot be estimated from the available data)

Very rare

- Local allergic and non-allergic reactions e.g:.
- Burning
- Swelling
- Redness
- Pruritus
- Urticaria
- Contact dermatitis
- Rashes
- Pain
- Taste disorders
- Loss of sensation
- Anaphylactic reactions and shock reactions with accompanying symptoms

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

Reporting of suspected adverse reactions
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

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.

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 patent; monitor blood pressure, pulse and pupil size; position the patient flat with the legs raised if there is an acute and threatening fall in blood pressure, administer a beta-sympathomimetic (e.g. isoprenaline); if seizures occur give diazepam (5 to 10 mg IV); if there is increased vagal activity (bradycardia) give atropine (0.5 to 1 mg IV); if necessary, administer oxygen, IV fluid replacement and resuscitation.

HOW SUPPLIED

Oracort E is supplied in tubes containing 5 g of dental paste.
Yellow, viscous, grainy paste.

Storage

Store below 25° in a cool dark place.

SHELF LIFE

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

Shelf-life after first opening: 3 months

MARKETING AUTHORISATION HOLDER AND MANUFACTURER

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

MARKETING AUTHORISATION NUMBER

Oracort E 037-10-22812-00

Revised in August 2022 according to MOH guidelines.