HAUTE AUTORITÉ DE SANTÉ

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TRANSPARENCY COMMITTEE

OPINION

12 April 2006

Oragix, periodontal gel
Box of 20 glass cartridges, each 1.7 g (CIP code: 367 881-4)

Applicant: Dentsply

prilocaine
lidocaine

List II
Professional use

Date of Marketing Authorisation: 17 February 2005

Reason for application: Inclusion on the list of drugs approved for hospital use

Health Technology Assessment Division

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

prilocaine
lidocaine

1.2. Indication

Oraqix is indicated in adults for local anaesthesia of periodontal pockets for diagnostic and treatment purposes (probing, scaling and/or root planing).

1.3. Dosage in adults (including the elderly)

Generally, one cartridge (1.7 g) or less of Oraqix is sufficient to treat one quadrant of the jaw. The maximum recommended dose of Oraqix for a treatment session is five cartridges, i.e. 8.5 g of gel containing 212.5 mg of lidocaine base and 212.5 mg of prilocaine base.

Fill the periodontal pockets with Oraqix using the blunt-tipped applicator included in the package, until the gel reaches the gingival margin. Wait 30 seconds before starting treatment (a longer waiting time does not improve the anaesthesia). Anaesthetic effect, as assessed by probing of pocket depths, lasts for approximately 20 minutes. If the anaesthesia starts to wear off, Oraqix may be re-applied if needed.

When applied, Oraqix should be a liquid. If it has formed a gel, it should be placed in a refrigerator until it becomes a liquid again. The bubble in the cartridge should move freely if the cartridge is turned upside down.

The use of Oraqix has not been studied in children and adolescents and is therefore not recommended in patients under 18 years of age.

2 SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification

N	: NERVOUS SYSTEM
N01	: ANAESTHETICS
N01B	: ANAESTHETICS, LOCAL
N01BB	: AMIDES
N01BB20	: Amide, combinations

2.2. Medicines in the same therapeutic category

Oraqix is the only local anaesthetic in the category of amides, consisting of a combination of prilocaine and lidocaine and intended for periodontal use.

2.3. Medicines with the same therapeutic aim

Local anaesthetics (topical anaesthetics and anaesthetics for injection) intended for use in dentistry and oral medicine.

3 ANALYSIS OF AVAILABLE DATA

The clinical dossier submitted by the company contains four trials:

- 3 double-blind randomised placebo-controlled trials (B1[a], B2[b], B3[c]) assessing the efficacy and safety of Oraqix in 337 patients;
- 1 open crossover trial (B4[d]) comparing Oraqix with a combination of lidocaine 2% and adrenaline administered by infiltration.

3.1. Efficacy

Controlled trials B1, B2, B3

The population in all three trials consisted of adults who had not had any periodontal care during the previous 6 (B3) or 12 months (B1, B2). In trials B1 and B2, all patients scheduled for scaling and root planing were included. Trial B3 included patients with pain sensitivity, defined as a pain score > 30 mm on a 100-mm visual analogue scale during mechanical probing of periodontal pockets.

The median dose give to patients was approximately one cartridge (1.7 g of gel) per quadrant of dentition treated. Treatment began 30 seconds after administration of the gel inside the periodontal pockets.

The main endpoint was score for procedure-related pain assessed by the patient on a 100-mm visual analogue scale (VAS) at the end of the procedure.

Secondary endpoints were:

- pain score for procedure-related pain assessed by the patient on a 5-point simple verbal scale (SVS) ranging from "no pain" to "very severe pain";
- number of patients requiring a further application of gel.

Results:

Procedure-related pain scores at the end of the procedure

Trial Number of patients	VAS Median global score			SVS Global score (%) “no pain” to "mild pain"		
	Oraqix	Placebo	p value	Oraqix	Placebo	p value
B1 (n=122)	7	17	< 0.0005	90	64	0.001
B2 (n=130)	5	13	0.015	78	76	0.230
B3 (n=85)	11	27	< 0.004	70	48	0.003

In all three trials, 92% of patients were able to receive all care without further application of gel.

Controlled trial (B4) comparing Oraqix with infiltration anaesthesia

The primary aim of this open trial was to assess patient preference for two types of anaesthesia, i.e. local application of Oraqix gel or injection of lidocaine 2% combined with adrenaline before procedures such as scaling and/or root planing.

[a] Jeffcoat MK, Geurs N, Magnusson I, et al.Intrapocket anesthesia for scaling and root planing: results of a double-blind multicenter trial using lidocaine prilocaine dental gel. J Periodontol 2001;72:895-900.

[b] Donaldson D, Gelskey SC, Landry RG, Matthews DC, Sandhu HS. A placebo-controlled multi-centred evaluation of an anesthetic gel (Oraqix) for periodontal therapy. J. Clin Periodontol 2003;30:171-5

[c] Magnusson L., Geurs NC, Harris PA, et al. Intrapocket anesthesia for scaling and root planing in pain-sensitive patients. J. Periodontol 2003;74:597-602.

[d] Van Steenberghe D, Bercy P, De Boever J, et al. Patient evaluation of a novel non-injectable anesthetic gel: a multicenter crossover study comparing the gel to infiltration anesthesia during scaling and root planing. J. Periodontol 2004;75:1471-8.

One hundred and seventy patients aged 18 years or over were included in the trial. Patients were randomised in a crossover design to receive Oraqix and lidocaine for injection administered on one side only to the upper and lower dental quadrants. The two treatment sessions were separated by one week without treatment.

Gel dose was 1.3–6.8 g. Treatment began 30 seconds after administration and lasted for a mean of 47 minutes.

The dose of injected anaesthetic was 28–190 mg of lidocaine 2% (1.4–9.5 ml) and mean duration of treatment was 44 minutes.

Treatment consisted of ultrasound as a first step, followed by scaling using traditional instruments.

The primary endpoint was type of anaesthesia preferred by the patient.

Results:
The majority of patients preferred application of Oraqix gel to injected anaesthesia (70% compared with 22%, $p<0.005$). However, the degree of anaesthesia induced by Oraqix was lower than that from infiltration anaesthesia.

3.2. Undesirable effects

No adverse events could be specifically attributed to Oraqix. The most common adverse events were local reactions in the mouth cavity. Frequency and type of reactions were similar with Oraqix and with placebo.

The local reactions reported such as tenderness, ulceration, irritation and redness are normal symptoms after scaling and root planing. Similar symptoms may also be associated with periodontitis.

No methaemoglobinaemia or allergic reactions were reported during the clinical trials carried out with Oraqix.

3.3. Conclusion

In trials B1, B2 and B3 assessing the efficacy of Oraqix in controlling procedure-induced pain during the treatment procedures of scaling and gingival curettage, the anaesthetic effect of an application of gel in the periodontal pockets was statistically higher than that of placebo. However, the degree of anaesthesia induced by Oraqix was low (reduction of approximately 10 mm in pain score compared with placebo on a 100-mm visual analogue scale).

In trial B4, comparing Oraqix with a combination of lidocaine and adrenaline administered by infiltration, the majority of patients studied (70%) preferred Oraqix even though the degree of anaesthesia obtained was lower. However, the endpoint of this trial is not clinically relevant when comparing Oraqix with injected anaesthesia, which has the benefit of reducing bleeding in the area of the procedure because of the vasoconstrictor combined with it.

In the different studies, Oraqix was well tolerated. The adverse events recorded were moderate and mainly local.

4 TRANSPARENCY COMMITTEE CONCLUSIONS

4.1. Actual benefit

Procedures related to the indications for this medicinal product are not life-threatening to the patient, do not cause serious complications, nor incapacity, nor marked degradation of quality of life.

The medicinal product is classed as adjuvant therapy for these treatment procedures.

The efficacy/side effects ratio for the drug is substantial.

The product is a first-line drug.

There are alternative drugs to this medicinal product.

Public Health Benefit

In view of the inconclusive nature of data on the prevalence of patients with an indication for the product Oraqix, the public health burden cannot be quantified.

Local anaesthesia of the periodontal pockets during these treatment procedures does not constitute a public health need.

In view of the data from clinical trials, it is not anticipated that the medicinal product will have any impact in terms of reducing pain related to the treatment procedure compared with existing forms of treatment, notably injected anaesthetics which include adrenaline.

Consequently, no public health benefit is anticipated for this medicinal product.

The actual benefit of this medicinal product is substantial.

4.2. Improvement in actual benefit

Oraqix does not contribute any improvement in actual benefit (ASMR V) compared with infiltration anaesthesia.

4.3. Therapeutic use

Non-surgical treatment for periodontal disease consists of cleaning by supragingival and subgingival scaling of the tooth surfaces to which plaque and tartar adhere. If periodontal pockets are present, the procedure is completed with subgingival curettage and planing.

Local anaesthesia, by whatever method, is only an adjuvant to the treatment procedure, and one which is not always necessary.

The choice of anaesthetic should then be guided by:

- the type of procedure to be performed (according to degree of severity of the disorder),
- patient and practitioner comfort,
- any benefit for the patient.

<u>Diagnostic procedures (probing) and treatment procedures (supragingival scaling)</u>

These procedures are superficial and do not require anaesthesia. Oraqix gel may be a first-line therapy in patients with sensitivity to or fear of pain related to the procedure.

<u>Treatment procedures (subgingival scaling and planing)</u>

These procedures are more invasive and are often associated with bleeding. Local infiltration anaesthesia has the benefit of reducing bleeding if the drug injected contains adrenaline.

Oraqix may be an alternative for patients with a contraindication to vasoconstrictors or fear of pain related to the injection.

4.4. Target population

The target population consists of patients with periodontal disease during the non-surgical phase of treatment and follow-up treatment procedures (periodontal maintenance), who could benefit from treatment with Oraqix.

Periodontal disease has been the subject of few epidemiological studies in the adult French population. The existing partial data[1] are too inconclusive to provide any estimate of the target population for Oraqix gel.

4.5. Transparency Committee recommendations

Approval of inclusion on the list of medicinal products approved for use in hospitals and various public services in the indications and at the doses given in the Marketing Authorisation.

[1] DGS /GTNDO – 2003: According to a study carried out in 1993 in a sample (established using a quota methods) of the French adult population aged 35–44 years and 65–74 years.