Application to widen the classification for topical oral benzocaine, tetracaine hydrochloride, lidocaine and prilocaine to allow access without prescription for oral health therapists and dental therapists registered with the Dental Council to use them in their practice

Dental Council
Te Kaunihera Tiaki Niho

Executive Summary

This reclassification application seeks to use an exception from prescription availability to make topical oral amethocaine (tetracaine), benzocaine, lidocaine (lignocaine) and prilocaine more readily available to dental therapists and oral health therapists. The application is being submitted by the Dental Council of New Zealand, the regulator of dental professionals practising in New Zealand. It follows work on scopes of practice for these professionals, and the 2017 widening of access to injected local anaesthetics to oral health therapists.

Topical and injected local anaesthetic agents are widely used in NZ and internationally by dentists and other dental professionals. They have clear consumer benefit in terms of comfort with dental procedures, which is important in encouraging people to receive dental care. Dental therapists have long used topical local anaesthetics and injectable local anaesthetics in treating children up to 18 years of age. Oral health therapists have been able to administer by injection local anaesthetics without needing standing orders or a dentist on site since 2017.

These agents are well-known in terms of use, contraindications, precautions and adverse effects. NZ spontaneous reports of adverse events have shown few concerns with the agents this application seeks to reclassify, with anaphylaxis and methaemoglobinaemia very rarely experienced.

The Dental Council previously consulted widely on the scope of practice for oral health therapists, which includes local anaesthetic administration without requiring a dentist to be on-site. Most submitters were supportive of the scope of practice consulted on.

Oral health therapists and dental therapists have had appropriate education in use of injected and topical local anaesthetics. They are trained, as are dentists, to CORE Immediate resuscitation level and must have oxygen and adrenaline available. Oral health therapists and dental therapists are increasingly working more independently in New Zealand and internationally, for example in Australia, UK, Singapore, and some states in the USA. The medicines affected by this application would be used on-site by the dental professionals concerned, there is no consumer self-use.

The proposed reclassification of four topical local anaesthetics (which are used in two marketed products) would enable dental therapists and oral health therapists to work more easily within their scopes of practice for the benefit of their patients.

The risk-benefit of this minor change to the classification statement is reasonable.

PART A

1. **International Non-proprietary Name of the medicine**

   a. Lidocaine (INN and BAN) also known as lignocaine. Named in the classification schedule as lignocaine
   b. Benzocaine
   c. Tetracaine (INN) also known as amethocaine. Named in the classification schedule as amethocaine
   d. Prilocaine

2. **Proprietary name (s)**

   The two products specifically targeted for this change are Oraqix and Zap gel.

3. **Name of company/organisation/individual requesting reclassification**

   Dental Council - New Zealand.
   Level 8
   Kordia House
   109-125 Willis Street
   Wellington 6011
   Ph: +64 4 499 4820

   The Dental Council is a responsible authority created by the Health Practitioners Competence Assurance Act 2003 to regulate the oral health professions. It ensures oral health practitioners meet and maintain its standards in order to protect the health and safety of the New Zealand public. The oral health practitioners it regulates are dentists, dental specialists, dental therapists, dental hygienists, clinical dental technicians, dental technicians, oral health therapists and orthodontic auxiliaries.

4. **Dose form(s) and strengths for which a change is sought**

   Dose form: topical oral gel
   See point 8 below for the strengths involved for each medicine.

5. **Proposed pack size, storage conditions and other qualifications**

   There are no qualifications required on pack size. We propose adding the qualification that the medicine can be used in practice by a dental therapist or oral health therapist registered with the Dental Council. See point 8 below for exact wording. No storage conditions need to be provided for the classification statement.

6. Indications for which change is sought

Rather than specifying the indications, the change for the classification statement will specify that the medicines are to be used in practice by a dental therapist or oral health therapist. Product licences and scopes of practice through the Dental Council will ensure appropriate usage better than the classification statement.

Benzocaine, prilocaine, lidocaine (lignocaine), and tetracaine (amethocaine) are used for local anaesthesia. In this application these active ingredients are used topically within the mouth.

Examples of the licensed indications of the products are below:
"ZAP Topical Anesthetic Gel [containing 18% benzocaine and 2% tetracaine hydrochloride] is indicated to reduce the discomfort of local anaesthetic injected into the mandibular mucobuccal fold and maxillary anterior sites, and to minimise pain in oral mucosal tissue arising from needle punctures, deep scaling procedures, prosthetic adjustments, clamp or crown placement, removal of primary teeth and suture removal. ZAP Topical Anesthetic Gel may also be used for the reduction of pharyngeal (gag) reflex associated with the placement of various dental materials into the oral cavity (impression trays, x-ray films)."

"Oraqix® [lidocaine 25 mg/g and prilocaine 25 mg/g] is indicated in adults for localised anaesthesia in periodontal pockets for probing, scaling and/or root planing."

NB: as lidocaine is the INN name and used in product data sheets, it is used throughout this application rather than lignocaine. It is noted that in the classification statement on the Medsafe website, a lidocaine search is referred to the lignocaine entry. Data sheets typically refer to lidocaine. Tetracaine is the INN name and used in the product data sheet, but it is referred to as amethocaine in the classification statement on the Medsafe website, so both names are included in this application to aid with clarity.

7. Present classification of the medicines

Table 1 Current classifications of medicines

Medicine	Current Classification
Benzocaine	**Prescription: except** when specified elsewhere in this schedule; **except** in dermal preparations containing 2% or less of total anaesthetic substances; **except** in lozenges containing 30 milligrams or less of total anaesthetic substances per dosage unit **Pharmacy Only:** in preparations for topical use, other than eye drops, containing 10% or less of total anaesthetic substances **except** in dermal preparations containing 2% or less of total anaesthetic substances; in divided preparations containing 200 milligrams or less of total anaesthetic substances per dosage unit **except** in lozenges containing 30 milligrams or less of total anaesthetic substances per dosage unit

	General Sale: in dermal preparations containing 2% or less of total anaesthetic substances; in lozenges containing 30 milligrams or less of total anaesthetic substances per dosage unit
Prilocaine	**Prescription**: for injection **except** when used as a local anaesthetic in practice by a dental therapist or oral health therapist registered with the Dental Council; **except** when specified elsewhere in this schedule **Pharmacy Only**: for dermal use in medicines containing 10% or less of local anaesthetic substances
Lidocaine (lignocaine)	**Prescription:** for injection **except** when used as a local anaesthetic in practice by a nurse whose scope of practice permits the performance of general nursing functions or by a podiatrist registered with the Podiatry Board or by a dental therapist or oral health therapist registered with the Dental Council; for ophthalmic use **except** when used in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board; for oral use **except** in throat lozenges in medicines containing 30 milligrams or less per dose form; for external use in medicines containing more than 10%; **except** in throat sprays in medicines containing 2% or less; **except** when specified elsewhere in this schedule **Pharmacy Only:** for urethral use; for external use in medicines containing 10% or less and more than 2% **General sale:** in throat lozenges in medicines containing 30 milligrams or less per dose form; for external use in medicines containing 2% or less; in throat sprays in medicines containing 2% or less
Tetracaine (Amethocaine)	**Prescription:** for internal use; for external use in medicines containing more than 10%; for ophthalmic use **except** when used in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board **Pharmacy Only:** for external use in medicines containing 10% or less and more than 2% **General Sale:** for external use in medicines containing 2% or less

8. Classification sought

Table 2 Proposed classifications of medicines (red shows the proposed changes)

Medicine	Current Classification
Benzocaine	**Prescription: except** when specified elsewhere in this schedule; **except** in dermal preparations containing 2% or less of total anaesthetic substances; **except** in lozenges containing 30 milligrams or less of total anaesthetic substances per dosage unit; **except** when containing 20% or less and used topically as a local anaesthetic in practice by a dental therapist or oral health therapist registered with the Dental Council **Pharmacy Only:** in preparations for topical use, other than eye drops, containing 10% or less of total anaesthetic substances **except** in dermal preparations containing 2% or less of total anaesthetic substances; in divided preparations containing 200 milligrams or less of total anaesthetic substances per dosage unit **except** in lozenges containing 30 milligrams or less of total anaesthetic substances per dosage unit **General Sale:** in dermal preparations containing 2% or less of total anaesthetic substances; in lozenges containing 30 milligrams or less of total anaesthetic substances per dosage unit
Prilocaine	**Prescription: except** when containing 2.5% or less and used topically as a local anaesthetic in practice by a dental therapist or oral health therapist registered with the Dental Council for injection **except** when used as a local anaesthetic in practice by a dental therapist or oral health therapist registered with the Dental Council; **except** when specified elsewhere in this schedule **Pharmacy Only:** for dermal use in medicines containing 10% or less of local anaesthetic substances
NB for prilocaine the current exemption for prescription for dental therapists or oral therapist relates to injection use not topical use.	
Lidocaine (lignocaine)	**Prescription:** for injection **except** when used as a local anaesthetic in practice by a nurse whose scope of practice permits the performance of general nursing functions or by a podiatrist registered with the Podiatry Board or by a dental therapist or oral health therapist registered with the Dental Council; **except** when containing 2.5% or less and used topically as a local anaesthetic in practice by a dental therapist or oral health therapist registered with the Dental Council; for ophthalmic use **except** when used in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board; for oral use **except** in throat lozenges in medicines containing 30 milligrams or less per dose form;

	for external use in medicines containing more than 10%; **except** in throat sprays in medicines containing 2% or less; **except** when specified elsewhere in this schedule **Pharmacy Only:** for urethral use; for external use in medicines containing 10% or less and more than 2% **General sale:** in throat lozenges in medicines containing 30 milligrams or less per dose form; for external use in medicines containing 2% or less; in throat sprays in medicines containing 2% or less
Tetracaine (Amethocaine)	**Prescription:** for internal use; for external use in medicines containing more than 10%; for ophthalmic use **except** when used in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board **except** when containing 2% or less and used topically as a local anaesthetic in practice by a dental therapist or oral health therapist registered with the Dental Council **Pharmacy Only**: for external use in medicines containing 10% or less and more than 2% **General Sale**: for external use* in medicines containing 2% or less

It is noted that dermal use does not include application within the mouth, while the term topical indicates being applied to a particular part of the body which can include areas such as the mouth.
*External use has been defined in the Medicines Regulations which states:

> *"…for external use, in relation to any medicine or related product, means for application to the anal canal, ear, eye, mucosa of the mouth, nose, skin, teeth, throat, or vagina, where local action only is required and where extensive systemic absorption will not occur; but nothing in these regulations relating to medicines or related products intended for external use shall apply to nasal drops, nasal inhalations, nasal sprays, teething applications, throat lozenges, throat pastilles, throat sprays, or throat tablets …"*

External use was noted to include topical use within the mouth when discussed previously for local anaesthetics by the Medicines Classification Committee [1]. Given the data sheet for Zap gel states: "tetracaine is readily absorbed through mucous membranes into the systemic circulation", it is possible that this could be deemed to fit the definition of extensive absorption. Martindale's Complete Drug Reference[2] reports 15% bioavailability after application of a 4% gel to intact skin, but does not specify the uptake for oral gel. Should Medsafe and the committee feel this is well covered in the current wording, and no change is required, the Dental Council would be happy to accept this viewpoint. However, we have suggested wording above that would enable use by dental therapists and oral health therapists in case this is necessary.

9. Classification status in other countries (especially Australia, UK, USA, Canada)

The Australian schedules for topical anaesthetics are somewhat aligned with New Zealand because of Trans-Tasman Harmonisation, although a small difference occurs in that Australia has a maximum of total local anaesthetic substances, while NZ does not specify that, and Australia sometimes uses the term "topical" while NZ has not used this for the medicines in this application. Dermal local anaesthetic preparations in Australia are frequently unscheduled for low doses. Tetracaine (amethocaine) is Schedule 2 (S2; pharmacy only) in preparations for topical use other than eye drops, containing 10% or less of total local anaesthetic substances, and unscheduled in dermal preparations containing 2% or less of total local anaesthetic substances. Benzocaine is Schedule 2 in preparations for topical use other than eye drops, containing 10% or less of total local anaesthetic substances, or in divided preparations containing 200 mg or less of total local anaesthetic substances per dosage unit. Benzocaine is unscheduled (general sales) in dermal preparations containing 2% or less of total local anaesthetic substances; or in lozenges containing 30 mg or less of total local anaesthetic substances per dosage unit. Otherwise benzocaine is a prescription medicine. This would make Zap gel a prescription medicine given it contains benzocaine 18% and tetracaine hydrochloride 2%.

In Australia, prilocaine is Schedule 2 in preparations for dermal use containing 10% or less of total local anaesthetic substances, and otherwise prescription. Lidocaine is Schedule 2 for topical use other than eye drops containing 10% or less of total local anaesthetic substances, and unscheduled in dermal preparations containing 2% or less of total local anaesthetic substances, in lozenges containing 30 mg or less of total anaesthetic substances per dosage unit, or in aqueous sprays for oromucosal use containing 0.6% of less of total local anaesthetic substances. Therefore, Oraqix, with 2.5% of prilocaine and 2.5% of lidocaine used topically (not dermally) would be a prescription medicine.

In Canada, tetracaine is schedule III (Pharmacy only equivalent) for "topical use on mucous membranes, except lozenges". Lidocaine is schedule II (Pharmacist only equivalent) "for ophthalmic or parenteral use, or topical use on mucous membranes, except lozenges". Prilocaine and its salts are schedule III (Pharmacy only equivalent) "for topical use on mucous membranes, except lozenges" or for lidocaine and prilocaine together. Benzocaine and its salts are schedule II (Pharmacist only) "for parenteral or ophthalmic use."

Oraqix is a prescription medicine in the UK. Zap gel does not appear to be available there.

Oraqix is available in the US where it is a prescription medicine. Zap gel is available in the US where it is a prescription medicine.

New Zealand varies from other countries in using the classification statement to allow different medicines to be used by various health practitioners.

In the UK, dental hygienists and dental therapists can independently administer local anaesthetics for their patients' needs under Patient Group Directions [3, 4]

In Australia, the Australian Dental Council outlines the scopes of practice for dental hygienists, dental therapists and oral health therapists, which includes administer pharmaceutical agents. In Victoria, Australia, a dental hygienist, dental therapist or an oral health therapist are generally

approved under the Health Practitioner Regulation National Law to have in their possession and use listed Prescription Medicines which are required for the provision of dental care [5]. These listed medicines include articaine, lignocaine, mepivacaine, and prilocaine.

10. Extent of usage in New Zealand and elsewhere (e.g. sales volumes) and dates of original consent to distribute

Topical oral local anaesthetics have extensive and long-time use in dental work, although they have changed over time.

The Medsafe website indicates that Zap gel was consented 21 Oct 2010 and Oraqix 24 April 2008. Sultan Topex gel containing 20% benzocaine was available from 2000-2020.

Sales data is not readily available, but some companies may choose to confidentially make this information available to the Medicines Classification Committee. However, these products have been very commonly used in everyday dental practice.

11. Local data or special considerations relating to New Zealand (if applicable)

See information in part B.

12. Labelling or draft labelling for the proposed new presentation(s)

Not applicable. The labelling would not need any update. The existing labelling is attached.

13. Proposed warning statements (if applicable)

There would be no need for any additional warning statements as usage is virtually unchanged.

14. Other products containing the same ingredient(s) and which would be affected by the proposed change

The products listed in Table 3 (below) containing the above active ingredients for topical use in dental procedures have Medsafe datasheets available.

Sultan Topex (20% benzocaine) oral topical gel was marketed 2000 to 2020 with the approval lapsed and product no longer marketed.

Table 3. Products affected by the proposed changes

Medicine	Brand	Sponsor
Benzocaine plus tetracaine hydrochloride	Zap Topical Anaesthetic Gel (benzocaine 18% w/w and tetracaine hydrochloride 2% w/w)	HealthCare Essentials Limited
Lidocaine plus prilocaine	Oraqix Periodontal Gel (lidocaine 25 mg/g and prilocaine 25 mg/g)	Dentsply Sirona (NZ) Limited

Lidocaine	Xylocaine® Viscous solution***** (lidocaine hydrochloride monohydrate 21.4 mg/mL equivalent to lidocaine hydrochloride 20 mg/mL)	Pharmacy Retailing

*****NB Xylocaine Viscous Solution is currently a pharmacy-only medicine according to the data sheet

PART B

Reasons for requesting classification change including benefit-risk analysis

This reclassification application follows the positive Medicines Classification Committee's consideration of a reclassification of injected local anaesthetics for oral health therapists in 2017 [6]. At this meeting, articaine, lignocaine and prilocaine with or without felypressin were reclassified to include use by oral health therapists without prescription. The minutes from this meeting reported a suggestion from the public submissions *"that topical anaesthetic agents such as those containing benzocaine could be considered for rewording to permit use by dental therapists and / or oral health therapists because topical anaesthetic agents can be more favourable in paediatric dental procedures."* This current application seeks to enable this work.

This is a minor change in classification with no greater risk than the last change. The practitioners concerned (oral health therapists and dental therapists) are already using injected local anaesthetics, and the risk of using a topical local anaesthetic on mucosal membranes is within their training with similar contraindications, precautions and adverse effects as for injected local anaesthetics.

This proposal will aid oral health therapists and dental therapists to work to their competencies without needing standing orders. A reclassification will be as safe as standing orders but reduce administrative burden. A reclassification will mean that they can continue to practise within their full scope without supervision by a dentist. When attending patients at residential care or other facilities, they will be able to treat the patient as appropriate for their scope of practice, and not need to refer some care that is within their scope to a dentist unnecessarily. It will also mean oral health therapists and dental therapists can purchase products from distributors or wholesalers legally directly instead of needing to go through a dentist.

Patient convenience arises from the increased likelihood of having all the care able to be provided in the one visit, rather than rebooking for part of the care with a risk of non-return or additional cost. A patient will be able to have a local anaesthetic administered topically rather than having to suffer from excessive pain to have all the necessary treatment at the time. There may be a saving to society in having oral health therapists and dental therapists able to work to their scope of practice rather than requiring a dentist present for work that an oral health therapist or dental therapist could have done, or risking further deterioration in the condition and a more costly procedure being required by delaying some of the treatment unnecessarily.

The risks have been managed through: appropriate undergraduate training; requiring practitioners to undertake resuscitation training every two years; and use of well-known and well-tolerated medicines commonly used in dental work. Dental therapists have a long history of local anaesthetics by injection without needing a dentist's supervision. Oral health therapists can administer local anaesthetics by injection in their work without needing a dentist's supervision. These facts give confidence in this expansion to local anaesthetics being used topically on mucosal membranes in the mouth and in periodontal pockets in dental care.

Below we provide background information on oral health therapists, dental therapists and dental hygienists and their use of local anaesthetics. Then we provide further information about the benefit-risk analysis.

Background on development of oral health therapy scope of practice

New Zealand was a leader in establishing the role of dental therapists, with school 'dental nurses' first introduced in NZ in 1923 [7]. Initially they provided dental prophylaxis, restorations, and extraction of primary teeth. Now called dental therapists, their work includes an extensive range of preventive and restorative services, and thus they frequently use local anaesthetics by injection and orally.

Internationally there is a move for dental therapists to undergo university degree-level education and to expand to treating adults [7]. Nash et al [7] reported that studies in Canada and Australia have shown good quality of work, and for Canada "there have been no reports of serious injuries or record of litigation or malpractice claims against dental nurses over the 50 years of their existence".

In New Zealand, oral health therapy is a relatively new practice, integrating the previous educational programmes of dental hygiene and dental therapy. The introduction of a three-year, tertiary level oral health degree, combining the previous dental hygiene and dental therapy programmes, marked a significant shift in the oral health workforce. Auckland University of Technology (AUT) introduced the new oral health programme in 2006, followed by the University of Otago in 2007.

There are no longer any standalone educational programmes for dental hygiene or dental therapy offered in New Zealand. The effect of the change in the university programmes is that, since 2007/08, there have been no new New Zealand educated dental hygienist or dental therapist graduates—only 'oral health therapists'. This means that the number of dental hygienists and dental therapists is declining over time.

The Dental Council believes that the oral health therapy scope of practice more accurately describes the oral health graduates' full set of capabilities and breadth of the new qualification, and now recognises these practitioners as a new profession within the oral health sector.

In the 2020 Annual Report, the Dental Council reported 661 oral health therapists and 424 dental therapists on its register with 609 oral health therapists and 378 dental therapists having annual practising certificates [8].

Administration of local anaesthetics by oral health therapists

Currently, oral health therapists can administer local anaesthetics to patients of all ages; while the dental therapy scope of practice allows administration of local anaesthetics to patients up to 18 years of age—without the requirement for supervision.

Oral health therapist graduates and dental therapists are well-versed with local anaesthetics – injected and topical, including their contraindications, precautions, adverse effects, indications and

dosage. They are also well-prepared to manage potential but rare side effects of local anaesthetics, whether administered topically or by injection.

For patients with a history of adverse reaction to medications, complex medical conditions or who are medically compromised, oral health therapists and dental therapists are expected to discuss a treatment plan with a dentist or dental specialist before commencement of treatment, irrespective of the need, or not, for local anaesthetic. The oral health therapy and dental therapy scope of practice is practised within a consultative professional relationship with at least one dentist or dental specialist—with the stated purpose of providing professional advice in relation to the treatment and management of patients, when needed.

Oral health therapy practitioners receive ongoing resuscitation training at the same level as other oral health practitioners (excluding dental technicians, and dentists/dental specialists providing sedation) to manage a medical emergency related to the administration of local anaesthesia. That is, NZRC CORE Immediate training (previously named CORE Level 4), or equivalent. Oral health therapists and dental therapists are expected to have a current certificate of NZRC CORE Immediate training.

TYPE OF ORAL HEALTH THERAPY SCOPE OF PRACTICE ACTIVITIES WHERE TOPICAL LOCAL ANAESTHETICS COULD BE ADMINISTERED

***Removing hard and soft deposits from all tooth surfaces*:** use in selected cases for the removal of hard deposits, where appropriate. For example, deep scaling of root surfaces, sensitive teeth and/or inflamed gum tissue.

***Restorative activities for patients up to age 18*:**

- ***Preparing cavities and restoring primary and permanent teeth using direct placement of dental materials***
- ***Extracting primary teeth***
- ***Performing pulpotomies on primary teeth***
- ***Preparing primary teeth for, and placing, stainless steel crowns***.

Prior to the procedures an injectable local anaesthetic is commonly provided. Use of the topical local anaesthetic prior to use of the injection can decrease the discomfort of the procedure and significantly reduce needle phobia and discomfort.

COMPETENCE NOTIFICATIONS RELATED TO THE ADMINISTRATION OF LOCAL ANAESTHETICS

A review of the Dental Council competence notifications for dental therapists and dental hygienists, shows few notifications for either profession, and nothing that would indicate that the proposed change to the classification statement would lead to increased harm.

THE MEDICINES AND BENEFIT-RISK OF THE RECLASSIFICATION

A brief note about the differences between the local anaesthetics

Lidocaine and prilocaine are amide-type local anaesthetics, while benzocaine and tetracaine are esters of para-aminobenzoic acid. Local anaesthetics vary in potency, and their onset and duration of action. For example, an update on dental topical anaesthesia [9] reported benzocaine has an onset of 30 seconds and duration of action of 5-15 minutes, and lidocaine 2% typically has an onset of 3-5 minutes and duration of 15 minutes. The eutectic mixture of lidocaine 2.5% and prilocaine 2.5% (Oraqix) has an onset of 30 seconds and duration of 20 minutes [9]. Hypersensitivity and metabolism also vary (more details below).

1. **Indications and dose**

   For both Oraqix and Zap gel, the indications are appropriate to the proposed classification statements. Oral health therapists' and dental therapists' scopes of practice already cover these areas and therefore there is minimal risk of inappropriate treatment. The consumer does not need to understand indications or dosing as they are not self-treating, these medicines are only administered during dental practice.

   Oraqix indications [10]:

   Oraqix® is indicated in adults for localised anaesthesia in periodontal pockets for probing, scaling and/or root planing.

   Zap indications [11]:

   Zap Topical Anesthetic Gel is indicated to reduce the discomfort of local anaesthetic injected into the mandibular mucobuccal fold and maxillary anterior sites, and to minimise pain in oral mucosal tissue arising from needle punctures, deep scaling procedures, prosthetic adjustments, clamp or crown placement, removal of primary teeth and suture removal. Zap Topical Anesthetic Gel may also be used for the reduction of pharyngeal (gag) reflex associated with the placement of various dental materials into the oral cavity (impression trays, x-ray films).

   Oraqix dose [10]:

   Adults

   On average, one cartridge (1.7 g) or less of Oraqix® will be sufficient for one quadrant of the dentition. The maximum recommended dose of Oraqix® at one treatment session is five cartridges, i.e. 8.5 g gel containing 212.5 mg lidocaine (lignocaine) base and 212.5 mg prilocaine base.

   The duration of anaesthesia, as assessed by probing of pocket depths, is about 20 minutes. If the anaesthesia starts to wear off, re-apply Oraqix® as needed.

   See the attached data sheet for further details.

Zapgel dose [11]:

Apply approximately 0.2 - 0.3 mL of gel to the desired area using a cotton swab or fingertip. The exact dosage depends on the area to be anaesthetised, the vascularity of the tissues at the application site, and the patient's tolerance. Do not exceed the recommended dosage or apply more than one application per procedure.

An appropriate paediatric dosage has not been established. Dosages should be reduced in the elderly, acutely ill, and very young patients.

2. Presentation

Oraqix is available as a periodontal gel containing lidocaine 25 mg/g and prilocaine 25 mg/g and is supplied in dental cartridges containing 1.7 g of gel with a sterile blunt-tipped applicator for each cartridge.

Zap gel is available as a gel containing benzocaine 18% w/w and tetracaine HCl 2% w/w. It is presented in a "magic" jar containing 30 g and 50 g – see the data sheet for more information.

These presentations are appropriate for the proposed classification statements, there is no consumer self-treatment. Both products are practical in their presentation.

Disposal will be as is usual for oral health therapists and dental therapists, there is no special consideration required here.

3. Consumer benefits

These medicines are used in many countries around the world as a usual part of dental care. The exact number of countries and number of users is unknown as this application is not being submitted by the manufacturers of these medicines.

Regular dental checks are needed to maintain health of teeth and gums. The New Zealand annual health survey 2014/2015 [12] found that 48% of all adults with natural teeth had visited a dental health care worker in the past 12 months. People in more deprived areas, or people of Māori, Asian or Pacific ethnicity have lower attendance than others. Most Pacific, Māori and Asian adults only visit for dental problems, not regular check-ups. Dental extraction for tooth decay, abscess, infection or gum disease was reported to have occurred in the last 12 months by at least 10% of Pacific and Māori adults. Dental extraction affects quality of life, and usually results from not seeking dental care (prevention or treatment) early.

Local anaesthetics (injected or topical) are widely used by dentists, dental specialists, dental therapists and dental hygienists. They are very effective in reducing pain during dental procedures [13]. As dental anxiety reduces the likelihood of routine attendance at the dentist [14], it is important to ensure patient comfort, including in people who are needle phobic. Injected local anaesthetics can be used by oral health therapists and dental therapists without a dentist on the premises, and it would be appropriate for this to be extended to topical local anaesthetics used on gums or in a periodontal pocket.

This extension would minimise the chances of treatment disruption or painful treatment. It will provide time savings for dentists, many of whom report time pressure stress [15]. It will be more efficient than standing orders which would not add any safety as they would allow product administration without a dentist on-site, and administration recorded in retrospect. Standing orders are cumbersome and time-consuming, and secondary dental services are over-burdened [16], so a reclassification is a better option.

It is also helpful for the oral health therapist and dental therapist for managing patients efficiently. A patient who needs a topical local anaesthetic and is rebooked may not return for the remainder of their treatment, so risk poorer care, in addition to inconvenience. The alternative approach of having a standing order in place would provide no greater safety than currently exists and is more burdensome on dentists and oral health therapists and dental therapists. The use of standing orders is not common in private dental practices. In the public sector, the scale of administration would be very difficult to manage effectively and safely, with approximately 500,000 children cared for under the community oral health services. The proposed change provides flexibility and aids quality care and patient convenience and has no greater risk than that which exists with injecting local anaesthetics which oral health therapists and dental therapists already do without a dentist present.

4. Contraindications and precautions

Table 4 Contraindications for the medicines

	Oraqix (lidocaine + prilocaine)	**Zap topical anaesthetic gel**
Hypersensitivity	Known history of hypersensitivity to local anaesthetics of the amide type or other component of the product	Known hypersensitivity to any ingredient in the product or local anaesthetics of the ester type
Other	Nil	Use outside the oral cavity. Tetracaine is hydrolysed in vivo to p-amino-benzoic acid (PABA) so should not be used in people taking sulphonamides

Table 5 Warnings and precautions (see full details in data sheets, attached)

	Oraqix (lidocaine + prilocaine)	**Zap topical anaesthetic gel (benzocaine + tetracaine)**
	Glucose-6-phosphate dehydrogenase deficiency or congenital or idiopathic methaemoglobinaemia	Do not apply to traumatised, inflamed or infected or highly vascular surfaces
	Avoid contact with eyes	Risk of systemic toxicity is greatest in small children and patients with pre-existing heart disease. Time and

		surface area increase systemic exposure
	Do not inject	Caution in paediatric, geriatric, acutely ill or debilitated patients. Do not use on children under 6 months or older patients with cardiac or anaemia problems
	Reduced sensation where used, care with inadvertent trauma or extreme hot or cold temperatures	Do not exceed the maximum recommended dosage
	Avoid contact to prevent allergy developing	Repeated and prolonged application may potentiate hypersensitivity.
	Hepatic impairment can cause increased half life of ingredients	Tetracaine is associated with a higher incidence of allergic reactions than other anaesthetics.
	Renal impairment can cause metabolites to accumulate	People sensitive to PABA, parabens or paraphenylenediamine may also be sensitive to benzocaine and tetracaine
		Do not eat for one hour after use because swallowing may be impaired
		Do not use under dentures or cotton rolls

For pregnancy, lidocaine and prilocaine are Category A with use by a large number of pregnant women without harm being observed [10]. Use of these agents in lactation is also expected to be reasonable owing to small exposure. The safety of benzocaine and tetracaine in pregnancy and lactation has not been fully established [11].

These contraindications and precautions are taught in under-graduate training within a pharmacology paper; these are also in the data sheets. The Oraqix product includes the prescribing information inside (see appendices). Zap gel packaging has application instructions attached. Dental therapists and oral health therapists will be asking about hypersensitivity and other medical conditions and referring if unsure about the appropriateness of a topical local anaesthetic for an individual.

These medicines will be administered by dental professionals, not consumers, and therefore contraindications and precautions are likely to be better managed than a person using a local anaesthetic themselves that has been purchased as a general sales medicine.

No effect on driving or operating machinery is expected. The only concern with food and drinks is that they are not too hot, but the numbness wears off quickly. Few drug interactions are of concern (see above).

Benzocaine at the recommended dose for Zap gel would provide up to 56 mg of benzocaine, when toxicity has been reported at 100 mg [17]. However, it is important to note that the doses are not repeated nor reliant on consumer compliance, minimising the risk. Tetracaine (amethocaine) is provided at a low strength because it is considered more potent.

5. Undesirable effects

Adverse effects of local anaesthetics are well-known. Local numbness could result in inadvertent burning of the mouth with a hot drink. Sensitivity reactions include local effects through to systemic effects, including anaphylaxis, which is rare. Serious effects are sufficiently rare to allow some forms of local anaesthetics to be general sales, and some to be pharmacy-only medicines.

The Oraqix data sheet reports that there were "no major differences in adverse events between Oraqix and placebo in clinical trials", with most reports being local reactions. See the data sheets for further information on adverse reaction frequencies.

Greenwood and Meechan in 2014 reported that anaphylaxis in dental practice was more likely to occur with latex or penicillin than with local anaesthetic use [18]. Hypersensitivity is rare and tends to affect the ester than amide-type local anaesthetics [19-21], although SMARs data, below, shows reports with both the ester and amide type of local anaesthetics in this proposal. Preservatives such as parabens or added sulphite for local anaesthetics combined with a vasoconstrictor, could cause allergy.

Topical use of local anaesthetic agents can cause sensitivity which could result in hypersensitivity with later administration e.g. by injection [19]. However, dermal local anaesthetic agents are available without prescription.

There are no withdrawal effects after using these medicines.

See below for regulatory action with regard to benzocaine and methaemoglobinaemia. Note also the Prescriber Update in NZ with methaemoglobinaemia and local anaesthetics (attached).

Methaemoglobinaemia

Local anaesthetics, along with nitrates, amyl nitrite, sulphonamides, infections, anaemia and certain foods are risk factors for methaemoglobinaemia [22-24]. Methaemaglobinaemia can occur with prilocaine at high doses (usually greater than 8 mg/kg) [21], but Becker and Reed [25] note that this effect is "unlikely to follow the administration of recommended doses".

Infants under 3 months, and people with haemoglobinopathies, and G6PD deficiency may be at greater risk of harm [19]. In methaemaglobinaemia, the iron in haemoglobin is oxidised to its ferric state, reducing the oxygen carrying capacity of the haemoglobin.

Symptoms include headache, fatigue, cyanosis, shortness of breath, tachycardia, confusion, and reduced consciousness, with serious outcomes including death possible. These can appear within minutes to 1-2 hours after use of an agent[26]. People with breathing problems or heart disease, or people who are elderly are at greater risk if experiencing methaemaglobinaemia.

The Food and Drug Administration (FDA) in 2018 stated that infants and children under two years of age should not have products containing benzocaine because of the risk of methaemaglobinaemia, and requested manufacturers stop manufacturing benzocaine-containing products for teething in this age group [26]. The FDA required a standardised methaemaglobinaemia warning to be used on labelling of benzocaine products, and noted that benzocaine was more problematic than other local anaesthetics, with more than 400 cases reported to the FDA or published in the literature since 1971. In contrast, Martindale's Complete Drug Reference suggests prilocaine has a greater incidence [19]. The FDA recommends "Health care professionals should warn patients of the possibility of methemoglobinemia and advise them of the signs and symptoms when recommending or prescribing local anesthetic products" [26]. The FDA also recommends health care professionals try to minimise the risk, including monitoring patients for signs and symptoms of methaemaglobinaemia, and having resuscitation equipment and medications readily available, including methylene blue. Note, many of the OTC benzocaine products used in the US were items for use by a consumer multiple times a day e.g. for teething or a sore throat spray (200 mg/mL[17]), as opposed to typically one-off usage by a dental professional with dental work.

In 2009, Prescriber Update in New Zealand warned of methaemoglobinaemia with various medicines including local anaesthetics, nitrates and sulphonamides[23], but did not provide advice on needing to keep methylene blue available where these medicines are used. SMARs data for the four medicines within this application reports one case of methaemaglobinaemia with benzocaine in 2007, one case with prilocaine injection in 2016, and no cases with the other two medicines. With local anaesthetics used very frequently in general practice, secondary care, and with dental professionals, the small number of SMARs reports is reassuring, and dental professionals will be first-aid trained and equipped. Additionally, children under 3 months (at particular risk)[19] will not be treated by dental therapists or oral health therapists.

NZ SMARs data

In New Zealand, SMARs data (2000-2020) reports four reactions for benzocaine, an 8 year old in 2007 with methaemaglobinaemia with benzocaine oral, a 7 year old with application site pain with benzocaine oral topical, a 4 year old with erythema, face oedema rash and somnolence in 2017 with Mepivacaine injection plus Zap gel topical, and a 51 year old in 2018 with agitation, flushing, tachycardia and tremor in 2018 with Zap gel topical.

SMARs data reports 25 reports for tetracaine (amethocaine), 22 of which are for Ametop, a dermal anaesthetic applied before a needle is inserted into a vein, and one for ophthalmic use. Most of these were local reactions, but four were systemic, including one case of

anaphylaxis and another with bronchospasm. Two reports were for topical oral use (Zap gel), as outlined above for benzocaine.

Lidocaine reports were 138 in total, including 34 cases of anaphylaxis or anaphylactoid reactions. Most reaction reports arose from injections, but over 30 cases involved topical lidocaine without anaesthetic injections, and these topical cases included anaphylaxis also or dyspnoea, with several such reports naming commonly sold non-prescription products as suspect medicines.

Prilocaine had 17 reports, including two cases of anaphylaxis, one bronchospasm, one tongue oedema, one laryngospasm and vocal cord paralysis and one methaemaglobinaemia (all injections). Six adverse reaction reports related to topical application, all skin reactions, e.g. urticaria or application site reaction.

None of the four medicinal ingredients had deaths reported in the SMARs data.

6. Overdose

Systemic toxicity from excessive dose or inadvertent intravascular administration provides excitation of the CNS which can be followed by depression [19]. Overdose with the local anaesthetic agent can cause headaches, light-headedness, dizziness, blurred vision, tinnitus, numb mouth, drowsiness, disorientation and loss of consciousness [27]. Adverse effects on the cardiovascular system are uncommon [21] but high systemic exposure can cause seizures and cardiac arrhythmias [11].

Martindale reports ready absorption of most local anaesthetics through mucous membranes, although the Zap gel data sheet reports minimal systemic absorption of benzocaine and higher systemic absorption of tetracaine [11, 19]. Anaesthetics of the ester type are hydrolysed by esterases in the plasma, while amides are metabolised in the liver. Oraqix reports 20-40% systemic absorption but minimal if swallowed due to first-pass effects, and a half-life of 3.6 hours for lidocaine and 2.8 hours for prilocaine after administration to mucosal surfaces[10].

7. Medication errors and abuse/misuse potential

Used by dental health professionals, there is no potential for abuse, misuse or unnecessary use. Errors would be unlikely given the limited area in which they are used and application aids. Errors may be more likely with injected local anaesthetics which could inadvertently be injected intravascularly, or by injection be administered too rapidly. If large amounts were used in error, systemic toxicity is possible. However, the application by dental professionals trained in their use, and dose aids for administration would help limit this potential.

We do not have access to manufacturer data regarding errors reported with these medicines post-marketing.

Import considerations are irrelevant for these medicines, as they would remain prescription medicines.

We are unaware of any potential for addiction with these medicines.

8. Communal harm and/or benefit

Communal benefit could arise from efficiency for these practitioners and the dentists responsible for standing orders because standing orders for these medicines would no longer be needed, and there would be easier arrangements for ordering by dental therapists and oral health therapists. Those without standing orders in place could provide services that are within their scopes.

No communal harm seems likely.

9. Integrated benefit-risk statement

This reclassification supports the appropriate use of topical local anaesthetics by dental therapists and oral health therapists in line with their scopes of practice. It will ensure good access for patients to appropriate pain relief when attending these practitioners, improving the acceptability of dental care and reducing the need for referral and potential for the person not to follow through with that referral (e.g. for financial or time reasons), creating a worse problem. Injected anaesthetic agents are already available for oral health therapists with a similar classification to that proposed here, therefore it is very logical to extend this to topical local anaesthetics for oral health therapists. It is similarly logical to extend it for dental therapists who are trained in the use of these medicines and use them extensively.

10. Risk mitigating strategies

Dental therapists and oral health therapists are both very familiar with using injected and topical oral local anaesthetics. This is within their scopes, and when used under standing orders, these dental professionals will already be working with no dentist on-site, using these medicines in their everyday practice. Therefore it is difficult to see that there is any greater risk than in the current situation.

The most serious risks are anaphylaxis, methaemaglobinaemia, and potential for overdose (e.g. using topical and injected local anaesthetics). Dental therapists and oral health therapists are trained to avoid these risks. They are aware of them, and ready to manage an emergency should it arise.

Registered oral health therapists and dental therapists will have received training on indications, contraindications and precautions for topical oral and injected local anaesthetics. They will be asking patients about relevant medical history, and in the case of a higher patient risk, they will consult with the dentist/dental specialist before

proceeding with the treatment, or refer if required. Similar professional judgment is required in all other areas of oral health therapy practice.

In the event of a medical emergency related to the administration of local anaesthesia, oral health students receive resuscitation training at the same level as other oral health practitioners, that is, NZRC CORE Immediate training (previously named CORE Level 4), or equivalent. This is required to be maintained following graduation, with the Dental Council requiring resuscitation training to the same level, every two years. Oral health practitioners declare compliance with this obligation as part of their annual practising renewal. Some first aid providers cater courses to dental practitioners with all of the dental practitioners doing these courses together.

Like dentists, dental therapists and oral health therapists need to have oxygen and adrenaline available when treating patients. Dental therapists have been treating children up to 18 years of age with local anaesthetics for decades. There are 500,000 children aged 0-12 years currently treated by the school dental services in NZ.

Research by Associate Professor Jonathan Broadbent from the University of Otago provides useful insights into medical emergencies in dentistry in New Zealand.[28] This survey of dentists, dental specialists, dental therapists, dental hygienists and clinical dental technicians found a low incidence of medical emergencies in dental practice in NZ, with an average of 2.9 per practitioner reported to have occurred in the last 10 years. Nine dentists (4.6%) reported one or more cases of anaphylaxis occurring in the last 10 years. Four dental specialists (14.8%) and no other dental practitioners reported anaphylaxis occurring in the last 10 years. In a 2000/2001 study of the readiness of New Zealand dentists for medical emergencies Broadbent and Thomson reported that seven anaphylaxis events were reported by dentists over the previous 10-year period, with three attributed to lignocaine (patient reported lidocaine use before without any reaction), adrenaline in local anaesthetic, and an unspecified local anaesthetic [29]. All patients made rapid and full recoveries, following emergency management. Fourteen patients received overdoses of anaesthetic agents during the same period. Details were provided for six of these events, of which three were due to excessive local analgesics administered.

To minimise risk, for Zap gel, approximately 0.2-0.3 mL of gel is applied, aided by a special pressure valve (see data sheet) [11]. The data sheet warns not to use more than one application per procedure. Containing 18% of benzocaine, this would be equivalent to about 36-54 mg of benzocaine. Toxicity is not seen until at least 100 mg [17].

Difficult work and extensive work is likely to be carried out either over multiple visits or is referred to a dentist instead, so multiple applications of local anaesthetics are unlikely. However, topical anaesthetics are likely to be used prior to injecting a local anaesthetic, and this is the most common use of the topical anaesthetic. The injectable would then be lignocaine, articaine or prilocaine.

11. **Potential risk of harm to the consumer as a result of the proposed change, and factors to mitigate this risk**

The proposed change is in line with the education and expertise of the graduates of the three-year oral health therapy degree courses from the University of Otago and Auckland University of Technology.

The main risks of harm of importance are anaphylaxis and methaemaglobinaemia. These are extremely rare, as noted above, and would be managed by the dental professional. These risks already exist with injected local anaesthetics which are used regularly by dental therapists and oral health therapists, and with their current use of topical local anaesthetics. Such risks also exist with use of various non-prescription medicines. For the considerable benefits of these agents, rarity of these reactions and ability to manage these reactions, the overall benefit-risk equation is very clearly favourable.

The Dental Council has a practice standard for medical emergencies in dental practice (see appendix 1) [30]. This document requires dental therapists and oral health therapists to have CORE (Certificate of Resuscitation and Emergency Care) Immediate or equivalent resuscitation training, revalidated every two years. The standard requires them to have written protocols for managing medical emergencies. It includes anaphylaxis management. Dental therapists, dental hygienists and oral health therapists are required to have an oxygen cylinder, bag mask device, basic airway device and adrenaline available. Medical history must be taken and recorded for all clients. The Standards document includes information about management of conditions that may occur in an emergency in dental care. It does not include signs, symptoms and management of methaemaglobinaemia, however, this will be considered for inclusion in the next update. We do not believe there is any need for methylene blue to be kept in a first aid kit, owing to the rarity of the reaction, having oxygen readily available, and being able to call immediately for an ambulance to get appropriate emergency care. No dental practitioner needs to stock this item.

There are no planned post-marketing surveillance activities. However, it would be noticed if there was an increase in reports of incorrect use by dental therapists or oral health therapists, and any such increase would be investigated. Given this is within their scopes and they are very familiar with these medicines, we do not expect any concerns to arise.

This application is from the Dental Council.

SUMMARY

This reclassification application seeks to use an exception from prescription availability to make topically applied tetracaine (amethocaine), benzocaine, lidocaine (lignocaine) and prilocaine more readily available to dental therapists and oral health therapists.

Local anaesthetic agents are widely used in NZ and internationally by dentists and other dental professionals. NZ has a long history of these agents being used topically and by injection by dental therapists for children up to 18 years of age, and by dental hygienists on all patients, with a dentist on-site. Oral health therapists have been able to administer by injection local anaesthetics without needing standing orders or a dentist on-site since 2017. NZ spontaneous reports of adverse events have shown few concerns. The Dental Council previously consulted widely on the scope of practice for oral health therapists, which includes local anaesthetic administration without requiring a dentist to be on-site. Most submitters were supportive of the scope of practice consulted on.

Oral health therapists and dental therapists have had appropriate education in use of injected and topical local anaesthetics. They are trained, as are dentists, to CORE Immediate resuscitation level and have oxygen and adrenaline available. Oral health therapists and dental therapists are increasingly working more independently, including in Australia, UK, Singapore, and some states in the USA. The proposed reclassification of four topical local anaesthetics (and two marketed products) enables dental therapists and oral health therapists to work more easily within their scopes of practice for the benefit of their patients.

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