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OncoZenge and the Dental Opportunity

by Impala Nordic
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Overview

OncoZenge AB (publ) ("OncoZenge" or the "Company") is developing BupiZenge™, a slow-dissolving bupivacaine lozenge, as a locally acting pain treatment for oral mucositis in cancer patients. The Company's Phase III programme is now in execution: European approval to start the pivotal BEAM-Pain trial (BZ003) was received in May 2026 and the first patient was enrolled on 7 July 2026. BEAM-Pain is a randomised, open-label registrational study of c. 150 patients at up to 12 sites in Norway, Sweden, Denmark and Germany, comparing BupiZenge™ with standard-of-care lidocaine. Management guides for full Clinical Study Report in early 2027, with a marketing authorisation application as soon as possible thereafter. Unless the Accelerated Assessment procedure is used standard EMA timelines would imply 2028 for a commercial launch in Europe. Commercialisation in Europe would be carried out by Molteni Farmaceutici, which holds European rights and pays OncoZenge milestones and a 15-20% on partner sales.

Beyond cancer treatment, OncoZenge has flagged dental care as a potential complementary indication following progress in the lead programme, and has filed intellectual property applications covering relevant dental use areas. The Company has not committed incremental development spend to a dental clinical programme, and states that any such programme would be planned together with a commercial partner. This analysis (the "Analysis") assesses where a lozenge-based, needle-free local anaesthetic could fit into dental pain management, focusing on selected subsegments. It has been developed in close dialogue with dental clinical experts.

Key takeaways

- **A differentiated pain-control concept**: The clinical logic is that a lozenge-based local anaesthetic reduces pain at its point of origin rather than relying on systemic symptom control, blocking transmission early in the pain pathway and maintaining local contact time where topical agents are often short-lived.
- **Recurring gaps in current treatment**: Dental pain control is still dominated by injectable local anaesthesia for reliable depth, while needle-free options are often constrained by limited duration, superficial effect, or procedural fit. Reported needle fear varies with definition: around one in four adults report clinically significant fear of dental injections, an estimated 5–10 % are needle-phobic, and around one in 20 avoid appointments because of it. Systemic analgesics remain common for post-procedure pain, supporting interest in opioid-sparing alternatives.
- **Three distinct use-case segments stand out**: (1) Scaling and root planing (SRP), where discomfort is common but injections are often perceived as disproportionate, (2) postoperative pain, which emerges as injection anaesthesia wears off, with dry socket a particularly severe, localised complication carrying a high revisit burden, and (3) recurrent aphthous stomatitis (RAS), a high-prevalence condition with intense pain and limited durable at-home options. The common thread is localised pain that today's options address incompletely.
- **Procedure volumes and disease prevalence**: Severe periodontitis is estimated to affect about 11 % of adults worldwide, underpinning recurring periodontal treatment volumes. Oral surgery adds a further high-volume layer, with around 5 million people estimated to undergo third-molar extraction annually in the US.
- **Supports a large addressable pool**: The global dental drug market is estimated at c. USD 5.5 billion in 2024, forecast to reach c. USD 8.3 billion by 2032. These are product-market figures: European rights to BupiZenge™ are licensed to Molteni Farmaceutici, so European revenue would reach OncoZenge as milestones and a 15–20 % royalty, not product sales.

Overview	
Ticker	ONCOZ
List	First North Stockholm
Share price	3,50 SEK
No. shares	14 820 865
MCAP	51,9 MSEK
Rights issue	3,00 SEK
Subscription	4–18 Sep 2026
Shares, post-issue	25 936 513
CEO	Stian Kildal
Chairman	Daniel Ehrenstråhle
Analyst	Ylber Rexhepi & Dlawar Kanabi

Contributing clinical experts

Dr Paul Murtagh *is an experienced dentist and clinic founder with international clinical experience across Ireland, the UK, Sweden, and the United States. He received his dental degree in 2001 and has been recognised for research in dental materials, including an award from the International Association for Dental Research (IADR). Dr Murtagh has completed advanced training in implant dentistry in the US and through Straumann and has founded and operated multiple dental clinics in Ireland and Sweden. He has also worked as a clinical supervisor within the Swedish Public Dental Service (Folktandvården) and has a strong personal focus on improving the patient experience in dental care. Dr Murtagh holds 158,000 shares in OncoZenge and has a subscription commitment of SEK 270,000 in the ongoing Rights Issue through Fenix Dental AB, and intends to subscribe.*

Dr Sayf Hosamaldin *is a dentist currently undertaking specialist training in maxillofacial surgery while pursuing medical studies at Linköping University Hospital, Sweden. He received his dental degree in 2019 and is expected to complete both medical licensure and specialist qualification by 2029. He serves as Chair of the Junior Section of the Swedish Association for Maxillofacial Surgery and is research-active across two university hospitals. In addition, Dr Hosamaldin has experience from both public and private healthcare settings and works as a consultant in dentistry and facial aesthetics through his own company. Dr Hosamaldin does not own shares in OncoZenge.*

Key Medical Terms

- Local anaesthetic = A medicine that makes a small area of your body numb so you don’t feel pain there.
- Bupivacaine = A strong, long-lasting numbing medicine.
- Lidocaine = A fast but short-lasting numbing medicine.
- Oral mucositis = Painful sores in the mouth (common in cancer patients).
- Topical anaesthesia = Numbing medicine put on the surface of the skin or mouth with no needle.
- Periodontal pockets = Deep spaces between the tooth and the gum caused by gum disease.
- Scaling and Root Planing (SRP) = A deep cleaning where a dentist or hygienist removes hardened plaque (calculus) from the teeth and from under the gums.
- Dry socket (alveolar osteitis) = A painful condition that develops in the days after a tooth is removed, when the blood clot over the socket is lost and the bone is exposed.
- Third-molar extraction = Removing a wisdom tooth.
- Breakthrough pain = Pain that returns despite ongoing pain treatment, for example when a numbing injection wears off.
- NSAIDs = Painkillers, like ibuprofen, that reduce swelling and pain.
- Opioid-sparing strategy = Treating pain in a way that avoids strong addictive painkillers.
- Systemic exposure = How much of a medicine enters the whole body through the blood.
- Pharmacokinetics = How the body takes in, moves, breaks down, and removes a medicine.
- Lipophilicity = How readily a medicine dissolves in fat. Higher lipophilicity generally means a longer-lasting local effect.
- Mucosal drug delivery = Giving a medicine through the moist lining of the mouth rather than by swallowing or injection.
- Patient-reported outcomes = What patients themselves say about their pain, comfort, or experience.
- Clinical workflow = How dentists and staff normally do their work step by step.
- Needle-free anaesthesia = Numbing without a needle, for example a gel or a lozenge.
- Subgingival scaling = Cleaning below the gumline on the root of the tooth.
- Supragingival cleaning = Cleaning above the gumline on the visible part of the tooth.

Introduction

OncoZenge's Potential Beyond Oncology

OncoZenge is a Swedish pharmaceutical company whose lead product, BupiZenge™, is a lozenge formulation containing the local anaesthetic bupivacaine, currently in Phase III. It is primarily being developed for the treatment of oral mucositis pain in cancer patients, where the Company has reported that BupiZenge™ outperformed standard of care in a Phase II study. The lozenge is designed to provide targeted pain relief through gradual release in the oral cavity, supporting a primarily local effect with minimal systemic exposure.[2]

While the current development focus in the ongoing Phase III study is on oncology, the underlying formulation and delivery concept of BupiZenge™ suggests broader potential for localized pain relief in the oral cavity. Among potential complementary areas, dental care stands out as a clinically relevant setting where pain control is central to both patient experience and procedural efficiency. In close dialogue with dental experts, Impala Nordic has assessed the potential for a future expansion of BupiZenge™ into dental care and identified several use cases that appear particularly relevant.

Opportunity for BupiZenge in the Dental field

The overarching rationale for BupiZenge™ in dental care is that pain control in routine clinical practice still involves clear trade-offs between efficacy, invasiveness and practicality. For many procedures, the standard of care remains injection-based local anaesthesia, which is reliable but inherently invasive and often associated with lingering soft-tissue numbness after the visit. At the same time, fear of injections is a tangible barrier in dental care. Studies show that 1 out of 4 adults experience significant needle fear, and nearly 5 % avoid or postpone dental visits due to this phobia,[3] which reinforces the demand for needle-free alternatives.

Needle-free local options exist and are often preferred by patients: in a randomised trial of a needle-free jet-injection system, a clear majority of patients favoured the needle-free technique over conventional syringe anaesthesia.[4] However, these options tend to be limited by short duration, shallow effect, or narrow procedural fit. For example, even though Oraqix® can reduce pain in non-surgical periodontal treatment and is often preferred by patients due to less post-procedure numbness, its anaesthetic effect is superficial and time-limited, lasting approximately 20 minutes.[5] Furthermore, conventional topical gels and sprays, such as lidocaine or benzocaine, are widely used as adjuncts, but are typically constrained by short residence time in the oral cavity and are easily diluted or removed during dental workflows. Finally, when local measures are insufficient, or when the primary burden is post-procedural pain, patients and clinicians rely on systemic analgesics.

Against this backdrop, a lozenge-based, locally acting anaesthetic like BupiZenge™ could be positioned as a meaningful tool that aims to deliver local pain control without injections, and potentially reduce reliance on repeated systemic dosing in selected scenarios. More on current treatment standards and their practical limitations is discussed in the next section.

BupiZenge is a Needle-Free Lozenge for Local Oral Anaesthesia

BupiZenge™ is a slow-dissolving lozenge containing bupivacaine, a potent long-acting local anaesthetic that has been used in clinical medicine for decades. Designed for targeted pain relief in the oral cavity, the formulation allows bupivacaine to be gradually released onto the mucosal surface, supporting local exposure over time rather than a short, rapidly washed-away topical contact, and providing effective anaesthesia with minimal systemic exposure. Relative to local anaesthetics like lidocaine, bupivacaine is generally considered longer-acting, which is relevant in oral settings where today's topical alternatives often provide only transient relief. In addition, expert input highlighted that, beyond pure anaesthesia, bupivacaine's anti-inflammatory properties could be clinically meaningful.

1. Impala Nordic. 2024. *Equity Analysis OncoZenge AB (publ).*
2. *Miroshnychenko et al. 2023. Injectable and topical local anesthetics for acute dental pain: 2 systematic reviews. Journal of the American Dental Association, 154*(1), 53–64.e14
3. Svensson, Lisa. 2020. *Dental anxiety: Prevalence, measurements and consequences* (Doctoral dissertation). University of Gothenburg, Sahlgrenska Academy, Institute of Odontology.
4. Vishwanathaiah et al. 2024. *Comparative Evaluation of New Needleless Local Anesthetic System (INJEX) and Conventional Syringe Needle Technique during Pulpotomy Treatment: A Randomized Clinical Trial*. Division of Pediatric Dentistry, Department of Preventive Dental Sciences, College of Dentistry, Jazan University, Jazan 45142, Saudi Arabia.
5. Friskopp, J et al. 2001. *The anesthetic onset and duration of a new lidocaine/prilocaine gel intra-pocket anaesthetic (Oraqix) for periodontal scaling/root planing.* Department of Periodontology, Public Dental Services, Kista, Sweden.

Dental care treatment

Current Standards of Care and Their Limitations

Injectable local anaesthetics (e.g., lidocaine, articaine, bupivacaine):

In dentistry, local anaesthesia is predominantly delivered via injection, most commonly with lidocaine-based agents for reliable, deep anaesthesia during operative procedures. Injectable anaesthesia is effective, but inherently invasive, requires administration by licensed personnel, and can result in prolonged soft-tissue numbness. Long-acting agents such as bupivacaine are already used in dental settings to extend postoperative pain control, but only in injectable form. This is relevant since OncoZenge's BupiZenge™ is built on the same active substance, yet aims to deliver local analgesia in a non-invasive lozenge format.

Oraqix® (lidocaine/prilocaine gel):

Oraqix® is a needle-free anaesthetic gel placed directly into periodontal pockets. While preferred by many patients over injections, Oraqix® offers only superficial mucosal anaesthesia with limited duration (approximately 20 minutes). Its use also requires a proprietary applicator, adding procedural complexity. Application has been described as uncomfortable and practical mainly for selected areas rather than generalized gingival sensitivity.[6]

Topical anaesthetics (e.g., lidocaine gel, benzocaine gels/sprays):

Conventional topical anaesthetics are frequently used to numb the injection site or provide brief surface-level relief, but their effect is limited by short duration and poor retention in the oral cavity. Aqueous lidocaine gels are readily diluted and tend to be washed away quickly by saliva and, in hygiene procedures, by water spray from ultrasonic scalers. Many patients also report unpleasant taste.[7] This in turn limits real-world efficacy when the goal is sustained comfort during scaling or when attempting to desensitize a larger area of inflamed tissue.

Painkillers (NSAIDs and paracetamol/ acetaminophen):

Systemic analgesics, primarily NSAIDs (nonsteroidal anti-inflammatory drugs) and paracetamol, are widely used as first-line treatment for acute dental pain, either alone or in combination, particularly after extractions and other invasive procedures.[8] However, the effectiveness of "normal painkillers" for mouth pain is often questioned and patients may end up taking high doses with limited relief, which is relevant when framing the rationale for a locally acting alternative. From a positioning standpoint, BupiZenge's intended value is not that systemic analgesics are obsolete, but that a local, first-order blockade approach could reduce pain burden at source and potentially lower reliance on repeated systemic dosing in selected use cases.

Where this leaves dental pain control today

Taken together, these four approaches cover dental pain reasonably well, but they force a trade-off between three things that cannot currently be had at once: depth of anaesthesia, duration, and freedom from needles and systemic exposure. Injection delivers depth, but is invasive and leaves lingering numbness. Needle-free topical options avoid the needle but are shallow and short-lived, around 20 minutes for Oraqix®, and are diluted or washed away by the oral environment.[9]

Systemic analgesics reach where local measures cannot, but act on the whole body, and the opioid component of that toolkit has been narrowing as prescribing scrutiny has increased.[10] It is this gap — local effect, useful duration, no injection — that defines the opportunity examined in the remainder of this Analysis.

6. Friskopp, J et al. 2001. The anesthetic onset and duration of a new lidocaine/prilocaine gel intra-pocket anesthetic (Oraqix) for periodontal scaling/root planing. Department of Periodontology, Public Dental Services, Kista, Sweden.
7. Lee, Hyo-Seol. 2016. Recent advances in topical anesthesia. Journal of Dental Anesthesia and Pain Medicine.
8. ADA. 2024. *Oral Analgesics for Acute Dental Pain.* Research Services and Scientific Information, ADA Library & Archives.
9. Ibid. (see note 6).
10. J Suda et al. 2020. *Overprescribing of Opioids to Adults by Dentists in the U.S.* American Journal of Preventive Medicine, 58(4), 473–486

Dental care treatment cont.

BupiZenge™ – Clinical and Practical Differentiation

Established active substance, novel needle-free delivery route

Bupivacaine is already widely used clinically as a local anaesthetic in injectable form. In that sense, the "novelty" in BupiZenge™ is primarily the lozenge delivery and intended local oral exposure. A bupivacaine-based lozenge, designed to deliver local anaesthesia without injections or proprietary applicators, may simplify chairside use and improve patient acceptance. The lozenge format provides even, controlled delivery without specialized equipment or trained administration, unlike many of the options used today.

Bupivacaine offers tissue penetration and sustained local action

Bupivacaine can, in practical terms, block pain at its source. There is also a theoretical potential to reduce tooth sensitivity if the active substance can access dentinal pathways. In practical terms, bupivacaine is generally regarded as more potent and longer acting than lidocaine, supporting an extended analgesic effect lasting for several hours. This duration profile is relevant both for longer chairside sessions and for post-procedure pain relief. Compared with lidocaine, onset may be slower, and, as with all local anaesthetics, safety remains dose dependent.[11]

Favourable systemic exposure profile in lozenge pharmacokinetic data

In clinical pharmacokinetic studies of bupivacaine lozenges, measured blood levels remained well below concentrations associated with systemic toxic symptoms, and modelling suggested that repeated dosing would still stay below those toxic thresholds. This supports the premise of a primarily local treatment effect at intended use and, since bupivacaine is a non-opioid local anaesthetic, it avoids opioid-type dependency risk.[12]

Flexible positioning across the dental patient journey

As a non-invasive local anaesthetic approach, the concept is compatible with both pre- and post-intervention pain management and symptomatic oral pain states, including routine hygiene appointments, surgical interventions, and oral mucosal pain conditions.[13]

Anti-inflammatory properties may add clinical relevance beyond anaesthesia

Local anaesthetics, including bupivacaine, have documented anti-inflammatory effects in experimental settings, and inhibition of inflammatory mediators has been demonstrated. This is directionally supportive of a positioning that extends beyond "numbing" alone, although clinical relevance in dental settings would need confirmation per indication.[14]

Clinical and Practical Differentiation

In summary, BupiZenge™ combines the established efficacy profile of bupivacaine with a patient-friendly, needle-free lozenge format intended for controlled local delivery. The concept is positioned to address several practical limitations of current approaches in dental pain management, where short-lived topical agents may offer only transient relief and injections, while effective, are invasive and often associated with unwanted lingering numbness. The oral cavity is also a uniquely demanding pain setting: it is highly innervated and continuously engaged in speaking, swallowing and chewing, meaning even localized pain can rapidly become function-limiting. A locally acting approach can therefore be clinically intuitive, aiming to reduce pain at the site of origin while limiting unnecessary systemic exposure.

11. Bronzato, Juliana D. Rordrigues, Guilherme A. 2025. *A narrative review on local anesthetics in dentistry: mechanism of action, characteristics, and clinical* considerations. Journal of Oral and Maxillofacial Anesthesia.
12. Mogensen, S. et al. 2017. Absorption of bupivacaine after administration of a lozenge as topical treatment for pain from oral mucositis. *Basic & Clinical Pharmacology & Toxicology, 120*(1), 71–78.
13. OncoZenge. 2024. *The case for BupiZenge (company material)*.
14. Weinschenk, S et al. 2022. Anti-inflammatory characteristics of local anesthetics: Inhibition of TNF-α secretion of lipopolysaccharide-stimulated leucocytes in human blood samples. *International Journal of Molecular Sciences, 23*(6), 3283.

Clinical Walkthrough

The figure below illustrates a simplified pain pathway from peripheral tissue to the brain. In dental settings, oral pain is often experienced as particularly intrusive because the soft lining of the mouth is densely supplied with nerves and is constantly engaged in everyday functions such as speaking, swallowing and chewing. This means that even small areas of irritation can become function-limiting. In some cases, the pain may even originate from within the tooth itself.

From a neurophysiology perspective, pain transmission can be viewed as a relay system. A signal in the affected tissue is picked up in the "first-order" neuron, the peripheral pain-carrying nerve. The "second order" neuron then relays that signal upward within the central nervous system (CNS), and the "third order" neuron carries it to the brain regions involved in conscious pain perception. In the mouth, the signal often starts in the mucosa, the soft tissue lining body canals and organs including the oral cavity, where nerve endings are dense and easily activated by irritation or injury. [15]

Clinical expert Dr Paul Murtagh explains that this framework is useful when contrasting local versus systemic pain control. He highlights that many commonly used treatments, i.e., systemic analgesics, modulate pain transmission later in the pathway, rather than preventing the signal from being generated at the source. In practical terms, systemic analgesics such as NSAIDs and paracetamol, and in some settings opioids, are described as working by dampening pain signalling higher up in the pathway by blocking receptors and reducing the impact of pain-related chemical messengers.

In addition to these mechanistic considerations, **clinical expert Dr Sayf Hosamaldin** highlights important medical limitations associated with systemic analgesic use. He notes that a subset of patients cannot tolerate NSAIDs due to contraindications such as asthma, gastrointestinal ulcer disease or other comorbidities. For these patients, effective pain control options are more limited, increasing the relevance of approaches that provide local pain relief without adding to systemic drug exposure.

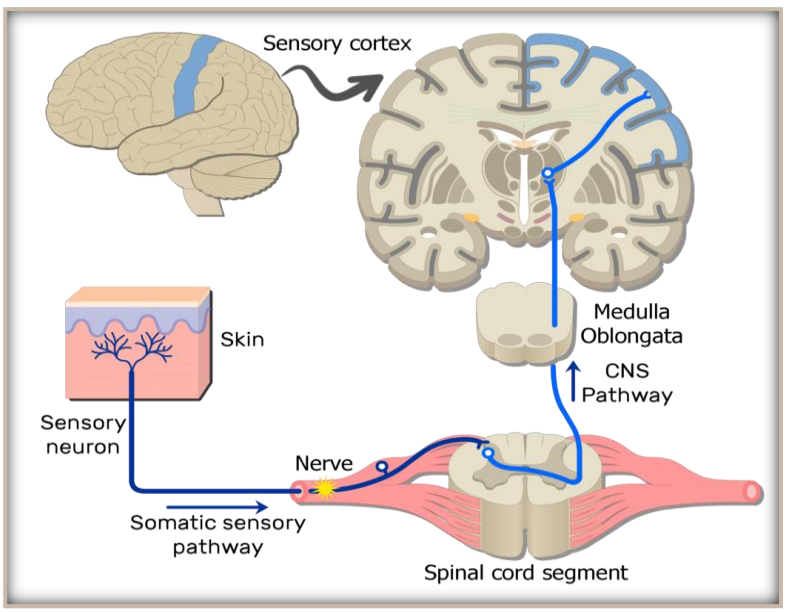
Dr Murtagh's core point is that blocking pain locally at the start of the pathway is fundamentally different from trying to dampen pain later once the signal has already been transmitted. In his explanation, the clinical aim is to prevent the pain signal from propagating beyond the first-order neuron, i.e. to block it at source in the affected oral tissue, such as the mucosa, rather than attempting to reduce signalling further upstream. He argues that this is where a bupivacaine lozenge, such as **BupiZenge™** could make a meaningful difference. This is because bupivacaine blocks the nerve's sodium channels and, due to its lipophilic characteristics, can provide a longer local effect, which he describes as lasting roughly four times longer than lidocaine in this context. A secondary implication in this framework is that a more localised approach reduces the need to rely on centrally acting pain medication, which is typically associated with broader systemic effects.

The oral mucosa aspect is central to the clinical logic here. When the protective epithelial surface is disrupted, nerve endings can become exposed, making even light contact painful. A lozenge format is intended to maintain contact with mucosal surfaces long enough to deliver a local anaesthetic effect where these nerve endings are located, without requiring injections or pocket-specific applicators.

Beyond soft tissue, Dr Murtagh also highlights a mechanistic hypothesis related to tooth sensitivity. Dentinal tubules (microscopic channels in dentin) are commonly reported to be on the order of 0.5–2.5 micrometres in diameter, and it is proposed that if the active substance can access these pathways, it could reduce sensitivity arising from the tooth itself. It should be stated that this remains theoretical and would require further confirmation in dental studies.

Taken together, the clinical thesis is that a locally acting bupivacaine lozenge aims to reduce pain at its point of origin, the first-order level, rather than relying primarily on treatment later in the pathway. This provides a structured lens for assessing where the approach could be most clinically meaningful across dental care, which is then developed in the subsequent use case discussion.

Pain Signaling Pathways. Adapted from Primary somatosensory cortex. [16]



15. Cleveland Clinic. 2022. *Mucosa*
16. Scott A. Sheffield . 2022. *Primary Somatosensory Cortex*

Dental Indications and Use Cases for BupiZenge™

Based on the underlying clinical needs in dentistry and the available scientific evidence on local anaesthesia and oral pain, Impala Nordic, following an assessment conducted in close dialogue with dental professionals and experts, has identified three primary areas within dental care where BupiZenge™ may offer meaningful clinical and commercial value. These categories reflect unmet patient needs, practical limitations of current approaches, and documented preferences for needle-free pain management. Below, we outline these areas and the supporting evidence.

Identified clinical use cases in dental care

Pre-dental use:
Pain Management Before or During Procedure

A large group of patients experience fear and anxiety related to dental injections, and this is one of the most frequently reported reasons for postponing or avoiding dental treatment as mentioned previously in this Analysis. Topical anaesthetic gels are sometimes applied to the mucosa before an injection, but their effect is typically superficial and short-lived, and they rarely alter the pain experienced during the procedure itself in a meaningful way. A bupivacaine lozenge represents a different conceptual approach, as it is intended to provide more sustained local anaesthesia across the oral cavity and, in selected low-invasiveness procedures, may reduce the need for injectable anaesthesia. For patients with injection-related anxiety, pre-procedural administration of a lozenge could therefore lower both perceived pain and stress without materially altering clinical workflow.

Post-dental Use:
Managing Pain After Procedures

Post-operative pain remains one of the most significant unmet needs in dental care, particularly after invasive procedures such as wisdom-tooth extraction, implant placement, or periodontal surgery. Studies demonstrate that bupivacaine provides better and longer-lasting post-extraction analgesia than lidocaine, and most patients preferred the longer-acting anaesthetic.[17] Post-dental pain is typically managed with NSAIDs or, in some instances, opioids. However, evidence shows that dentists account for a notable share of unnecessary opioid prescriptions, and many opioid tablets dispensed after dental procedures remain unused, contributing to risks of misuse and diversion. A long-acting, locally administered anaesthetic lozenge could meaningfully reduce reliance on systemic analgesics by providing extended mucosal pain relief as the injected anaesthesia wears off.

Oral Mucosal Pain and Disease-Related Indications

Beyond procedure-related pain, many patients suffer from acute or chronic pain originating in the oral mucosa. These include aphthous ulcers, oral lichen planus, traumatic lesions, prosthesis-related irritation, and Burning Mouth Syndrome (BMS). BMS alone affects approximately 1.7 % of the global population, with markedly higher prevalence among older women.[18] Available systemic treatments often provide limited benefit, and several clinical analyses suggest that local anaesthetics can offer meaningful symptomatic relief, although current formulations are short-acting. A bupivacaine lozenge could provide sustained local analgesia without systemic exposure, positioning it as a potential option for both episodic and chronic mucosal pain management.[19]

Taken together, these three indications illustrate a coherent platform opportunity. It is our understanding that BupiZenge™ aligns with several identifiable pain points within dentistry: needle aversion, insufficient duration of topical gels, reliance on systemic painkillers, and a lack of effective options for mucosal pain. Its formulation and pharmacological profile suggest the potential to simplify clinical workflow, improve patient comfort, and reduce downstream medication use. These characteristics create a compelling rationale for further exploration of BupiZenge™ within dental care.

Furthermore, according to clinical expert Dr. Paul Murtagh, oral mucosal and disease-related pain conditions are estimated to affect approximately 5 % of the global population at any given time. A substantial proportion of these conditions are recurrent or chronic, leading to repeated episodes of discomfort that often require ongoing symptom management. While a range of topical and systemic treatment options are available, their effectiveness is frequently limited by short duration of action, tolerability issues, or practical constraints in routine use. As a result, symptom relief is often partial or temporary, highlighting an unmet need for local, well-tolerated solutions that can provide sustained analgesia without increasing systemic exposure.

17. Balakrishnan, K et al. 2015. *Bupivacaine versus lignocaine as the choice of local anesthetic agent for impacted third molar surgery: A review. Journal of Pharmacy & Bioallied Sciences, 7*(Suppl 1), S230–S233.
18. Wu, S et al. 2022. *Worldwide prevalence estimates of burning mouth syndrome: A systematic review and meta-analysis. Oral Diseases, 28*(6), 1431–1440
19. Liu, Y et al. 2018. *Burning mouth syndrome: A systematic review of treatments. Oral Diseases, 24*(3), 325–334.

Dental Indications and Use Cases for BupiZenge™ cont.

Clinical use cases- Selected subsegments

Dental pain is not a single, uniform condition, but arises in distinct and recurring clinical situations along the dental care pathway. These situations differ in pain characteristics, duration, treatment setting and workflow requirements, yet share a common limitation: While current pain management options provide sufficient control in many procedures, they leave clear gaps in routine dental care where solutions are either invasive, short-acting, systemically focused, or operationally burdensome.

To assess the relevance of a needle-free, long-acting local anaesthetic lozenge such as BupiZenge™ within dentistry on a more nuanced level, Impala Nordic has, based on an assessment conducted in close dialogue with dental professionals and subject-matter experts, structured the Analysis around three clearly defined and clinically meaningful subcategories. Together, these subcategories cover the primary unmet pain-related needs in routine dental care:

- ☑ Pre-dental use – Pain management before or during procedures
- ☑ Post-dental use – Managing pain after procedures
- ☑ Non-procedural mucosal pain – Oral Mucosal pain and disease-related indications

Each subcategory is analysed from five perspectives:

(1) Clinical background and pain characteristics,

(2) Current treatment landscape and its limitations,

(3) The specific rationale for a bupivacaine lozenge in that setting, and

(4) Financial and market implications.

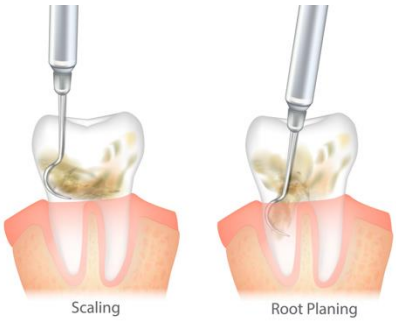
Integrated expert insights are included to reflect real-world clinical considerations, and adoption dynamics. This structure allows for a nuanced assessment of where BupiZenge™ could add value clinically, operationally and commercially, while also illustrating how these distinct use cases together form a broader and coherent opportunity within dental pain management.

Segment I: Scale and Polish / Scaling and Root Planing

Clinical Background and Characteristics

Scale and polish procedures, including scaling and root planing (SRP), are among the most frequently performed interventions in dentistry and constitute the backbone of periodontal care. SRP is the standard non-surgical treatment for periodontitis and is not a one-time intervention, but a recurring component of long-term disease management. Patients with periodontal disease typically undergo SRP at regular intervals over many years, often multiple times per year.

Scaling and Root Planing - illustration



Source: Parkway Periodontics. 2023. SRP and Osseous Surgery

Pain during SRP is well documented and closely linked to inflammatory status, exposed root surfaces and depth of periodontal pockets. Clinical studies indicate that approximately 20–30 % of patients experience pain of sufficient intensity to justify analgesic support.[20] Subgingival scaling, which targets inflamed tissue and root surfaces below the gumline, is consistently perceived as more painful than supragingival cleaning. The pain is often described as diffuse (widespread) rather than focal (specific spot), persists throughout the procedure and is amplified by tissue inflammation and hypersensitivity. Despite this documented pain burden, SRP is frequently performed without anaesthesia. Many patients tolerate discomfort to avoid injections, which are perceived as disproportionate for a routine hygiene visit. Needle anxiety further reinforces this behaviour. From a clinical perspective, this creates a structural mismatch between experienced pain and the use of analgesic support, particularly in preventive and maintenance-oriented care where injections are viewed as excessive, invasive and workflow-disruptive.

Current Treatment Landscape and Limitations

Injection-based local anaesthesia provides reliable and deep pain control but is rarely used in SRP. Its invasive nature, requirement for licensed administration and impact on clinical workflow make it poorly suited to routine hygiene visits. For dental hygienists in particular, injections introduce additional time, procedural complexity and patient anxiety, all of which conflict with the efficiency-driven structure of periodontal maintenance appointments.

Needle-free alternatives such as Oraqix® have demonstrated strong patient preference and can reduce discomfort during treatment. However, their clinical utility is constrained by superficial depth of anaesthesia and limited duration of action, which as mentioned is typically around 20 minutes. This restricts effectiveness during longer or more demanding SRP sessions. Conventional topical gels face further limitations related to dilution by saliva, displacement during ultrasonic scaling and inconsistent retention at the treatment site, resulting in variable real-world efficacy.

As a result, SRP remains a high-volume procedure category with a well-documented discomfort burden but limited penetration of effective, durable and workflow-compatible local analgesic solutions.

Rationale for BupiZenge™

A bupivacaine lozenge offers a differentiated approach in this setting. By providing broader mucosal coverage and longer duration of action than existing topical alternatives, BupiZenge™ could improve patient tolerance during SRP without requiring injections. The lozenge format enables even distribution of the active substance across the oral cavity and sustained local exposure throughout the procedure, which is particularly relevant in diffuse pain states such as periodontal inflammation.

Pre-procedural administration aligns well with hygienist workflows and avoids procedural disruption. The lozenge can be administered before treatment, for example in the waiting room, allowing onset of analgesia without adding chair time. This is critical in high-throughput hygiene settings, where any additional procedural steps represent a barrier to adoption.

Barriers to Adoption and Requirements for Uptake

Adoption will require clear clinical evidence that the lozenge provides meaningful pain reduction and allows a substantial proportion of SRP procedures to be completed without injection. Onset of action must be predictable and compatible with hygiene appointment scheduling. In addition, the product must be perceived as simple, intuitive and non-disruptive, requiring minimal training and no changes to established workflows. Clear communication with patients is also important, positioning the lozenge as a comfort-enhancing measure rather than an indicator of a more complex or invasive procedure.

EXPERT INSIGHT

Dr Paul Murtagh *notes that discomfort during scaling and root planing (SRP) is often underestimated in everyday practice but can be clinically meaningful for a subset of patients. He emphasises that a needle-free analgesic option could gain traction provided that onset of action is predictable and use does not complicate the clinical visit. In particular, needle-phobic patients, estimated to represent approximately 5–10 % of the patient population, could benefit significantly from a lozenge-based approach. He highlights that a BupiZenge™ lozenge could offer a patient-friendly way to desensitise inflamed gingival tissue prior to scaling, improving comfort without injections. If patients experience improved comfort when using the lozenge shortly before treatment, they are likely to request it again at subsequent visits. Adoption, in his view, will therefore be driven primarily by individual patient experience rather than by changes in clinical protocol.*

EXPERT INSIGHT

Dr. Hosamaldin *notes that in clinical practice, scaling and root planing is often performed in segments rather than across the entire dentition in a single visit. In patients with advanced periodontal disease and deep pockets, treatment is typically limited to one quadrant per appointment, as adequate pain control requires injectable local anaesthesia during deep subgingival instrumentation. In these cases, a lozenge-based local anaesthetic such as BupiZenge™ may still play a supportive role by reducing discomfort associated with the injection itself. In patients with less advanced disease and shallower pockets, it is often clinically feasible to treat an entire jaw, or even both jaws, in one visit. Here, multiple injections can be uncomfortable and disproportionate, leading to unnecessarily deep and prolonged numbness. In this setting, BupiZenge™ could offer a needle-free alternative that improves comfort during treatment while allowing sensation to return more quickly afterward.*

20. Pihlstrom, B. L. et al. 1999. *Pain after periodontal scaling and root* planing. Journal of the American Dental Association.

Segment I: Scale and Polish / Scaling and Root Planing cont.

The Market – Scale and Polish

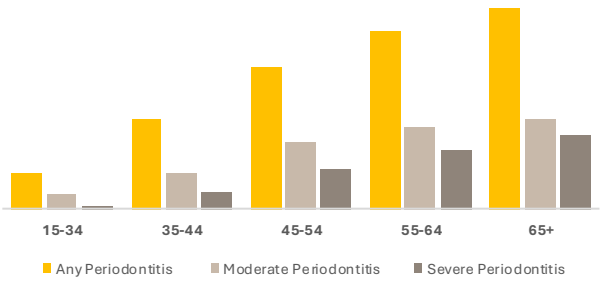
Scaling and root planing is one of the most frequently performed dental procedures globally, driven by the chronic and widespread nature of periodontal disease. Severe periodontitis affects approximately 11 % of adults worldwide (about 743 million people), making it one of the most prevalent non-communicable diseases. Prevalence increases sharply with age, rising from below 10 % in adults under 45 to more than 25 % among individuals over 65. This demographic dynamic creates a durable and structurally expanding need for non-surgical periodontal therapy.[21]

SRP is estimated to account for approximately 26 % of the total periodontal market, valued at around USD 12.2 billion in 2025. That figure covers periodontal treatment as a whole, including services and devices, and is not an addressable market for an anaesthetic product.[22] Given the high frequency of SRP procedures, there is a clear and recurring need for effective pain management. Local anaesthesia and pain-relief products should therefore be viewed as an integrated component of everyday periodontal treatment, rather than a standalone niche. These products form part of the broader global dental drug market, valued at approximately USD 5.5 billion in 2024, which includes injectable and topical local anaesthetics as well as systemic analgesics used before, during and after dental procedures.[23]

Procedure volumes are substantial across developed dental markets. NHS England utilisation data provide a useful anchor. In 2023/24, approximately 34 million courses of dental treatment were delivered within the NHS system, of which roughly three quarters were adult courses. Around 31 % of adult courses included scale and polish or periodontal treatment, which implies in the order of 7–8 million such procedures annually in England alone. Note that scale and polish is a routine hygiene procedure and is not equivalent to SRP, so this figure is an upper bound on SRP activity rather than a direct measure of it.[24]

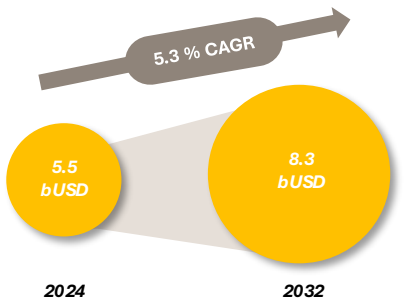
Despite this scale, SRP appears underpenetrated by local anaesthesia. Trial-level evidence suggests that only a minority of SRP procedures, on the order of 15–25 %, are performed with any form of anaesthesia, and adoption of needle-free options is particularly limited. We note that this estimate derives from a single clinical trial rather than from utilisation data, and should be treated as indicative. The structural point stands: a high-volume procedure category with a well-documented discomfort burden and a comparatively small anaesthesia market.[25]

Periodontitis prevalence by age group



Source: Richards, D. 2014, reporting Kassebaum et al. Severe periodontitis affects c. 11 % of adults. Categories overlap: "any" includes moderate and severe.

Global Dental Drug Market Size (bUSD)



Source: Intel Market Research. 2025. Dental Drug Market

21. Richards, D. 2014. *Review finds that severe periodontitis affects 11 % of the world population. Evidence-Based Dentistry, 15(3), 70–71.*
22. Future Market Insight. 2025. *Periodontal Market Size and Share Forecast Outlook 2025 to 2035.*
23. Intel Market Research. 2025. *Dental Drug Market.*
24. NHS. 2025. *Dental Statistics – England 2023/2024.*
25. Moraes, G et al. 2019. *Liposomal anesthetic gel for pain control during periodontal therapy in adults: A placebo-controlled randomized clinical trial. Journal of Applied Oral Science, 28,* e20190025.

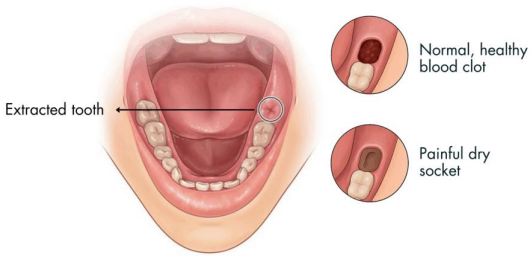
Segment II: Postoperative Pain Following Dental Surgery

Clinical Background and Characteristics

Postoperative pain following dental surgery represents one of the most predictable and clinically relevant pain states in dentistry. Procedures such as third-molar extraction, implant placement and periodontal surgery routinely result in moderate to severe pain once injected anaesthesia wears off, typically several hours after discharge. This pain often emerges when patients are no longer under direct clinical supervision and may intensify during the first postoperative evening, making breakthrough pain a major driver of patient dissatisfaction, unplanned follow-up contacts and additional medication use.

Within this broader postoperative pain category, alveolar osteitis (dry socket) represents a distinct and particularly burdensome clinical scenario. Dry socket occurs when the blood clot that forms over the extraction site is lost or fails to develop in the days after the tooth is removed, leaving bone exposed. While the condition affects a minority of patients in absolute terms, it is associated with severe, persistent and highly localised pain that is often disproportionate to the initial procedure and poorly responsive to standard systemic analgesics. Incidence is estimated at approximately 3 % of routine extractions, increasing to 20–30 % following surgical removal of mandibular third molars (wisdom tooth) and reaching even higher levels in high-risk groups such as smokers.[26] Pain typically develops several days after extraction, often after routine follow-up has ended, and can persist for more than a week if not adequately managed. Clinically, this delayed onset and prolonged symptom duration make dry socket one of the most disruptive postoperative pain states in dental care.[27]

Dry Socket after Tooth Extraction - illustration



Source: Seaforth Oral Surgery Montreal. 2025. Dry Socket: Symptoms, Treatment and Prevention After a Tooth Extraction

Current Treatment Landscape and Limitations

Intraoperative pain control relies almost exclusively on injectable local anaesthetics, often supplemented with longer-acting agents such as bupivacaine at the end of surgery. While effective initially, these injections inevitably wear off. Postoperative pain management is therefore dominated by systemic analgesics, primarily NSAIDs and paracetamol, with opioids still used in some regions despite declining prescription rates.

As described in the **Clinical Walkthrough**, systemic analgesics mainly act by dampening pain processing later in the pain pathway rather than blocking pain where it originates. In dental surgery, pain typically arises from localised, inflamed tissue in the mouth and jaw that is rich in nerve endings. As a result, systemically acting medication may provide incomplete relief, particularly once injected anaesthesia has worn off, leading to breakthrough pain.

These limitations are evident in dry socket. Analgesic therapy does not constitute curative treatment, and definitive management requires local clinical intervention such as irrigation and dressing placement. However, systemic analgesics often provide limited relief given the intensity and localisation of the pain. Patients frequently require multiple unplanned clinic visits, and dry socket disproportionately consumes clinical resources relative to its incidence. Importantly, there is currently no effective at-home local analgesic option that allows patients to manage dry socket pain independently between visits.

Rationale for BupiZenge™

A bupivacaine lozenge could extend localised pain control into the postoperative period by acting directly at the level of the oral mucosa, where pain signals are initiated in densely innervated and inflamed tissue. This local-first approach is designed to block nerve conduction at the source rather than modulating pain further along the pathway, potentially reducing the intensity of breakthrough pain once injected anaesthesia wears off. In routine postoperative pain, this could improve patient comfort during the vulnerable hours after discharge and reduce reliance on additional systemic medication. In the context of dry socket, the rationale is even clearer. Dry socket pain is entirely local, severe and prolonged, yet does not require deep nerve blockade. A long-acting local anaesthetic lozenge could provide sustained mucosal analgesia at the site of pain, allowing patients to manage symptoms between clinic visits. From an operational perspective, this has the potential to reduce unplanned follow-ups, ease chair-time burden and improve overall patient experience, while positioning the lozenge as a non-invasive adjunct rather than a replacement for established surgical or in-clinic treatments.

Barriers to Adoption and Requirements for Uptake

Adoption will depend on clear clinical evidence demonstrating that the lozenge meaningfully reduces breakthrough postoperative pain and provides consistent relief in high-intensity subsegments such as dry socket. In dry socket specifically, clinician confidence will depend on predictable analgesic effect and clear dosing guidance, given the severity and persistence of symptoms. From a practical standpoint, use must be straightforward and easy to explain to patients recovering from surgery. Importantly, the product would need to integrate naturally into existing postoperative protocols as a complement to standard care, rather than as a substitute for definitive clinical intervention.

EXPERT INSIGHT

Dr Murtagh *highlights that breakthrough pain as injected anaesthesia wears off is a common driver of patient dissatisfaction and unplanned postoperative contact. Once local injections subside, postoperative soft-tissue pain is often inadequately controlled by systemic analgesics, which may require repeated dosing while still providing incomplete relief. In this setting, he views locally acting anaesthesia, such as the BupiZenge™ lozenge, as better aligned with the underlying pain mechanism, as it targets pain at its source. Predictable duration of action and simple dosing are important for both patient adherence and clinician confidence, while local administration avoids systemic side effects associated with high analgesic intake.*

EXPERT INSIGHT

Dr Hosamaldin *adds that dry socket represents one of the most painful postoperative complications following tooth extraction, with severe localised pain that often persists despite standard systemic analgesics. While definitive management requires local clinical intervention, effective pain control is critical between visits. He notes that systemic analgesics have important limitations, particularly in patients with NSAID intolerance or polypharmacy. In this context, a locally acting lozenge could provide meaningful supportive relief, reducing patient discomfort and easing clinical chair-time burden while complementing existing in-clinic treatment.*

26. Tandon, P et al. 2024. *Dry socket prevalence and risk factors in third molar extractions: A prospective observational study. Cureus, 16*(3), e56721.
27. Malamed, S. F. 2023. *Pain management following dental trauma and surgical procedures. Dental Traumatology, 39(4), 295–303.*

Segment II: Postoperative Pain Following Dental Surgery cont.

The Market – Postoperative Pain

Post-extraction and postoperative dental pain constitute the largest definable segment within dental pain management, driven primarily by the high global volume of dentoalveolar surgical procedures. Third-molar removal is the single most significant contributor and remains one of the most frequently performed oral surgeries worldwide.[28] Available epidemiological and procedural data illustrate the scale of this category. In the United States, an estimated 5 million patients undergo third-molar removal annually, corresponding to approximately 10 million extracted teeth. In Europe, population-based reviews indicate that 7–12 % of adults undergo at least one third-molar extraction during their lifetime, translating into approximately 3–4 million procedures per year across the European Union.[29]

The market for postoperative dental pain management, dominated by NSAIDs, paracetamol and adjunct opioid formulations, has been estimated at approximately USD 4–5 billion annually, or roughly 10 % of the global postoperative pain management market, which exceeds USD 40 billion across all surgical specialties. This figure is not directly comparable with the USD 5.5 billion dental drug market cited elsewhere in this Analysis: it counts general analgesics consumed for dental pain, most of which are sold over the counter and are not classified as dental pharmaceuticals. Taken at face value the two would be inconsistent, and we regard the narrower dental drug market as the more relevant reference point for a prescription anaesthetic.[30] At the same time, prescribing behaviour is undergoing structural change. Declining opioid prescription rates in dental care in both the United States and Europe reflect increasing regulatory scrutiny and a broader shift toward opioid-sparing treatment strategies. This transition increases the relevance of alternative, locally acting analgesic options that can deliver effective pain control without reliance on systemic opioids.[31]

Within this broader postoperative segment, alveolar osteitis (dry socket) represents a small but high-intensity addressable market, defined more by the severity and duration of symptoms than by patient numbers. Epidemiological studies report that dry socket develops in approximately 3 % of routine extractions, rising to 20–30 % following surgical removal of mandibular third molars and up to 40 % in high-risk groups such as smokers. Applied to the third-molar volumes above, those rates imply in the order of 0.8–1.4 million cases per year in the United States and the European Union alone, before routine extractions are counted. Global extraction volumes are not reliably enumerated, so any worldwide figure should be read as an order-of-magnitude estimate rather than a measured market. These patients often experience severe, persistent pain that responds poorly to systemic analgesics and frequently require multiple unplanned follow-up visits for irrigation and dressing placement.[32]

- Low patient numbers but high treatment intensity
- High willingness to pay due to pain severity
- Meaningful economic burden for clinics driven by unplanned revisit rates and chair time consumption
- Absence of an at-home local analgesic option

From a commercial perspective, the opportunity is therefore less about broad volume capture and more about addressing a concentrated, high-need pain state where unmet clinical need, patient burden and operational inefficiencies converge. A local analgesic option that allows patients to manage dry socket pain between visits could reduce chair time, ease procedural load for providers and deliver meaningful symptomatic relief in a segment where current solutions remain largely clinic dependent.

28. Brilhante-Neto et al. 2023. *Postoperative pain after third molar extraction surgery in patients with and without bruxism: An observational study*. *Acta Odontologica Latinoamericana, 36*(1), 47–52.
29. Friedman, J. W. 2007. The prophylactic extraction of third molars: A public health hazard. *American Journal of Public Health, 97*(9), 1554–1559.
30. Mordor Intelligence. 2025. *Post-Operative Pain Management Market Share & Share Analysis - Growth Trends and Forecast (2026 - 2031)*.
31. Han, C et al. 2022, *Trends in opioid prescribing by general dentists and dental specialists in the United States, 2012–2019. American Journal of Preventive Medicine, 63*(1), 3–12.
32. Noroozi, A.-R., & Philbert, R. F. 2009. Modern concepts in understanding and management of the "dry socket" syndrome: Comprehensive review of the literature. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology, 107(1), 30–35.

Segment III: Recurrent Aphthous Stomatitis

Clinical Background and Characteristics

Recurrent aphthous stomatitis (RAS) is one of the most common causes of painful ulcers in the oral mucosa and represents one of the clearest non-procedural pain indications within dentistry.[33] The most common presentation consists of minor aphthae (<1 cm) that typically last 10–14 days, resolve on their own, and recur intermittently, often months later. Despite the self-limiting nature of individual lesions, RAS has a reported prevalence of approximately 5–20 % in the general population, affecting both teenagers and adults.[34]

Stomatitis - illustration

Source: Lois Zoppi. 2019. What is Stomatitis?

Clinically, RAS is associated with intense, localised pain that can materially impair eating, speaking and swallowing. As outlined in the Clinical Walkthrough, the oral mucosa is densely supplied with nerve endings and is constantly involved in everyday functions. As a result, even small ulcers can become function-limiting. Pain in RAS originates directly at the mucosal surface, activating peripheral first-order neurons early in the pain pathway, which helps explain why symptoms are often experienced as severe despite the limited size of the lesions.

Current Treatment Landscape and Limitations

The current standard of care for RAS is widely regarded as inadequate. Management typically relies on topical corticosteroids, antiseptic or anaesthetic gels, mouth rinses and protective pastes. These treatments may reduce inflammation or provide short-term symptom relief, but their effects are often short-lived, inconsistent and insufficient, particularly for patients with moderate to severe pain.[35] Importantly, there is no established at-home, long-acting local analgesic specifically designed to control RAS pain throughout the full symptomatic period. In teenagers, treatment is further complicated by dosing and safety considerations, which require careful clinical definition. As a result, RAS represents a high-incidence condition with a persistent pain burden and limited effective pain-control options.

Rationale for BupiZenge™

From a neurophysiological perspective, RAS closely aligns with the treatment logic described in the Clinical Walkthrough. Pain originates at the first-order level, in exposed or inflamed oral mucosa, and is transmitted centrally unless blocked locally. Systemic analgesics act later in the pain pathway and may therefore provide incomplete relief in this setting. A long-acting local anaesthetic lozenge such as BupiZenge™ is designed to block pain at its source, preventing signal propagation beyond the peripheral nerve endings. By maintaining contact with the mucosal surface, the lozenge format is intended to deliver sustained local anaesthesia without injections or systemic exposure. This positions BupiZenge™ as a complementary option to anti-inflammatory treatments, addressing pain directly rather than dampening perception further upstream.

Barriers to Adoption and Requirements for Uptake

Adoption of BupiZenge™ in RAS will depend on clear clinical evidence demonstrating meaningful and durable pain relief in typical presentations of minor aphthous ulcers. Given the episodic and recurrent nature of the condition, studies must be designed to capture both pain intensity and duration during an active episode.

From a practical perspective, collaborative studies with university dental hospitals or specialised oral medicine centres are likely required to achieve sufficient patient volumes, as individual practices typically see too few RAS patients to support robust standalone studies. Clear and predictable dosing regimens will also be important, particularly for teenage patients.

Because the lozenge is intended to act locally at the level of the oral mucosa, with limited systemic exposure, tolerability and suitability for repeated use are likely to be key considerations in a recurrent condition such as RAS. Overall, successful adoption will depend on demonstrating reliable local pain control, good tolerability and ease of use in an at-home setting without adding complexity to existing care pathways.

EXPERT INSIGHT

Dr Murtagh *highlights that RAS is, in his view, one of the clearest and most under-recognised pain indications within dentistry. Despite the self-limiting nature of individual episodes, the condition has a high incidence rate and is associated with significant pain that interferes with eating, speaking and daily function. Current standards of care are largely inadequate and often provide only partial or inconsistent relief. RAS affects both teenagers and adults, although dosing and safety considerations in younger patients would need to be defined carefully. Generating meaningful clinical evidence would require collaboration with university dental hospitals, as single-practice patient volumes are typically insufficient for robust studies.*

EXPERT INSIGHT

Dr. Hosamaldin *notes that RAS represents a common yet substantially undertreated source of oral-mucosal pain. In clinical practice, the most effective symptomatic strategy is often simply to avoid contact with the ulcer altogether—an approach that is inherently impractical, as it restricts eating, speaking and normal oral function. These limitations can significantly affect quality of life, particularly in patients experiencing frequent or severe episodes. A long-acting local anaesthetic lozenge such as BupiZenge™ has the potential to provide meaningful, sustained pain reduction, allowing patients to maintain everyday activities without discomfort.*

33. Scully, C., & Porter, S. 2008. *Oral mucosal disease: Recurrent aphthous stomatitis.* British Journal of Oral and Maxillofacial Surgery, 46(3), 198–206.
34. Plewa, M. C., & Chatterjee, K. 2023. *Recurrent aphthous stomatitis.* StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
35. Edgar, N. R., Saleh, D., & Miller, R. A. 2017. *Recurrent aphthous stomatitis: A review.* Journal of Clinical and Aesthetic Dermatology, 10(3), 26–36.

Segment III: Recurrent Aphthous Stomatitis cont.

The Market – RAS

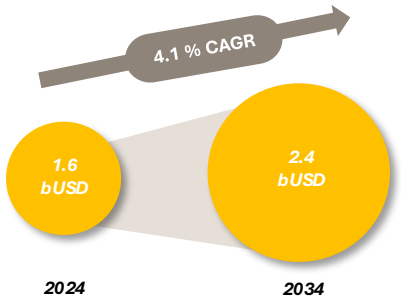
In terms of the addressable market, RAS is best viewed as a subset of the broader mouth-ulcer treatment market. The global mouth-ulcer treatment market was valued at approximately USD 1.6 billion in 2024, projected to grow to approximately USD 2.4 billion by 2034, implying a compound annual growth rate of approximately 4.1 %. This category includes treatments for oral ulcers of various causes, with RAS representing the most prevalent non-viral indication.[36] Geographically, the market is concentrated in regions with high healthcare access and diagnosis rates. North America and Europe together account for approximately 2/3 of global market value.

From a formulation perspective, the mouth-ulcer treatment market is currently dominated by topical gels, which account for approximately 35 % of total market value, followed by mouthwash and sprays. Lozenges already represent around 19 % of the market, so the format itself is established rather than novel. The relevant gap is narrower: existing lozenges are predominantly antiseptic or mild surface-analgesic products, and none is a long-acting local anaesthetic. Gels, while widely used, often have a short duration of action, dilution by saliva and inconsistent retention at the lesion site, particularly in mobile areas of the oral mucosa.[36] Commercially, this points to a clear gap in current treatments. Despite representing a minority share today, lozenge-based products, particularly lozenge offering longer-lasting local analgesia, could capture market share by offering prolonged mucosal contact, simple administration and suitability for at-home use.

Unlike procedural dental pain segments, RAS is characterised by high prevalence, recurrent demand and relatively low per-episode spend, with current expenditure fragmented across low-cost topical products with limited efficacy. The commercial opportunity is therefore driven not by procedure volume, but by the combination of a large patient population, repeated episodes and an unmet need for effective, durable local pain control in an at-home setting.

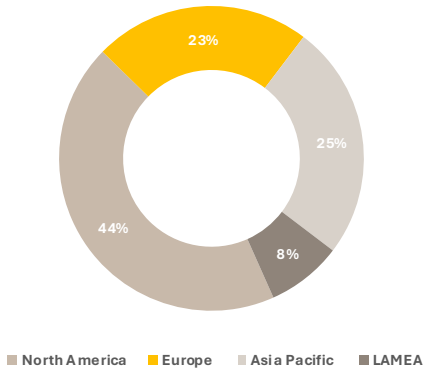
Within the broader dental pain management platform described in this Analysis, RAS complements the procedural segments (SRP, postoperative pain and dry socket) by extending the relevance of BupiZenge™ beyond the dental chair. While RAS is unlikely to match postoperative dental pain in absolute market size, its prevalence, recurrence and alignment with a local-first pain-pathway approach make it a strategically attractive complementary growth indication with potential to broaden the overall addressable market.

Mouth Ulcer Treatment Market Size growth (bUSD)



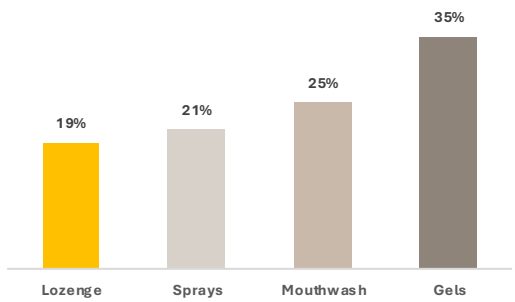
Source: Precedence Research. 2025. *Mouth Ulcer Treatment Market*

Mouth Ulcer Treatment Market Share, By Region, 2024 (%)



Source: Precedence Research. 2025. *Mouth Ulcer Treatment Market*

Mouth Ulcer Treatment Market Share, By Formulation, 2024 (%)



Source: Precedence Research. 2025. *Mouth Ulcer Treatment Market*

36. Precedence Research. 2025. *Mouth Ulcer Treatment Market*.

Global Dental Pain Market – The Addressable Market

The global dental anaesthesia market is estimated at approximately USD 2.3 billion in 2024, expected to grow by approximately 5 % per year until 2032, and is currently driven primarily by restorative and surgical procedures.[37] The global dental pain management market extends well beyond the local anaesthesia segment alone and encompasses a broad range of products used to control pain before, during and after dental treatment. The global dental drug market was valued at approximately USD 5.5 billion in 2024, and is forecast to reach approximately USD 8.3 billion by 2032, a compound annual growth rate of approximately 5.3 %.[38] This market includes injectable and topical local anaesthetics, NSAIDs, paracetamol and other analgesic products used in connection with dental care.[39]

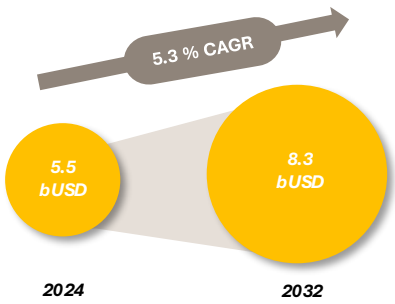
Europe accounts for a substantial share of this market, although published estimates vary with scope. Combined spending on dental pain-related products in the region has been estimated at approximately USD 2.0–2.5 billion, which would represent 36–45 % of the global dental drug market. The narrower dental anaesthesia data shown opposite imply a European share closer to 25 %. The wider figure evidently captures over-the-counter analgesics used for dental pain; for a prescription anaesthetic the narrower measure is the more appropriate anchor. The United States represents the single largest national market, while Europe displays similar structural demand patterns, particularly within periodontics, implantology and oral surgery.[40]

From a volume perspective, demand is primarily driven by the high and persistent burden of dental and periodontal disease. Severe periodontitis affects approximately 11 % of adults worldwide, corresponding to roughly 743 million people, and is recognised as one of the most prevalent non-communicable diseases globally. This creates a large and recurring need for periodontal maintenance, scaling and root planing and other interventions commonly performed under local anaesthesia.[41]

Oral surgery volumes add a further major demand layer. Third-molar (wisdom tooth) surgery remains one of the most frequently performed surgical procedures in outpatient dentistry. Classic public health analyses estimate that approximately 5 million patients undergo third-molar extraction annually in the United States, corresponding to roughly 10 million extracted teeth. More recent observational and registry-based data suggest comparable proportional rates in Europe, where 7–12 % of adults undergo at least one third-molar extraction during their lifetime, translating into approximately 3–4 million procedures per year across the European Union. When combined with other high-volume interventions such as implant placement, periodontal flap surgery, apical surgery and complex extractions, global oral surgery volume likely exceeds 25–30 million procedures annually.[42]

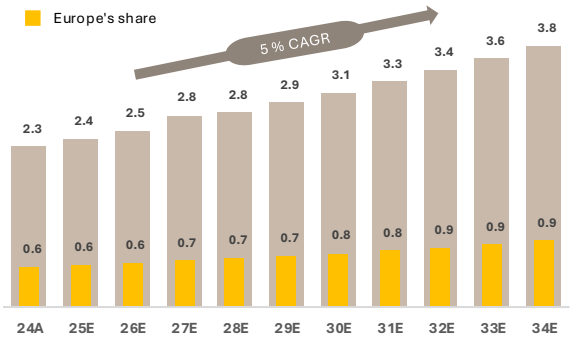
At the same time, there is increasing scrutiny of systemic analgesic use in dental care. Multiple studies indicate that dentists account for a notable share of opioid prescriptions, particularly among adolescents and young adults following procedures such as wisdom tooth extraction, and that early exposure is associated with elevated risk of later misuse. This has resulted in growing professional and regulatory pressure to adopt opioid-sparing treatment pathways and to rely more heavily on non-opioid analgesics such as NSAIDs and paracetamol as first-line therapy.[43]

Global Dental Drug Market Size (bUSD)



Source: Intel Market Research. 2025. Dental Drug Market

Dental Anesthesia Market Size Projection Global (bUSD)



Source: Precedence Research. 2025. Dental Anesthesia Market

37. Precedence Research. 2025. Dental Anesthesia Market https://www.precedenceresearch.com/dental-anesthesia-market
38. Intel Market Research. 2025. Dental Drug Market. https://www.intelmarketresearch.com/dental-drug-market-market-16430
39. Precedence Research. 2025. *Dental Market Size and Forecast 2025 to 2034*.
40. Grand View Research. 2025. *Dental Anesthesia Market (2023-2030)*.
41. Kassebaum, N et al. 2014. *Global burden of severe periodontitis in 1990–2010: A systematic review and meta-regression. Journal of Dental Research, 93*(11), 1045–1053.
42. Friedman, J. W. 2007. The prophylactic extraction of third molars: A public health hazard. *American Journal of Public Health, 97*(9), 1554–1559.
43. Schroeder, A et al. 2019. *Association of opioid prescriptions from dental clinics for US adolescents and young adults with subsequent opioid use and abuse. JAMA Internal Medicine, 179*(2), 145–152.

Impala Nordic's Concluding View

Dental care is a large and recurring market where pain management remains shaped by clear trade-offs. Injectable local anaesthetics remain the backbone for reliable, deep anaesthesia, but they are invasive and often associated with lingering numbness and patient reluctance. Needle-free topical options exist, yet they are typically constrained by limited duration, superficial effect, or narrow procedural fit. These limitations become most apparent at three recurring points of care discussed in this Analysis: discomfort during SRP, local pain after procedures, including dry socket as a painful post-extraction complication, and RAS. For patients, these gaps translate into avoidable discomfort, anxiety and, in some cases, delayed or postponed care, while also affecting recovery experience and overall satisfaction with treatment.

Based on this background, Impala Nordic views a long-acting, needle-free local anaesthetic lozenge as a concept that could be relevant in selected dental care settings, provided that effect, dosing and usability translate well outside the oral mucositis context. The potential value is not framed as replacing injections in complex procedures, but as complementing today's toolkit in situations where prolonged local pain relief is desirable and where current topical options often fall short. Beyond the direct patient benefit, there may also be a health-economic upside in specific scenarios, for example if improved at-home pain control reduces need for unplanned follow-ups and repeat clinic visits.

For OncoZenge, the proposed expansion into dental care appears strategically consistent with the underlying treatment principle of BupiZenge™: sustained, localised pain relief in the oral cavity. Several of the pain characteristics described in this Analysis overlap with the Company's lead indication in terms of local origin, need for targeted delivery and limitations of systemic pain medication in certain contexts. At the same time, commercial relevance will depend on how convincingly the concept can be demonstrated in dental-specific settings and whether adoption can be achieved without creating friction in everyday clinical workflows.

From an investment case perspective, three things determine what the dental opportunity is worth to shareholders, and none of them is the size of the dental pain market itself.

First, economics. European commercialisation rights to BupiZenge™ are held by Molteni Farmaceutici, which pays OncoZenge milestones and a royalty of 15–20 % on partner sales. The scope of that agreement across indications is not specified in the Company's public disclosure, and both outcomes are plausible. If it covers all indications in Europe, a dental label extension would be commercialised by an existing partner without a new transaction, and the value to OncoZenge would be the royalty on incremental volume. If it is limited to oral mucositis, European dental rights would be unencumbered and available to license separately. The distinction matters to how a dental expansion should be valued.

Second, funding. As of 30 June 2026 the Company held SEK 0.7 million in cash. The ongoing Rights Issue is expected to provide net proceeds of approximately SEK 27.8 million, allocated 65 % to completing the Phase III trial and extending runway, 25 % to MAA preparation and 10 % to general corporate purposes, business development and patents. None of it is earmarked for dental development, and the Company has not committed incremental development spend to a dental clinical programme. We read that as a deliberate choice rather than an omission: on the current plan a dental indication is a partnering or licensing opportunity rather than something OncoZenge funds from its own balance sheet, and it sits behind the Phase III readout in sequence.

Third, evidence and optionality. BEAM-Pain compares BupiZenge™ directly with standard-of-care lidocaine, and that comparison underpins much of the clinical argument in this Analysis, which makes the trial the most transferable source of evidence into dental settings. Separately, we would note that a defined label-expansion path can carry value well before any dental study begins. The Company has filed intellectual property applications covering relevant dental use areas, and a credible indication-expansion route strengthens a licensor's position in commercial and licensing discussions that are already under way. In our view that is a nearer-term channel for the dental work to matter than dental revenue itself. How much of it accrues in Europe again depends on the scope of the Molteni agreement; outside Europe it applies in full.

Taken together, dental care is in our view a credible long-term expansion area for BupiZenge™ rather than a near-term value driver, and we do not regard it as reflected in near-term estimates. Execution risk is tied to Phase III progress, the regulatory pathway, the terms on which dental rights are held, and real-world adoption in dental workflows. One practical objection would also need to be resolved in dental-specific studies: a lozenge anaesthetises the oral cavity broadly rather than a defined target site, with consequent effects on the tongue, cheeks and pharynx. That is a meaningful drawback in settings such as routine hygiene appointments, and it is not addressed by the evidence available today.

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