VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Remarkable progress in oral health care has been made and pain control by means of local anaesthesia is now an intrinsic part of clinical practice in dentistry. A wide range of dental treatments and odontological surgery, including procedures performed in children, is now accompanied by a local anaesthesia. Besides improving dental procedures, this increases the patient's comfort and facilitates his/her cooperation.

Local anaesthetics are drugs that temporary interrupt the propagation of nerve impulses, producing insensitivity to painful stimuli in the area supplied by that nerve. Articaine is a widely used local anaesthetic, belonging to the class of so-called amide-type local anaesthetics.

Vasoconstrictors are often combined with local anaesthetics to delay their absorption, which prolongs the duration and improves the depth of anaesthesia. Vasoconstrictors also prevent bleeding by constricting small local blood vessels. Adrenaline is the agent most commonly used for this purpose.

VI.2.2 Summary of treatment benefits

Clinical trials performed by Septodont indicate that SEPTANEST® is effective as a local dental anaesthetic in adults. Anaesthesia is achieved within the first few minutes after the injection of the drug and persists over an adequate time for routine dental treatments. Of note, the rate of success of anaesthesia is higher for upper jaw. A study with 60 patients achieved 95.2% success rate of anaesthesia, whereas another study with 47 patients achieved 75.8%. For lower jaw interventions, a study in 30 patients achieved 47.6% success rate, and another study in 16 patients achieved 25.8%. This difference is due to the difference in innervation of upper vs lower jaw.

Further clinical trials performed by Septodont demonstrate that SEPTANEST® effect is similar to other local anaesthetics. Overall, in the three studies, 1,326 patients were randomised and 1,325 were treated: 882 with SEPTANEST® and 443 with lidocaine. The primary efficacy parameter was the subjective evaluation of pain experienced by the subject during the procedure, rated immediately after the procedure by both the subject and the investigator using a visual analogue scale (VAS), ranging from 0 = "no pain" to 10 = "worst pain imaginable." No statistical difference was found between the two treatment groups with respect to either subject or investigator ratings of pain.

Fifty subjects aged between 4 and 12 years of age were treated with articaine and 20 with lidocaine; these subjects represented 5% of the study population.

VI.2.3 Unknowns relating to treatment benefits

Children have been treated with SEPTANEST®, but the effects in children below 4 years have not been investigated. It is, therefore, not known if the SEPTANEST® would be equally safe and effective and what is the best dose to use.

Retrospective studies of pregnant women received local anaesthetics for emergency surgery early in pregnancy have not shown that local anaesthetics cause birth defects. However no controlled studies have been carried out on pregnant women.

VI.2.4 Summary of safety concerns

Risk	What is known	Preventability
Persistent tingling, burning and loss of feeling in the nerves (Persistent paraesthesia)	Persistent tingling, burning or loss of feeling in the nerves inervating the mouth and jaws may occur. Based on large surveys reported in literature, it is very rare and is reported approximately in 1 in 600,000 to 800,000 non-surgical interventions. This effect may be either due the anaesthetic or due to needle injury. For surgical interventions, the rate is higher, in which case injury contributes.	If the effect is dose related, the use of minimal required dose would decrease the number of events. Needle injury may be prevented by minimal risk injection technique

VI.2.5 Summary of additional risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

SEPTANEST® manufacturer will put in place a web site providing further guidance ot health care professionals on SEPTANEST® safe and effective use. This is an additional risk minimisation measure.

These additional risk minimisation measures are for the following risks: **Persistent tingling, burning and loss of feeling in the nerves (Persistent paraesthesia).**

Risk minimisation measure(s)
Objective and rationale
Summary description of main additional risk minimisation measures SEPTANEST® manufacturer believes that paraesthesia may be prevented by: • Decreasing the dose administered to the minimum necessary dose; • Decreasing the risk of traumatic nerve injury. The Company will create a website which will be educational and at the same time facilitating reporting of suspected adverse reactions to Septodont.

Risk minimisation measure(s)

VI.2.6 Planned post authorisation development plan

Not applicable. There is no study planned and no study is a condition of the marketing authorisation.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable (first submission)