Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Xylonor, 50 mg/g + 1.5 mg/g, gingival gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 gram of gingival gel contains 50 mg of lidocaine and 1.5 mg of cetrimide.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Gingival gel.

White to ivory translucent gel with a mint odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Xylonor is indicated for the production of topical anaesthesia in the buccal cavity, especially in the following procedure:

- Anaesthesia of the mucous membrane before injection, lancing of abscesses, or scaling.
- Surface anaesthesia for the extraction of mobile, deciduous or permanent teeth.
- Prevention of gagging during impression taking.

Xylonor is indicated in adults and in children and adolescents aged 4 to 18 years of age.

4.2 Posology and method of administration

For professional use by dentists and stomatologists only.

Posology

For all populations, the lowest dose leading to effective anaesthesia should be used. The necessary dosage must be determined on an individual basis.

- *Adults*

The recommended dose is 0.10 g to 0.20 g of gel (about the size of a small hazelnut) to cover an area of about 1 cm^2 to 2 cm^2, corresponding to 5 to 10 mg of lidocaine.

Depending upon the surface to be anaesthetised and the status of the patient (age, physical condition), the dose of the gel used may be increased, up to 0.5 g.

The maximum daily administration of the medicinal product should not exceed 4 g, equivalent to 200 mg of lidocaine.

- *Paediatric population (from 4 years of age)*The recommended dose is 0.10 g to 0.20 g of gel (about the size of a small hazelnut) to cover an area of about 1 cm^2 to 2 cm^2, corresponding to 5 to 10 mg of lidocaine. The maximum daily administration for a paediatric population should not exceed 4 mg/kg of lidocaine.

- *Elderly patients or patients with hepatic function disorders* When liver activity is reduced, the minimum effective anaesthetic dose should be used when applied before anaesthetic injection.

Method of administration

The medicinal product is for gingival use (local use) and can be occasionally used by oromucosal route.
Prior to use, the area of administration should be thoroughly dried.
Just before the procedure, a cotton bud should be impregnated with the medicinal product and applied on the mucosa.

Debilitated, elderly patients, acutely ill patients and children should be given reduced doses commensurate with their age and physical status (see section 4.4).

The total dose of all administered local anaesthetics should not exceed the lowest maximum recommended dose of each local anaesthetic (see sections 4.4 and 4.5).

4.3 Contraindications

Hypersensitivity to the active substances, lidocaine and cetrimide, or to any of the excipients listed in section 6.1.

Hypersensitivity to local anaesthetics of the amide type.

4.4 Special warnings and precautions for use

The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions and readiness for emergencies.

Although the passage of lidocaine into systemic circulation is expected to be negligible, Xylonor must be used with caution if there is an inflamed, infected or extremely traumatised mucosa in the area of application, since under such conditions there is potential for rapid systemic absorption of lidocaine.

Moreover, when Xylonor gel is used concomitantly with other products containing lidocaine such as injection of lidocaine adrenaline, the toxicity of local anaesthetics is additive.

Patients with defective glucose-6-phosphate dehydrogenase, hereditary or idiopathic methemoglobinemia may be at increased risk of developing methemoglobinemia when concurrently exposed to oxidizing agents (e.g. other local anaesthetic, nitric oxide, sulfonamides, sodium valproate, paracetamol.)

The availability of resuscitation equipment should be ensured before the onset of dental anaesthesia with local anaesthetics.

Precautions to be taken before and after handling or administering the medicinal product:

- Saliva aspiration is required alongside isolation with a cotton bud of the site to be treated with the local anaesthetic.
- The risk of biting trauma (lips, cheeks, tongue) does exist, but it is expected to be very low with the medicinal product due to the limited application area. When it is associated with injectable local anaesthetics, the patient should be told to avoid chewing gum or eating until sensation is restored.

The oropharyngeal use of topical anaesthetic agents may interfere with swallowing and thus enhance the danger of aspiration, particularly in children.

4.5 Interaction with other medicinal products and other forms of interaction

Lidocaine should be used with caution in patients receiving other local anaesthetics or antiarrhythmic drugs. Known interactions that usually occur with lidocaine (beta-blocking agents, inhibitors of CYP1A2, sedatives) are not expected to occur when the product is used locally on the oral mucosa. However, when the oral mucosa is injured, lidocaine may be released into the systemic circulation and lead to a risk of toxicity.

Additive interactions with other local anaesthetics:

Local anaesthetic toxicity is additive. This is not directly applicable in topical dental anaesthesia but may be a concern when associated with injectable anaesthetics in cases of unintended intravascular injection or rapid systemic resorption, especially in children.

The total dose of all administered local anaesthetics should not exceed the lowest maximum recommended dose of each local anaesthetic.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or a limited amount of data from the use of lidocaine and cetrimide in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

The product is applied locally on gingival tissues. No effects during pregnancy are anticipated, since the systemic exposure to lidocaine and cetrimide is negligible. The product can be used during pregnancy

Breastfeeding

The product is applied locally on gingival tissues. Lidocaine is excreted in human milk, but at therapeutic doses of the product, no effects on breastfed newborns/infants are anticipated. The transfer of cetrimide into human milk is expected to be negligible, no effects on breastfed newborns/infants are anticipated. The product can be used during breastfeeding.

Fertility

This drug is applied locally on gingival tissues. No effects on fertility are anticipated since the systemic exposure to lidocaine and cetrimide is negligible.

4.7 Effects on ability to drive and use machines

Xylonor has no or negligible influence on the ability to drive and use machines

4.8 Undesirable effects

a) Summary of the safety profile

The adverse reactions following the administration of lidocaine/cetrimide are similar to those observed with other amide local anaesthetics. These adverse reactions are mainly local application site reactions and hypersensitivity reactions.

Systemic adverse reactions are extremely rare with topical lidocaine. However, they may result from high plasma levels due to excessive dosage, or rapid absorption (see section 4.9) particularly when associated with injectable local anaesthetics. Such reactions may also result from hypersensitivity, idiosyncrasy, or diminished tolerance.

Drowsiness following the administration of lidocaine is usually an early sign of high lidocaine plasma levels and may occur as a consequence of rapid absorption.

Serious adverse reactions are generally systemic.

b) Tabulated list of adverse reactions

The reported adverse reactions come from spontaneous reporting and the literature.

The frequency classification follows the convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000) and "not known" (cannot be estimated from the available data).

MedDRA System Organ Class	***Frequency***	***Adverse Reactions***
Blood and lymphatic system disorders	Not known	Methemoglobinemia
Immune System disorders	Rare	Hypersensitivity including anaphylactic shock
Nervous System disorders	Not known	Local hypoesthesia
Respiratory, thoracic and mediastinal disorders	Not known	Bronchospasm
Gastrointestinal disorders	Not known	Gingival ulceration Oral mucosal exfoliation
Skin and subcutaneous tissue disorders	Not known	Angioedema Erythema Face oedema Rash Pruritus Urticaria
General disorders and administration site conditions	Not known	Application site oedema Application site burn

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

At normal doses and under normal conditions of administration, overdose is unlikely to occur with a product for local use only.

However, caution should be taken when using the product in association with injectable local anaesthetics, as the risk of CNS toxicity and cardiovascular toxicity may occur with high plasma levels of lidocaine due to excessive dosage, or rapid absorption. To date, no cases of overdose have been reported when the topical products were used alone.

Symptomatology:
The following reactions may occur with high plasma levels of lidocaine due to excessive dosage or rapid absorption, in particular when associated with the use of injectable local anaesthetics:

Central Nervous System (CNS):
High plasma levels may cause CNS stimulation (including seizures) followed by CNS depression (including respiratory arrest) and may be characterized by the following signs and symptoms of escalating severity: circumoral paresthesia, light-headedness, nervousness, anxiety, apprehension, euphoria, confusion, dizziness, drowsiness, hyperacusis, tinnitus, blurred vision, vomiting, nausea, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations (e.g., twitching, tremors, and convulsions) may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.

Cardiovascular System:
The cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, arrhythmia and cardiovascular collapse, which may lead to cardiac arrest. Hypertension, tachycardia and angina may be caused by concomitant use with an injectable local anaesthetic containing adrenaline.

Overdose can rarely lead to methemoglobinemia, the clinical signs are cyanosis of the nail beds and lips, fatigue and weakness.

Treatment of overdose:
The availability of resuscitation equipment should be ensured before the onset of dental anaesthesia with local anaesthetics.
If signs of acute toxicity are suspected, the medicinal product should be rinsed away immediately.
Oxygen should be administered rapidly, and assisted ventilation used if necessary. The patient's position should be changed to supine if necessary.

In cases of cardiac arrest, cardiopulmonary resuscitation should be immediately initiated.

In case of methemoglobinemia, if methemoglobinemia does not respond to administration of oxygen, administration of methylene blue intravenously 1-2 mg/kg body weight over a 5-minute period is recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Nervous System / Anaesthetics / Local anaesthetics / Amides / Lidocaine combinations, ATC code: N01BB52

The medicinal product is a combination of:

- Lidocaine: an amide local anaesthetic. When applied to the oral mucous membrane, it provides surface anaesthesia by controlling the painful stimulation occurring in or just beneath the mucosa. The local anaesthetic effect of lidocaine occurs via a reversible blockade of nerve fibre impulse propagation.
- Cetrimide: a quaternary ammonium disinfectant with antiseptic properties. This action occurs via protein denaturation, enzyme inactivation and damage of bacterial membranes

Xylonor combines both these ingredients in a non-irritant, water miscible excipient. This gel effects local topical anaesthesia. The onset of action is 2-5 minutes. The duration of anaesthesia is 10-20 minutes. This anaesthetic effect is complemented by a disinfecting action.

The intended use dosage is unlikely to cause systemic toxicity, as it falls well below the concentrations associated with systemic toxicity.

5.2 Pharmacokinetic properties

Lidocaine:
Absorption: the results from published studies performed in patients using various topical lidocaine-based preparations applied to healthy oral mucosa show that measured serum lidocaine levels remain well below the toxic range (< 5 µg/mL). Studies evaluating peak plasma levels of lidocaine using topical lidocaine patches (23 mg) or lidocaine sprays (200 mg) have determined the peak levels to be 0.016 µg/mL and 0.35 µg/mL, respectively.

Distribution: lidocaine is 60% to 80% bound to plasma protein, primarily to alpha-1-acid glycoprotein. Topical bioavailability averages 3%.

Biotransformation: lidocaine is principally metabolized in the liver by the cytochrome P450 system. Consequently, after a topical dose of lidocaine is applied to the oral mucosa, any swallowed fraction is significantly metabolized before entering into the systemic circulation. This accounts for the low plasma lidocaine concentrations following the intraoral administration of lidocaine.
Elimination: lidocaine and its metabolites are excreted by the kidneys, 90% as metabolites and 10% as unchanged drug. The elimination half-life of lidocaine following an intravenous bolus injection is typically of 100 minutes.

Cetrimide:
No pharmacokinetic information regarding cetrimide is available. As cetrimide is only to be used topically and at low concentrations, plasma concentrations are expected to be extremely low and therefore not clinically significant. Consequently, it can be extrapolated that systemic exposure to cetrimide is negligible.

5.3 Preclinical safety data

Effects in non-clinical general toxicity studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

The available repeat-dose toxicity data do not raise any safety concerns for lidocaine or cetrimide used as acute topical administrations in dentistry.

Lidocaine and cetrimide are not genotoxic.

Carcinogenicity studies have not been performed for lidocaine or cetrimide. Studies are not required due to short term administration in humans.

The available non-clinical data do not indicate direct or indirect harmful effects of parenteral administration of lidocaine with respect to reproductive toxicity or fertility.

Some teratogenic effects were reported at high oral dose of cetrimonium bromide, however there was no evidence of teratogenicity with the chloride salt of cetrimonium after dermal application at 2% in rabbits. At the low concentration used in the final product (0.15%), the systemic exposure associated with topical cetrimide is expected to be negligible, with no anticipated risk when used during pregnancy

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Saccharin (E954)
Spearmint flavour
Macrogols 300, 1500 and 4000

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25^{o}C.
Keep tube tightly closed.

6.5 Nature and contents of container

Aluminium tube internally coated with epoxy varnish, with a polyethylene screw cap. Contents: 15g.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Septodont
58 Rue Du Pont De Creteil
Saint-Maur-Des-Fosses
94100
France

8 MARKETING AUTHORISATION NUMBER

PA0196/014/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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