SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Xylonor Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1g of 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

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

- 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 Gel is indicated in adults, and in children 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

To be used only once from 0.1 to 0.5 g by topical local application with a cotton pellet.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 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.

Removal of excess saliva with cotton rolls or saliva ejector minimises dilution of the gel and permits maximum penetration

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

4.3 Contraindications

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

Hypersensitivity to any local anaesthetics of the amide type.

4.4 Special warnings and precautions for use

Special warnings

Although the passage of lidocaine into systemic circulation is expected to be negligible, the medicinal product must be used with caution when applied to an inflamed or infected area due to the risk of a rapid systemic absorption of lidocaine.

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.

4.5 Interaction with other medicinal products and other forms of interaction

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.

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

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

Breast-feeding

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 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 is negligible.

4.7 Effects on ability to drive and use machines

Xylonor gel 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***
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 the national reporting system:

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

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.

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Xylonor Gel 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 Gel 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 disinfectant 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

The data from pre-clinical studies show that products containing lidocaine or cetrimide are safe to be used in combination as a topical local anaesthetic agent before routine dental treatment in humans.

Systemic effects in non-clinical studies were observed only at exposures exceeding the maximum human exposure. Such exposures have therefore little relevance to clinical use. These systemic manifestations of lidocaine toxicity are expected to spontaneously resolve upon discontinuation of lidocaine and such adverse events are unlikely to happen with a single topical application of the medicinal product.

Cetrimide was associated with mild irritation upon dermal application for 48h in rabbits, but this is unlikely to happen with a single topical application of the medicinal product.

Regarding the genotoxicity, carcinogenicity, and reproductive toxicity, no cases have been reported in literature in neither animals nor humans. Considering the history of use of lidocaine and cetrimide, such toxicity is not expected.

No major toxicity is expected upon use of the medicinal product, at the recommended doses, in eligible patients.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Saccharin (E954)

Spearmint oil

Macrogol

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25ºC.

Store in a dry place.

Keep tube tightly closed.

6.5 Nature and contents of container

Aluminium tube with internal epoxy varnish and polyethylene screw cap containing 15 g of gel.

6.6 Special precautions for disposal

Always discard any unused portion taken from the tube. Tightly close after use.

7 MARKETING AUTHORISATION HOLDER

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