Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Xylocaine 2% w/v with Adrenaline (Epinephrine) 1:80,000 DENTAL Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains Lidocaine Hydrochloride equivalent to lidocaine hydrochloride anhydrous 20 mg (44 mg per 2.2 ml cartridge), and Adrenaline (Epinephrine) Tartrate equivalent to adrenaline (epinephrine) 12.5 micrograms (27.5 micrograms per 2.2 ml cartridge).

Excipients - contains sodium metabisulphite (E223).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
A clear colourless sterile aqueous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Xylocaine 2% with Adrenaline (Epinephrine) 1:80,000 DENTAL is a local anaesthetic solution for use in dental infiltration anaesthesia and all dental nerve block techniques.

4.2 Posology and method of administration

Route: Infiltration by injection

Posology

Xylocaine 2% with Adrenaline (Epinephrine) 1:80,000 DENTAL has a rapid onset of action after infiltration, with an average of 2-3 minutes. Mandibular block requires 5 minutes or more to take full effect. The duration of effective anaesthesia varies in individuals and depends on the type of anaesthetic technique. The average duration of useful anaesthesia after infiltration is 60 minutes. After successful regional anaesthesia, e.g. mandibular block, anaesthesia lasts for 2 hours or longer.

The lowest dosage that results in effective anaesthesia should be used. The dosage will also depend on the area of the oral cavity to be anaesthetised, the vascularity of oral tissue and the technique of anaesthesia. The total dose must be adjusted to the age, size and physical status of the patient.

A combination of high pressure induced by the use of a dental cartridge system and a rapid rate of injection may lead to complications *(see section4.9)* even after the injection of small amounts of local anaesthetic due to the high concentration, especially following accidental injection, when the injection drug could travel in a retrograde manner along the vessel and, in cases of intra-arterial injection in the head and neck area, reach the brain without the same degree of dilution that occurs with an intravenous injection.

It must be noted that adrenaline (epinephrine), when added to local anaesthetic solution is less active as a localising agent in the highly vascular oral environment than elsewhere in the body.

Adults and children above 12 years of age

For effective local anaesthesia in most dental procedures, an adequate dose of Xylocaine 2% with Adrenaline (Epinephrine) 1:80,000 DENTAL solution should be injected by infiltration into the oral tissue at the following doses. More complicated dental procedures may require doses towards the higher end of the range given below:

1-5 ml (= 20-100 mg lidocaine hydrochloride)

The maximum single dose of Xylocaine when given with adrenaline is 500 mg as a total.

Special populations

Older people
Consider dose adjustment in older and frail patients.

Patients with renal impairment
Lidocaine and its metabolites are excreted in urine. Elimination, especially of metabolites, may be reduced in patients with renal impairment. Dose adjustment should be considered in patients with severe renal impairment.

Patients with hepatic impairment
Dose adjustment should be considered in patients with advanced liver disease, in whom the metabolism and clearance of lidocaine may be decreased.

Paediatric population

The quantity injected must be determined based on the age and weight of the child and the extent of the procedure. The dose may be calculated as 1.33 mg of lidocaine per kilogram of body weight in children under 10 years of age.

In children under 10 years of age, an adequate dose per treatment session should be:
1-2 ml (= 20-40 mg lidocaine hydrochloride)

Particular caution should be exercised in children under 4 years of age.

In adolescents (12-18 years of age), the recommended doses are same as for the adults.

Method of administration
Xylocaine with adrenaline should be injected slowly to avoid intravascular injection. Rapid injection, even of small amounts, especially if intravascular, may lead to complications (see section 4.9).
After opening the cartridge, the solution must be used at once.

4.3 Contraindications

Hypersensitivity to lidocaine or other amide type local anaesthetic agents or to any of the excipients listed in section 6.1.

Hypersensitivity to sulphite (see section 4.4) especially in steroid dependent asthma patients who may develop bronchospasm and anaphylactic shock.

Xylocaine with adrenaline should not be given intravenously.

4.4 Special warnings and precautions for use

Before administration of a local anaesthetic drug, make sure that resuscitative equipment, such as equipment required for oxygenation and assisted ventilation, and drugs for the treatment of toxic reactions are immediately available.

The patients should be advised to exert caution to avoid inadvertent trauma to the lips, tongue, cheek mucosa or soft palate when these structures are anaesthetized. The ingestion of food should therefore be postponed until normal function and sensation returns.

Incommon
withotherlocalanaesthetics,Xylocainewithadrenalineshouldbeusedcautiouslyinpatientswithepilepsy,impairedcardiacconduction, impairedrespiratoryfunction,andinpatientswithimpairedrenal and hepaticfunction especially ifthedoseorsiteofadministrationislikelytoresultinhighbloodlevels.

In the head and neck area the intravascular injection of even small doses of local anaesthetics may cause systemic adverse reactions similar to those seen after the inadvertent intravascular injection of larger doses in other areas.

The incidence of neurological adverse reactions associated with local anaesthetics is very low.

Even if the dose of Xylocaine 2% with Adrenaline (Epinephrine) 1:80,000 DENTAL in dental practice is generally small, some patients may require special attention to reduce the risk of dangerous side effects:

-Xylocaine with adrenaline should be used with caution in patients with cardiovascular disease and conditions where lidocaine may depress cardiovascular function or in patients in whom adrenaline may cause adverse haemodynamic effects e.g. those with angina pectoris.

-Patients treated with class III anti-arrhythmic drugs (e.g. amiodarone) should be under close surveillance (see section 4.5).

-The clearance of lidocaine and its metabolites may be reduced in patients with severe hepatic or renal impairment. Accumulation is not anticipated following a single dose.

-The elderly and patients with epilepsy or those in poor general condition (see section 4.2).

Xylocaine with adrenaline should be used with caution in patients taking tricyclic antidepressants, phenothiazines, butyrophenones, and non-selective β-blockers, which can interact with adrenaline to cause severe hypertension and potentially cause stroke or myocardial infarction (see section 4).
Acidosis or hypoxia can increase the risk of CNS and cardiovascular toxicity (see section 4.9).

Use of Xylocaine with adrenaline in hyperthyroid states may cause additive effects (tachycardia, arrhythmia, increased cardiac output and cardiac ischemia).

Local anaesthetic containingadrenaline (such as Xylocaine 2% w/v with Adrenaline)shouldbeusedwherepossible as adrenaline has been shown to cause local vasoconstriction and as a resulttoprolonganaesthesiaandreducesystemicabsorption of the anaesthetics. Thisisparticularlyimportantinhighlyvascularareas such as oral and dental tissues.

Local anaesthetics, especially those containing adrenaline (epinephrine), should be administered with caution to patients with severe or untreated hypertension, severe heart disease, uncontrolled diabetes, hyperthyroidism, severe anaemia or circulatory failure from whatever cause or any other pathological condition that might be aggravated by the effects of adrenaline (epinephrine). Local anaesthetics should be avoided when there is inflammation in the region of the proposed injection.

The possibility of hypersensitivity to other amide type local anaesthetics or sulphite should be considered (see section 4.3). Such reactions include oedema and chills. More severe manifestations include anaphylactic shock, dyspnoea, and circulatory collapse.

Rash, erythema and arthralgia may occur. Allergic reactions to sodium metabisulfite are rare and more common in patients with steroid-dependent asthma (see section 4.3).

4.5 Interaction with other medicinal products and other forms of interactions

Pharmacodynamic Interactions
Lidocaine should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics e.g. certain anti-arrhythmics such as mexiletine because of additive systemic effects, and in patients treated with class III anti-arrhythmic drugs (e.g. amiodarone) (see section 4.4).

Solutions containing adrenaline (epinephrine) should generally be avoided or used with care in patients receiving monoamine oxidase inhibitors or tricyclic antidepressants since severe, prolonged hypertension may result. In addition, the concurrent use of adrenaline (epinephrine)-containing solutions and oxytocic drugs of the ergot type may cause severe, persistent hypertension and possibly cerebrovascular and cardiac accidents. Phenothiazines and butyrophenones may reduce or reverse the pressor effect of adrenaline (epinephrine).

Serious cardiac arrhythmias may occur if preparations containing a vasoconstrictor, such as adrenaline (epinephrine), are employed during or following the administration of volatile inhalation anaesthetics, such as halothane.

Non-cardioselective betablockers such as propanolol enhance the pressor effects of adrenaline, which may lead to severe hypertension and bradycardia.

Pharmacokinetic Interactions
Lidocaine is metabolized by cytochrome P450 isoenzymes CYP3A4 and CYP1A2 (see section 5.2) and has the potential to interact with other drugs metabolized by these isoenzymes.

4.6 Fertility, pregnancy and lactation

Pregnancy
Reproductive toxicity has not been identified in animal studies (see section 5.3).

Lidocaine crosses the placenta. Foetal concentrations are lower than maternal, but the foetal half-life may be longer and it is possible that foetal depression could occur following overdose.

The addition of adrenaline may potentially decrease uterine blood flow and contractility, especially after inadvertent injection into maternal blood vessels.

Althoughthereisnoevidencefromanimalstudiesofharmtothefoetus,aswithalldrugs,lidocaineshouldnotbegiveninearlypregnancyunlessthebenefitsareconsideredtooutweighttherisks.

Breast-feeding
Lidocaine is excreted in human milk; no effects on the breastfed infant are anticipated at therapeutic doses of Xylocaine with adrenaline.

It is not known whether adrenaline is excreted in human milk or not; however it is unlikely to affect the breast-fed child.

Fertility
There are no animal or human data on potential adverse effects of lidocaine or adrenaline on fertility.

4.7 Effects on ability to drive and use machines

Besides the direct anaesthetic effect, local anaesthetics have a very mild effect on mental functions and coordination, even in the absence of overt CNS toxicity and can therefore temporarily impair locomotion and alertness.

Therefore, driving is not advised if the patient experiences certain CNS side effects such as dizziness, blurred vision, convulsion etc. (see section 4.8).

Therapeutic doses of Xylocaine with adrenaline are not expected to have significant effect on the ability to drive and use machines.

4.8 Undesirable effects

There are no controlled trials assessing the nature or frequency of undesirable effects attributable to Xylocaine with adrenaline. The undesirable effects listed below are based on post-marketing experience and published data. The frequency of these undesirable effects cannot be estimated from available data.

Immune system disorders: Anaphylactic reaction, Hypersensitivity (see section 4.4)

Psychiatric disorders: Anxiety, Disorientation, Restlessness

Nervous system disorders: Nervousness, Tinnitus, Blurred vision, Convulsion, Dizziness, Dysgeusia, Headache, Unconsciousness

Eye disorders: Eye pain, Lacrimal disorder, Visual impairment

Ear and labyrinth disorders: Vertigo

Cardiac disorders: Palpitations, Tachycardia, Cardiac arrest, Bradycardia, Hypotension, Myocardial depression

Respiratory, thoracic and mediastinal disorders: Dyspnoea, Respiratory arrest

Gastrointestinal disorders: Nausea, Vomiting

Skin and subcutaneous tissue disorders: Erythema, Rash macular

Musculoskeletal and connective tissue disorders: Arthralgia, Muscle spasms

General disorders and administration site conditions: Face oedema, Chills, Injection site pain, Injection site ulcer, Injection site necrosis, Paresthesia (sensation of tingling, tickling, pricking, or burning of skin) and numbness of tongue or around the mouth at the injection site.

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, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms and Signs
Lidocaine can cause acute toxic effects if high systemic concentrations occur due to unintentional intravascular injection, excessively rapid absorption, or overdose. Intravascular injection of local anaesthetics may cause immediate (seconds to a few minutes) systemic toxic reactions. In overdosage, systemic toxicity appears later (15–60 minutes after injection) due to the slower increase in blood concentration.

Systemic toxic reactions primarily involve the CNS and the cardiovascular system. CNS reactions are similar for all amide local anaesthetics, while cardiac reactions are quantitatively and qualitatively more dependent on the drug. Signs of CNS toxicity generally precede cardiovascular effects, unless the patient is receiving a general anaesthetic or is heavily sedated with drugs such as benzodiazepines or barbiturates.

CNS toxicity is a graded response with symptoms and signs of escalating severity. Initial symptoms are usually circumoral paraesthesia, numbness of the tongue, light-headedness, hyperacusis, tinnitus and visual disturbances. Dysarthria, muscular twitching or tremors are more serious and precede the onset of generalized convulsions. Unconsciousness and grand mal

convulsions may follow and may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly following convulsions due to increased muscular activity and interference with respiration. In severe cases, apnoea may occur. Acidosis, hyperkalaemia, hypocalcaemia and hypoxia increase and extend the toxic effects of local anaesthetics.

Recovery is due to redistribution of the drug from the CNS with subsequent metabolism and excretion. Recovery may be rapid unless large amounts have been injected.

Cardiovascular toxicity may occur in severe cases and is generally preceded by signs of CNS toxicity; however, prodromal CNS symptoms may be absent in patients under heavy sedation or general anaesthesia. Hypotension, bradycardia, arrhythmia and cardiac arrest may occur as a result of high systemic lidocaine concentrations; in rare cases, cardiac arrest has occurred without prodromal CNS effects.

Adrenaline excess can cause vasoconstriction, increased cardiac output, hypertension, and arrhythmia.

In children, early signs of toxicity may be difficult to detect if the block is given during general anaesthesia.

Management

If signs of acute systemic toxicity appear, the injection should be stopped immediately. CNS symptoms (convulsion, CNS depression) must be treated with appropriate respiratory support and anticonvulsant drugs.

If circulatory arrest occurs, immediate cardiopulmonary resuscitation should be instituted, with ventilation and circulatory support and treatment of acidosis.

Cardiovascular depression (hypotension, bradycardia) should be treated appropriately with intravenous fluids, vasopressor, chronotropic and/or inotropic agents.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:Anaesthetics, local, amides,ATC code:N01BB02

Mechanism of action

Like other local anaesthetics, lidocaine causes a reversible blockade of the impulse propogation along nerve fibers by preventing the inward movement of sodium ions through the nerve membrane. Local anaesthetics of the amide type are thought to act within the sodium channels of the nerve membrane.

Local anaesthetics can have a similar effect on excitable membranes in the brain and myocardium. If excessive amounts of drug reach the systemic circulation rapidly, symptoms and signs of toxicity will appear, emanating mainly from the central nervous and cardiovascular systems.

Central nervous system toxicity occurs at a lower plasma concentrations (see section 4.8), and usually precedes the cardiovascular effects. All local anaesthetics stimulate the CNS and may produce anxiety, restlessness and tremors. At high doses lidocaine has a quinidine like action on the myocardium i.e. cardiac depressant. Direct effects of local anaesthetics on the heart include slow conduction, negative inotropism, and eventually cardiac arrest.

5.2 Pharmacokinetic properties

Absorption
Lidocaineisreadilyabsorbedfromthegastro-intestinaltract,frommucousmembranesandthroughdamagedskin.Itisrapidlyabsorbed frominjectionsitesincludingmuscle.

Absorption is considerably slowed by the addition of adrenaline (epinephrine), although it also depends on the site of injection. Peak plasma concentrations are reduced by 50% following subcutaneous injection, by 30% following epidural injection and by 20% following intercostal block if adrenaline (epinephrine) 5 µg/ml is added.

Biotransformation
Lidocaineundergoesfirstpassmetabolismintheliver.

Elimination
Eliminationhalf-lifeis2hours.Lessthan10%ofadoseisexcretedunchangedviathekidneys.

5.3 Preclinical safety data

Genotoxicity tests with lidocaine showed no evidence of mutagenic potential. A metabolite of lidocaine, 2,6-dimethylaniline, which has carcinogenic potential in preclinical toxicological studies with chronic exposure, showed weak evidence of activity in some genotoxicity tests. Risk assessment comparing the calculated maximum human exposure from intermittent use of lidocaine with animal exposure indicates a wide margin of safety for clinical use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium metabisulfite (E223)
Sodium hydroxide
Hydrochloric acid
Water for injections

6.2 Incompatibilities

Additions to Xylocaine with adrenaline solution for injection are not recommended. Similarly, Xylocaine with adrenaline should not be mixed with other drug products.

6.3 Shelf life

18 months.
For single use only. Discard any unused contents after first use.

6.4 Special precautions for storage

Storebelow25°C. Do not freeze. Keep the container in the outer carton in order to protect from light.

6.5 Nature and contents of container

Glassstandarddentalcartridges2.2 m1,inboxesof 50 or 100.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Adequate precautions should be taken to avoid prolonged contact between local anaesthetic solutions containing adrenaline (low pH) and metal surfaces (e.g. needles or metal parts of syringes), since dissolved metal ions, particularly copper ions, may cause severe local irritation (swelling, oedema) at the site of injection and accelerate the degradation of adrenaline.

The solution must be used immediately after opening the cartridge.

The dental cartridge should be disinfected by wiping with a pledget moistened with disinfectant. The cartridge should not be immersed in disinfectant solution.

Xylocaine with adrenaline cartridges should not be autoclaved.

7 MARKETING AUTHORISATION HOLDER

DENTSPLY DeTrey GmbH
De-Trey-Strasse 1
78467 Konstanz
Germany

8 MARKETING AUTHORISATION NUMBER

PA1045/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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