3M ESPE

Prescription Medicine

Xylestesin™-A

Solution for injection
(local anesthetic for dentistry)
INFORMATION FOR USE

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Germany

44000736262/05

1. NAME OF THE MEDICINAL PRODUCT

Xylestesin-A
20 mg/mL + 12.5 micrograms/mL
Solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

	1 mL solution for injection contains	1.7 mL solution for injection contains
Lidocaine hydrochloride	20 mg	34 mg
Epinephrine (adrenaline) as Epinephrine (Adrenaline) hydrochloride	12.5 micrograms	21.25 micrograms
Excipients with known effect		
Sodium sulphite (E221)	0.6 mg	1.02 mg
Sodium*	1.71 mg	2.91 mg

* Sodium content of sodium sulphite and sodium chloride

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection

The solution is a clear, not opalescent, colourless liquid with a pH value of 3.6 to 4.4.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Local anaesthesia (infiltration and nerve-block anaesthesia) in dentistry.

Xylestesin-A is indicated in adults, children and adolescents.

4.2 Posology and method of administration

Xylestesin-A is exclusively recommended for use in dentistry.

Posology

The smallest possible volume of solution which will lead to an effective anaesthesia should be used.

Adults:

The dosage should be individually determined from case to case depending on the method used and special characteristics of the particular case.

In oral infiltration and/or mandibular block, initial dosages of 1.0–4.0 mL are usually sufficient.

Special populations:

Elderly population: Increased plasma levels of Xylestesin-A can occur in older patients due to diminished metabolic processes and reduced distribution volume. The risk of accumulation of Xylestesin-A is increased after repeated administration in particular.

Dosages should be reduced from adult recommendations, taking into consideration any cardiac or liver disease (see section 4.4).

Patients with hepatic impairment: Lidocaine is metabolized by the liver. Lower doses of lidocaine may be required in patients with hepatic dysfunction due to prolonged effects and systemic accumulation (see section 4.4).

Patients with renal impairment: Lidocaine and its metabolites are mainly eliminated in urine. Lower doses of lidocaine may be required in patients with severe renal dysfunction due to prolonged effects and systemic accumulation (see section 4.4)

Other relevant special populations: The dose has to be likewise reduced in patients with certain pre-existing diseases (angina pectoris, arteriosclerosis, see section 4.3 and 4.4) and patients taking contemporary medications known to interact with lidocaine and/or adrenaline see section 4.4 and 4.5).

Dose recommendation for special populations: A lower dosage range is thus recommended in all such cases (i.e. minimum volume of Xylestesin-A for sufficient anaesthetic effect).

Paediatric population:

Xylestesin-A is indicated in adults, children and adolescents. Special care has to be exercised when treating children below 4 years. The quantity to be injected should be determined by the age and weight of the child and the magnitude of the operation. The anaesthesia technique should be selected carefully. Painful anaesthesia techniques should be avoided. The behaviour of the child during treatment has to be monitored carefully. The average dose to be used is in the range of 20 mg to 30 mg lidocaine hydrochloride per session. The dose in mg of lidocaine hydrochloride which can be administered in children may alternatively be calculated from the expression: child's weight (in kilograms) x 1.33.

Dose recommendation for children and adolescents of 13 – 18 years:

Body weight (kg)	**Recommended dosage**	
	lidocaine hydrochloride/ mg/child	solution for injection mL/child
20 – <30	5 – 20 mg	0.25 mL – 1 mL
30 – <40	10 – 40 mg	0.5 mL – 2 mL
40 – <50		
50 – <60	10 – 60 mg	0.5 mL – 3 mL
60 – <70	20 – 80 mg	1 mL – 4 mL
70 – <80		

Due to the fact that lidocaine diffuses rapidly into tissues and the density of bones is lower in children compared to adults, infiltration anaesthesia instead of conduction anaesthesia can be preferred in paediatric population.

Maximum Recommended Dosage:

Adults:

For healthy adults, the maximum dose of the active ingredient lidocaine hydrochloride with vasoconstrictor admixture is 7 mg/kg body weight.

Example: The maximum dose for a 70 kg patient is 500 mg. However, due to the addition of adrenaline 1:80,000, the maximum administered quantity of 16 mL solution for injection or 9 cartridges (equivalent to 0.2 mg adrenaline, maximum dose) must not be exceeded.

Children:

The quantity to be injected should be determined by the age and weight of the child and the magnitude of the operation. Do not exceed the equivalent of 5 mg lidocaine hydrochloride/kg BW or 0.250 mL Xylestesin-A/kg BW.

Maximum recommended dosage of Xylestesin-A in children and adolescents of 13 – 18 years:

Body weight (kg) (Corresponding paediatric age groups according to ± limits of growth tables)	**Maximum** allowed dose based on 5 mg/kg BW	
	Lidocaine hydrochloride mg/child	solution for injection mL/child
20 – <30	100	5
30 – <40	150	7.5
40 – <50	200	10.0
50 – <60	250	12.5
60 – <70	300	15.0
70 – <80	350	16.0

Method of administration

Dental use

To avoid intravascular injection, aspiration control at least in two planes (rotation of the needle by 180°) must always be carefully undertaken, although a negative aspiration result does not safely rule out an unintentional and unnoticed intravascular injection.

The injection rate should not exceed 0.5 mL in 15 seconds, i.e. 1 cartridge per minute.

Major systemic reactions as a result of accidental intravascular injection can be avoided in most cases by an injection technique – after aspiration slow injection of 0.1 – 0.2 mL and slow application of the rest – not earlier than 20 – 30 seconds later.

Opened cartridges must not be used in other patients. Residues must be discarded (see section 6.6).

4.3 Contraindications

Xylestesin-A must not be used in the event of

- hypersensitivity to the active substances, sodium sulphite (E221) or to any of the excipients listed in section 6.1.

Due to the active substance lidocaine, Xylestesin-A must not be used in the event of

- known allergy or hypersensitivity to local anaesthetics of the amide type,
- severe, uncontrolled or untreated excitation and conduction disorders of the heart (e.g. grade II and III AV block, pronounced bradycardia),
- acutely decompensated heart failure,
- severe hypotension

Due to the content of adrenaline as a vasoconstrictor admixture, Xylestesin-A must not be used in the event of

- Heart diseases such as:
  - unstable angina pectoris,
  - recent myocardial infarction,
  - recent coronary artery bypass surgery,
  - refractory arrhythmias and paroxysmal tachycardia or high-frequency, continuous arrhythmia,
  - untreated or uncontrolled severe hypertension,
  - untreated or uncontrolled congestive heart failure,
- concomitant treatment with monoamine oxidase (MAO) inhibitors or tricyclic antidepressants (see section 4.5).
- Xylestesin-A is not allowed to be used in acra of extremities.

Due to the content of sulphite as excipient, Xylestesin-A must not be used in the event of

- allergy or hypersensitivity to sulphite,
- severe bronchial asthma.

Xylestesin-A can provoke acute allergic reactions with anaphylactic symptoms (e.g. bronchospasm).

4.4 Special warnings and precautions for use

Special warnings

Xylestesin-A must be used with particular caution in the event of

- severe impairment to the renal and hepatic function,
- angina pectoris (see section 4.2 and 4.3),
- arteriosclerosis,
- considerably impaired blood coagulation or concomitant treatment with anticoagulants or platelet aggregation inhibitors (e.g. heparin or acetylsalicylic acid). The overall risk of bleeding is increased.
- haemorrhagic diatheses – increased bleeding risk particularly with nerve-block anaesthesia,
- uncontrolled or untreated hyperthyroidism,
- narrow-angle glaucoma,
- diabetes mellitus,
- lung diseases – particularly allergic asthma bronchiale,
- pheochromocytoma,
- methemoglobinemia,
- impaired cardiovascular function due to decreased ability to compensate prolonged A-V conduction,
- epilepsy (Avoid high doses!),
- blood screening tests on athletes as Xylestesin-A may show up positive results. Lidocaine is not listed in the current WADA list. The listed adrenaline can be used in local anaesthetics.

This medicinal product contains less than 1 mmol (23 mg) sodium per 1.7 mL, i.e. essentially "sodium free".

E221 sodium sulphite: May rarely cause severe hypersensitivity reactions and bronchospasm.

Precautions for use:

- Information to the patients: The patient should be advised to exert caution to avoid inadvertent trauma to the lips, tongue, cheek mucosae or soft palate when these structures are anaesthetized. The ingestion of food should therefore be postponed until normal function returns.
- The lower blood flow in the pulp tissue due to the content of adrenaline and thus the risk to overlook an opened pulp has to be taken into account regarding cavity or crown preparations.
- Injection into an inflamed area should be avoided due to reduced penetration of lidocaine into an inflamed tissue.
- Dental practitioners who employ local anaesthetic agents should be well versed in diagnosis and management of emergencies which may arise from their uses.
- Inadvertent intravascular application must be avoided (see section 4.2). Accidental intravascular injection or accidental overdose may be associated with convulsions, followed by central nervous system depression or cardiorespiratory arrest (see section 4.9).
- Each time a local anaesthetic is used the following medicinal products/ therapy as well as an indwelling venous cannula set should be available:
  - Anti-convulsant medicines (benzodiazepines e.g. diazepam), myorelaxants, glucocorticoids, atropine and vasopressors or adrenaline as well as an electrolyte solution for a severe allergic or anaphylactic reaction.
  - Resuscitating equipment (in particular a source of oxygen) enabling artificial ventilation if necessary.
- Careful and constant monitoring of cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness should be performed after each local anaesthetic injection. Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression, or drowsiness may be early warning signs of central nervous system toxicity (see section 4.9).

4.5 Interaction with other medicinal products and other forms of interaction

Interactions affecting the use of this medicinal product:

- Contraindications of concomitant use:

  Patients taking MAO inhibitors or tricyclic antidepressants

  The sympathomimetic effect of adrenaline can be intensified by the simultaneous intake of MAO inhibitors or tricyclic antidepressants (see also section 4.3).

- Concomitant use is not recommended:

  Patients taking phenothiazines and butyrophenones

  Phenothiazines and butyrophenones may reduce or reverse the pressor effect of adrenaline.

  Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

  Patients taking non-selective beta-blockers

  The concomitant administration of non-cardioselective β-blockers can lead to an increase in blood pressure due to the adrenaline in Xylestesin-A.

  Inhalational anaesthestics

  Certain inhalational anaesthetics, such as halothane, can sensitise the heart to catecholamines and therefore induce arrhythmias following administration of Xylestesin-A.

  The use of Xylestesin-A during or following treatment with general anaesthesia should be avoided, if possible.

  Patient taking vasopressor and ergot-type oxytocic medicines

  Lidocaine hydrochloride with adrenaline 1:80,000 or other vasopressors should not be used concomitantly with ergot-type oxytocic medicines, because a severe persistent hypertension may occur.

- Precaution including dose adjustment

  Local anaesthetics

  Caution is advised if lidocaine with adrenaline is used concurrently with other local anaesthetics. The toxic effects of local anaesthetics are additive. A major cause of adverse reactions appears to be excessive plasma concentrations, which may be due to accidental intravasal administration, slow metabolic degradation or overdosing.

Interactions resulting in clinically relevant changes on the use of other medicinal products:

- Concomitant use is not recommended:

  Patients taking oral antidiabetics

  Adrenaline can inhibit insulin release in the pancreas and thus diminish the effect of oral antidiabetics.

Paediatric population

No significant differences can be expected regarding medicine interactions between adult and paediatric population.

4.6 Fertility, pregnancy and lactation

Pregnancy

For Xylestesin-A no clinical data on exposed pregnancies are available. Lidocaine animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). Animal studies carried out with adrenaline have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown.

Caution should be exercised when administering to pregnant women. Xylestesin-A should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breast-feeding

Lidocaine is excreted in breast milk with a milk: plasma ratio of 0.4. No information is available on the use of adrenaline during breast feeding.

A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Xylestesin-A should be made taking into account the benefit of breast-feeding to the child and the benefit of Xylestesin-A therapy to the women. Therefore, nursing mothers should milk and discard the first mother's milk following anaesthesia with lidocaine.

Fertility

In animal studies no effects on fertility were seen (see section 5.3).

4.7 Effects on the ability to drive and use machines

Although test patients have shown no impairment of their normal reactions when driving a vehicle, the dentist has to assess in each case the possible impairment of safety when operating a motor vehicle or machinery. The patient should not leave the dental office earlier than 30 minutes after the injection.

4.8 Undesirable effects

a) Summary of the safety profile:

In general, the therapeutic use of Xylestesin-A can be regarded as very safe. The causality assessment in case of adverse events is difficult, because either the underlying dental disease or the dental procedure or the local anaesthetic may be the reason of an adverse event, and an explicit differentiation is not possible. The description of the safety profile of Xylestesin-A is based on data identified in published clinical studies and on the postmarketing surveillance data of the manufacturer.

In clinical studies, the most frequently observed adverse events were hypoaesthesia oral (74%), followed by medicine ineffective (8.5%) as well as pain, procedural pain, toothache (0.25–1.26%). Nerve disturbances were in clinical studies with exception of hypoaesthesia oral not observed, which may be explained by the low patient number. Postmarketing surveillance data confirm the pattern described in published clinical studies in general, but indicated a lower overall incidence of adverse events. However it has to be considered that spontaneous reporting systems did not allow incidence calculation.

The overall risk of nerve disturbances (e.g. hypoaesthesia, paraesthesia, taste disorders) is low according to the postmarketing experience. In the case of suspected hypersensitivity reactions, allergy testing is recommended including testing of the single components of the medicinal product.

b) Tabulated summary of adverse reactions:

The tabulated summary is based on data from published controlled clinical studies (N = 1,990 patients) and completed by postmarketing data (5-years-interval):

Very common (>1/10)
Common (≥ 1/100, <1/10)
Uncommon (≥ 1/1'000, <1/100)
Rare (≥ 1/10'000, <1/1'000)
Very rare (<1/10'000)
Not known (frequency cannot be estimated from the available data)

System organ class	
Infections and infestations	*Uncommon* Oral herpes
Immune system disorders	*Not known** anaphylactic reaction, anaphylactic shock, type I hypersensitivity
Psychiatric disorders	*Not known** confusional state
Nervous system disorders	*Uncommon* dizziness
	Rare headache, somnolence
	*Not known** facial palsy, paresis, syncope, dysarthria
Eye disorders	*Not known** accommodation disorder, blindness, diplopia, eye swelling, vision blurred, eyelid ptosis, mydriasis, ophthalmoplegia
Cardiac disorders	*Rare* palpitations
Vascular disorders	*Rare* haematoma
	*Not known** pallor
Respiratory, thoracic and mediastinal disorder	*Not known** bronchospasm, laryngeal oedema, respiratory failure, throat tightness, wheezing, dyspnoea, cough
Gastrointestinal disorders	*Very common* hypoaesthesia oral
	Uncommon toothache, nausea
	*Not known** tongue oedema, vomiting
Skin and subcutaneous tissue disorders	*Rare* haemorrhage subcutaneous
	*Not known** dermatitis bullous, dermatitis contact, hypoaesthesia facial, pruritus, rash, swelling face
General disorders and administration site conditions	*Common* drug ineffective, pain
	Uncommon injection site swelling, injection site haematoma
System organ class	
Investigations	*Not known** allergy test positive, heart rate increased, heart rate irregular
Injury, poisoning and procedural complications	*Uncommon* procedural pain, mouth injury

* data from postmarketing surveillance representing 5 years of observation

c) Description of selected adverse events:

Two types of adverse events are of special clinical interest, but not the most frequently reported adverse events. The presentation is based mainly on postmarketing surveillance data.

Nerve disturbances

Nerve disturbances in dentistry may have different reasons, caused by underlying dental disease, by dental procedure, but also by direct adverse events of dental local anaesthetics. With an observation frequency of one event per 10 millions of sold carpules the risk of such disturbances is low. In the data compilation given above the most frequently reported nerve disturbance in clinical studies was oral hypoaesthesia (mainly lip numbness). It should be taken into account that the high number of oral hypoaesthesia reported in clinical studies may reflect only an individually increased duration of action of Xylestesin-A. During postmarketing surveillance, cases of facial palsy, hypoaesthesia facial and different adverse eye events (e.g. diplopia, accommodation disturbances) were identified indicating possibly anaesthesia related nerve disturbances. All of these adverse events were reversible.

Hypersensitivity reactions

Hypersensitivity reactions were only rarely identified in the postmarketing surveillance (6.41 events per 10 millions sold carpules). Mostly the reactions were non-serious (4.56/10 millions sold carpules), but life-threatening reactions cannot be fully excluded. The reactions included anaphylactic reactions/shock, skin reactions and respiratory symptoms.

In the case of suspected hypersensitivity reaction, allergy testing is recommended including testing of the single components of the medicinal product.

d) Paediatric population

The observation during postmarketing surveillance does not reveal differences in the safety profile in children compared with those in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions is an important way to gather more information to continuously monitor the benefit/risk balance of the medicinal product. Any suspected adverse reactions should be reported via your local 3M contact or to pharmacovigilance@mmm.com (Germany).

4.9 Overdose

Acute emergencies from local anaesthetics are generally related to high plasma levels encountered during therapeutic use or unintended and fast intravasal administration of local anaesthetics. Symptoms of overdose may appear either immediately, caused by accidental intravascular injection or abnormal absorption conditions, e.g. in inflamed or intensive vascularised tissue, or later, caused by true overdose following an injection of excessive quantity of anaesthetic solution, and manifest themselves as central nervous and/or vascular symptoms.

Symptoms probably caused by lidocaine:

Cardiovascular symptoms (SOC Cardiac disorders, Vascular disorders, Investigations): blood pressure decreased, bradycardia, cardiac arrest, conduction disorder.

Central nervous symptoms (SOC Psychiatric disorders, Nervous system disorders, Ear and labyrinth disorders, Gastrointestinal disorders, Musculoskeletal and connective tissue disorders, Investigations): anxiety, coma, confusional state, dizziness, dysgeusia, grand mal convulsion, muscle twitching, nausea, respiratory paralysis, respiratory rate increased, restlessness, somnolence, tinnitus, tremor, vomiting.

The most dangerous symptoms regarding the outcome of such an event are: blood pressure decreased, cardiac arrest, conduction disorder, grand mal convulsion, respiratory paralysis, and somnolence/coma.

Symptoms probably caused by epinephrine (adrenaline):

Pressure symptoms (SOC Vascular disorders, Investigations): blood pressure systolic increased, blood pressure diastolic increased, venous pressure increased, pulmonary arterial pressure increased, hypotension.

Cardiac symptoms (SOC Cardiac disorders): bradycardia, tachycardia, arrhythmia (e.g. atrial tachycardia, atrioventricular block, ventricular tachycardia, premature ventricular contractions).

These symptoms can result in life threatening situations as well as pulmonary oedema, cardiac arrest, kidney failure, and metabolic acidosis.

Therapy

If symptoms of overdose arise the application of the local anaesthetic has to be stopped.

General basic measures:

Diagnostics (respiration, circulation, consciousness), resuscitation and/or maintenance of the vital functions (respiration and circulation), administration of oxygen, intravenous access.

Special measures:

Hypertension:	Elevation of the upper body, if necessary sublingual nifedipine.
Convulsions:	Protect patients from concomitant injuries, if necessary benzodiazepines (e.g. diazepam iv).
Hypotension:	Horizontal position, if necessary intravascular infusion of a whole electrolyte solution, vasopressors (e.g. etilefrine iv).
Bradycardia:	Atropine iv.
Anaphylactic shock:	Contact emergency physician, in the meantime shock positioning, generous infusion of a whole electrolyte solution, if necessary epinephrine iv, cortisone iv.
Cardiovascular arrest:	Immediate cardiopulmonary resuscitation, contact emergency physician.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anaesthetics, local, ATC code N01B B52

Mechansim of action:

Xylestesin-A contains lidocaine which is a local anaesthetic of the amide type for dentistry and leads to a reversible inhibition of the irritability of vegetative, sensory and motor nerve fibres. The blocking of voltage dependent Na^+ channels on the membrane of the nerve fibre is supposed to be the mechanism of action of lidocaine.

Adrenaline leads locally to vasoconstriction and reduced blood supply, whereby the absorption of lidocaine is delayed. The result is a higher concentration of the local anaesthetic at the site of action over a longer period, as well as the reduction of systemic adverse side effects.

Pharmacodynamic effects:

Onset of local anaesthetic effects of Xylestesin-A occurs after a short latency period of 1–3 min with infiltration and after somewhat longer latency period with nerve block anaesthesia (2 to 4 minutes after injection). The duration of complete anaesthesia with Xylestesin-A in pulpal anaesthesia is 30 to 60 minutes, and in soft-tissue anaesthesia 120 to 180 minutes.

Clinical efficacy and safety:

Success rates of anaesthesia with Xylestesin-A differ, depending on the kind of anaesthesia and the factors already mentioned before. In general, success rates of about 90% or higher may be expected after single use if the medicine is administered as indicated. The inferior alveolar nerve block has the greatest failure rate. Repeated or supplementary injections may be necessary in the event of failure or in the event of prolonged dental procedures and surgery. Special conditions, e.g. acute irreversible pulpitis of mandibular molars, may require special or alternative anaesthetic techniques. Articaine 4% with adrenaline may provide better clinical efficacy in such cases as reported by different authors. Xylestesin-A is usually tolerated well however, adverse reactions cannot be fully excluded (see section 4.8), in the event of overdose in particular (see section 4.9).

Paediatric population:

The use of Xylestesin-A in paediatric population is considered for routine treatment. Dosages in paediatric population should be reduced considering age, body weight, physical condition and the magnitude of the treatment (see section 4.2), together with complex measures to prevent painful experience and to reduce anxiety, including sedation.

Since paediatric patients suffer relatively often traumatic injury to their still (residual) anaesthetized soft tissue following local anaesthesia administration in the dental office (reportedly 13%), local anaesthesia providing the appropriate duration of efficacy should be used.

5.2 Pharmacokinetic properties

Absorption:

Lidocaine is rapidly and extensively absorbed. The maximum plasma level of lidocaine from intraoral injection is achieved approximately after 10–20 minutes. Exogenous administered adrenaline, also in dental use, may increase the adrenaline serum concentration in a dose dependent manner with a rapid decline within few minutes after administration.

Distribution:

Lidocaine is bound up to 60 to 80 % in the serum to plasma proteins. Lidocaine and adrenaline are widely distributed within the organism.

Biotransformation and elimination:

Lidocaine is largely metabolised in the liver and any alteration in liver function or hepatic blood flow can have a significant effect on its pharmacokinetics and dosage requirements. Metabolism in the liver is rapid and about 90 % of the given dose is dealkylated to form monoethylglycinexylidide and glycinexylidide. Less than 10 % is excreted unchanged. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-dimethylaniline. The elimination half-life is 1.5 to 2 hours.

Lidocaine crosses the blood-brain and placental barriers.

Adrenaline is rapidly catabolized in the liver and other tissues. The metabolites are excreted renally.

Special populations:

Effect of age: Lidocaine has been extensively investigated in elderly patients. A significantly longer half-life was found for lidocaine in elderly patients. Reduced clearance was detected only in elderly men, while the values in females did not differ significantly from younger individuals. Dose reduction was sometimes suggested for elderly patients (reduction by approximately 1/3 to ½).

According to the age of the child differences to adults in regard of metabolism and distribution volume has to be considered.

For children it seems preferable to use medicines with higher protein binding and a high hepatic extraction ratio such as articaine.

Renal and hepatic insufficiency:

The elimination half-life of lidocaine following an intravenous bolus injection is typically 1.5 to 2.0 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. The half-life may be doubled or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites.

5.3 Preclinical safety data

There is evidence that 2,6-xylidine, a metabolic product arising from lidocaine, can have mutagenic effects in the rat, and possibly also in man. This evidence is obtained from in-vitro tests in which the said metabolite was used at very high, almost toxic concentrations. There is no reason to believe at this time that the parent substance, lidocaine, is itself also mutagenic.

A carcinogenicity study of transplacental exposure and postnatal treatment of animals for two years with 2,6-xylidine in rats demonstrated malignant and benign tumors predominantly in the nasal cavities (ethmoturbinalia) by means of this highly sensitive test system (transplacental exposure and postnatal treatment of animals for two years with very high doses). It does not seem totally unlikely that these findings will be relevant to humans. For this reason high doses of Xylestesin-A (lidocaine) should not be administered over longer periods.

Lidocaine has evidently no teratogenic potential if used in recommended doses (see section 4.6).

Adrenaline was potentially teratogenic in rats albeit at doses 25 times the human therapeutic dose (see section 4.6).

While supratherapeutic doses of lidocaine and adrenaline administered under in vitro or in vivo experimental conditions to laboratory animals may affect fertilization and foetal development, harmful or other effects on female or male fertility is no expected based on animal studies at therapeutic doses of lidocaine and adrenaline (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous sodium sulphite (E221)
Sodium chloride
Hydrochloric acid 14% (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf-life

2 years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Cartridge made of colourless neutral glass I.
Stopper and rubber disc are made of butyl rubber.
Green coloured aluminium cap made of aluminium-iron-silicon-alloy.

Tin with 50 cartridges of 1.7 mL each.

6.6 Special precautions for disposal and other handling

The product should be inspected visually for particulate matter, discoloration or damage of container prior to administration. The product should not be used if such defects are observed.

The product is for single use only. Any unused product should be disposed immediately after first use in accordance with local requirements.

MEDICINE CLASSIFICATION

Prescription Medicine

NAME AND ADDRESS

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