

Data Sheet

UBISTESIN

4% Articaine with Adrenaline 1/200 000

UBISTESIN FORTE

4% Articaine with Adrenaline 1/100 000

Presentation

UBISTESIN and UBISTESIN FORTE are sterile isotonic aqueous solutions for injection. They contain sodium sulphite as an antioxidant. The pH of the solutions is 3.6-4.4. The cartridges are free from preservatives and are intended for single-use only.

Uses

Actions

Articaine is a local anaesthetic of the amide type. Local anaesthetics produce reversible loss of sensation by preventing or diminishing the conduction of sensory nerve impulses by decreasing the permeability of the nerve cell membrane to sodium ions. Articaine is thought to act by blocking the voltage dependent Na⁺ channels on the membrane of the nerve fibre.

Adrenaline is a vasoconstrictor added to retard diffusion and limit absorption of the local anaesthetic, thereby prolonging the duration of effect and lessening the danger of toxicity.

Complete anaesthesia can be achieved within 1-3 minutes of administration. The mean duration of effect in pulpal anaesthesia is 48-54 minutes for UBISTESIN and at least 75 minutes for UBISTESIN FORTE. For surgical interventions in soft tissue the mean duration of effect is 120-240 minutes.

Pharmacokinetics

Articaine is rapidly and almost completely absorbed. The maximum plasma level from intraoral injection is achieved after approximately 10-15 minutes. The volume of distribution is 1.67L/kg, and the elimination half-life is approximately 20 minutes. Upto 95% of Articaine is bound to plasma proteins. Articaine is rapidly hydrolysed by plasma cholinesterases to its primary metabolite articainic acid, which is further metabolised to articainic glucuronide. Excretion is via the kidneys.

Adrenaline undergoes rapid enzymatic degradation in the liver and other body tissues. The metabolites are excreted in the urine.

Indications

Infiltration anaesthesia and nerve block anaesthesia in dentistry. UBISTESIN FORTE is especially indicated for more complex dental procedures requiring prolonged anaesthesia.

Dosage and Administration

The following dosage instructions apply:

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

For extraction of maxillary teeth, 1.7mL UBISTESIN or UBISTESIN FORTE per tooth suffices in most cases, thereby avoiding painful palatal injections. A smaller injection volume is often possible for serial extractions of neighbouring teeth.

If a cut or suture is required in the palate, a palatal injection of approximately 0.1mL per puncture is indicated.

For smooth extractions of mandibular premolar teeth, infiltration anaesthesia of 1.7mL UBISTESIN or UBISTESIN FORTE per tooth is mostly sufficient; in single cases a buccal re-injection of 1 to 1.7mL is required. In rare cases an injection into the mandibular foramen can be indicated.

Vestibular injections of 0.5-1.7mL per tooth enable cavity and crown stump preparations.

Nerve-block anaesthesia should be used in the treatment of mandibular molar teeth.

Generally, in children weighing about 20-30kg, doses of 0.25-1mL are sufficient; and in children weighing 30-40kg, 0.5-2mL. UBISTESIN and UBISTESIN FORTE must not be used in children under the age of 4 years.

Increased plasma levels can occur in older patients due to diminished metabolic processes and lower distribution volume. The risk of accumulation is increased, in particular after repeated administration (eg re-injection). A similar effect can ensue where the general condition of the patient is poor, and in severely impaired hepatic and renal function (see *Warnings and Precautions*). In these cases a lower dose range (minimum quantity for sufficient anaesthetic depth) is recommended

The dose should also be reduced in patients with certain pre-existing diseases (angina pectoris, arteriosclerosis) (see *Warnings and Precautions*).

Maximum Recommended Dosage

Adults: For healthy adults the maximum dose is 7mg/kg body weight articaine (500mg for a 70kg patient), equivalent to 12.5mL UBISTESIN or UBISTESIN FORTE. The maximum dose represents 0.175mL of solution per kg.

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 7mg articaine/kg (0.175mL/kg) of body weight.

UBISTESIN FORTE may be more appropriate for procedures of longer duration and when there is a risk of significant bleeding into the operative field (see *Uses/Actions* for information on duration of analgesia). The duration of anaesthesia during which an operation can be performed using UBISTESIN FORTE is up to 75 minutes.

Method of Administration

For injection / oromucosal use in dental anaesthesia only.

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

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

Major systemic reactions resulting from accidental intravascular injection can in most cases be avoided by the injection technique: after aspiration slow injection of 0.1-0.2mL followed by slow injection of the remainder no sooner than 20-30 seconds later.

Opened cartridges must not be used in other patients. Residues must be discarded.

Contraindications

Use in children under the age of 4 years. Hypersensitivity to any ingredients. In general patients with demonstrated hypersensitivity to articaine and other amides should receive an ester-group local anaesthetic for subsequent procedures.

Due to the local anaesthetic ingredient articaine, do not use in the event of:

- known allergy or hypersensitivity to local anaesthetics of the amide type;
- severe impairment of the nerve impulses and conduction system of the heart (eg grade II and III AV block, pronounced bradycardia);
- acutely decompensated cardiac insufficiency;
- severe hypotension;
- patients who are known to have a deficiency in plasma cholinesterase activity;
- haemorrhagic diatheses, particularly with nerve-block anaesthesia.

Do not inject into inflamed or infected areas.

Due to the content of adrenaline as a vasoconstrictor admixture, do not use in the event of:

- heart disease 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 hypertension, untreated or uncontrolled congestive heart failure;
- concomitant treatment with monoamine oxidase (MAO) inhibitors or tricyclic antidepressants (see *Interactions*).

UBISTESIN and UBISTESIN FORTE must not be used in persons who are allergic or hypersensitive to sulphite, as well as in persons with severe bronchial asthma. UBISTESIN and UBISTESIN FORTE can provoke acute allergic reactions with anaphylactic symptoms (eg bronchospasm).

Warnings and Precautions

Use with particular caution in the event of:

- severe impairment to renal function;
- angina pectoris (see *Dosage and Administration* and *Contraindications*);
- arteriosclerosis;
- considerably impaired blood coagulation (see *Interactions*);
- thyrotoxicosis;
- narrow-angle glaucoma;

- diabetes mellitus;
- lung diseases, particularly allergic asthma;
- pheochromocytoma.

Accidental intravenous injection may be associated with convulsions, followed by central nervous system or cardiorespiratory arrest. Resuscitative equipment, oxygen and other resuscitative drugs should be available for immediate use.

Since amide-type local anaesthetics are metabolised in the liver, use with caution in patients with hepatic disease. Patients with severe hepatic disease are at greater risk of developing toxic plasma levels.

Administer with caution in patients with impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by these drugs.

Administer with caution to patients with a history of epilepsy.

There is the possibility of a positive doping test result.

Inadvertent vasopuncture can lead to serious bleeding during treatment with anticoagulants (eg heparin or acetylsalicylic acid), and in general haemorrhagic tendency is increased.

Avoid inadvertent intravascular injection (see *Dosage and Administration*).

In the case of cavity or crown preparations the risk of overlooking an opened pulp must be taken into account since adrenaline reduces blood flow in the pulp tissue.

Precautions for Use

Before a local anaesthetic is used the following drugs/therapy should be available: anti-convulsant medicines (benzodiazepines or barbiturates), myorelaxants, atropine and vasopressors or adrenaline for a severe allergic or anaphylactic reaction; resuscitating equipment (in particular a source of oxygen) enabling artificial ventilation if necessary.

Cardiovascular and respiratory vital signs and the patient's state of consciousness should be monitored after each local anaesthetic injection. Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression or drowsiness may be early signs of central nervous system toxicity and require rapid corrective measures to prevent possible worsening (see *Overdose*).

Patients taking phenothiazines:

Phenothiazines may reduce or reverse the pressor effect of adrenaline. Concurrent use of these agents should generally be avoided. In situations where concurrent therapy is necessary, careful patient monitoring is essential.

Patients taking non-selective beta-blockers:

The concomitant administration of non-cardioselective beta-blockers can lead to an increase in blood pressure due to adrenaline (see *Interactions*).

The administration of large doses of articaine may produce methaemoglobinaemia in patients with subclinical methaemoglobinaemia.

Use in Pregnancy and Lactation

No clinical experience of use in pregnant and lactating women is available. Safe use of local anaesthetics during pregnancy with respect to adverse effects on foetal development has not been established. The medicine should only be used if the expected benefit to the patient outweighs the risk to the foetus.

The excretion of articaine and its metabolites in human milk is unknown. Preclinical safety data suggests that the amount of articaine in breast milk does not reach clinically relevant levels. It is recommended that nursing mothers express and discard the first mother's milk following anaesthesia with articaine.

Effect on ability to Drive and Use Machines

Although trial patients have shown no impairment of their normal reactions when driving, possible impairment on the ability to drive or operate machinery should be assessed. The patient should not leave the dental surgery earlier than at least 30 minutes after the injection.

Adverse Effects

The following adverse effects can occur as a result of the local anaesthetic ingredient articaine or to the content of adrenaline, and are presented at a frequency of:

Rare: $\geq 1/10,000$ and $< 1/1000$

Very Rare $< 1/10,000$

Cardiovascular disorders: *Rare:* Bradycardia, hypotension, cardiac impulse conduction disorders, asystole, cardiovascular arrest, heat sensation, sweating, heart racing, migraine-like headache, hypertension, anginal disorders, tachycardia, tachyarrhythmia, cardiovascular arrest and acute oedematous thyroid swelling.

Central Nervous System disorders: *Rare:* Metallic taste, tinnitus, dizziness, nausea, vomiting, restlessness, anxiety, yawning, shaking, nervousness, nystagmus, headache, hyperventilation, paraesthesia of the lip and/or tongue. More severe symptoms are drowsiness, confusion, tremor, muscular twitching, seizures, coma and respiratory paralysis.

Respiratory disorders: *Rare:* Tachypnea, then bradypnea, which could lead to apnoea.

Allergic Reactions: *Very Rare:* Rash, oedema, pruritis, erythema; nausea, diarrhoea, wheezing and anaphylaxis as a result of hypersensitivity to articaine.

Methaemoglobinaemia (see *Warnings and Precautions*). Allergic or hypersensitivity reactions to sulphite, particularly in bronchial asthmatics, are manifested as vomiting, diarrhoea, wheezing, acute asthma attacks, clouding of consciousness or shock.

2 Weeks delayed onset of facial nerve paralysis has been described with articaine/adrenaline, the event still occurring after 6 months.

Interferences in the clinical picture can result from the simultaneous occurrence of various complications and adverse effects.

Interactions

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

Adrenaline can inhibit insulin release in the pancreas and thus diminish the effect of oral anti-diabetics. The concomitant administration of non-cardioselective beta-blockers can lead to an increase in blood pressure due to the adrenaline in UBISTESIN and UBISTESIN FORTE.

Certain inhalational anaesthetics, such as halothane, can sensitise the heart to catecholamines and therefore induce arrhythmias following administration of UBISTESIN or UBISTESIN FORTE.

Haemorrhagic tendency is increased during treatment with anti-coagulants (see *Warnings and Precautions*).

Cross-reactivity to articaine has been reported in a patient with delayed hypersensitivity to prilocaine.

Overdosage

Symptoms and Signs

Toxic effects may occur either immediately, caused by unintentional intravascular injection or rapid absorption eg in inflamed or intensive vascularised tissue, or delayed caused by excessive dosage, and manifest themselves as CNS and/or cardiovascular symptoms.

Milder CNS symptoms include metallic taste, tinnitus, dizziness, nausea, vomiting, restlessness, anxiety, initial hyperventilation. More severe symptoms are drowsiness, confusion, tremor, muscular twitching, seizures, coma and respiratory paralysis. Cardiovascular symptoms are characterised by heat sensation, sweating, migraine-like headache, angina pectoris disorders, tachycardia and tachyarrhythmias. Severe cardiovascular episodes are seen in the form of hypotension, cardiac impulse conduction disorders, bradycardia and cardiovascular arrest.

General Basic Measures:

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

Special Measures:

- Hypertension: Elevation of the upper body, sublingual nifedipine if necessary.
- Convulsions: Protect patients from concomitant injuries, diazepam i.v if necessary.
- Hypotension: Horizontal position, intravascular infusion of an electrolyte solution if necessary, vasopressors (eg etilefrine i.v).
- Bradycardia: Atropine i.v.
- Anaphylactic Shock: Contact emergency physician. In the interim shock positioning, generous infusion of an electrolyte solution, if necessary adrenaline i.v, cortisone i.v.
- Cardiac shock: Elevation of the upper body, contact emergency physician.
- Cardiovascular arrest: Immediate cardiopulmonary resuscitation, contact emergency physician.

Pharmaceutical Precautions

Store below 25°C. Store in the original package in order to protect from light.

Medicine Classification

Prescription Medicine

Package Quantities

50 cartridges of 1.7mL each.

Further Information

Keep out of reach of children.

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