3M ESPE

Ubistesin™

Solution for Injection
Oromucosal use

FOR USE IN DENTAL ANAESTHESIA ONLY

3M Deutschland GmbH
Carl-Schurz-Straße 1
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Germany

44000799161/01

PACKAGE LEAFLET

COMPOSITION

1 ml solution for injection contains:

Active ingredients:

Articaine hydrochloride	40 mg
Adrenaline hydrochloride	0.006 mg
(equivalent to 0.005 mg adrenaline)	

Other ingredients:

Anhydrous sodium sulphite	max. 0.6 mg
(equivalent to max. 0.31 mg SO_2)	

Sodium chloride
Water for injections
Hydrochloric acid and sodium hydroxide for adjusting the pH-value

PHARMACEUTICAL FORM AND CONTENT

Solution for injection; one tin contains 50 cartridges of 1.7 ml each

Local anaesthetic (agent that abolish sensation affecting a particular area of region) of the amide type with vasoconstrictive (narrowing of blood vessel) component for administration in dentistry

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THERAPEUTIC INDICATIONS

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

CONTRAINDICATIONS

Ubistesin is not allowed to be used in the event of

- children under 4 years of age
- hypersensitivity (allergic) to any of the components

Due to the local anaesthetic ingredient articaine, Ubistesin is not allowed to be used in the event of

- known allergy or hypersensitivity to local anaesthetics of the amide type
- severe impairment of the impulse initiation and conduction system of the heart (e.g. grade II and III AV block, pronounced bradycardia (slow heart rate))
- acutely decompensated cardiac insufficiency (acute failure of cardiac performance)
- severe hypotension (low blood pressure)
- patients who are known to have a deficiency in plasma cholinesterase activity (a naturally occurring chemical in the body)
- haemorrhagic diatheses (tendency to bleed) – particularly with nerve-block anaesthesia
- injection into an inflamed area

Due to the content of adrenaline as a vasoconstrictor admixture, Ubistesin is not allowed to be used in the event of

- Heart diseases such as:
  - unstable angina pectoris (pain in the center of the chest)
  - recent myocardial infarction (death of a segment of heart muscle)
  - recent coronary artery bypass surgery (heart surgery)
  - refractory arrhythmias (disturbance of regular heart beat) and paroxysmal tachycardia (an abrupt increase of the heart rate) or high-frequency continuous arrhythmia (very fasten irregular heartbeat)
  - untreated or uncontrolled severe hypertension (high blood pressure)
  - untreated or uncontrolled congestive heart failure (failure of cardiac performance)
- concomitant treatment with monoamine oxidase (MAO) inhibitors or tricyclic antidepressants (drugs for treating depression) (see section "Interactions")

Due to the content of sulphite as excipient, Ubistesin is not allowed to be used in the event of

- allergy or hypersensitivity to sulphite
- severe bronchial asthma

Ubistesin can provoke acute allergic reactions with anaphylactic symptoms (e.g. bronchospasm (narrowing of bronchi)).

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Ubistesin must be used with particular caution in the event of

- severe impairment to the renal function
- angina pectoris (pain in the center of the chest) (see section "Posology and method of administration" and "Contraindications")
- arteriosclerosis (hardening of the arteries)
- considerably impaired blood coagulation (see section "Interactions")
- thyrotoxicosis (syndrome due to excessive amounts of thyroid hormones in the bloodstream)
- narrow-angle glaucoma (condition in which loss of vision occurs because of an abnormally high pressure in the eye)
- diabetes mellitus (disorder in which sugars in the body are not oxidized due to a lack of pancreatic hormone insulin)
- lung diseases – particularly allergic asthma
- pheochromocytoma (a form of cancer that effects the adrenal gland)

Accidental injection may be associated with convulsions, followed by damping of 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 also metabolised by the liver, Ubistesin should be used with caution for patients with hepatic diseases. Patients with severe hepatic diseases are at greater risk of developing toxic plasma concentration.

The product should be administered with caution for 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.

The product should be administered with caution for patients with history of epilepsy (disorder of brain function characterized by recurrent seizures).

There is a possibility of positive results on doping tests performed on sportsmen.

It should be taken into consideration that during treatment with blood coagulation inhibitors (drugs which prevent blood clotting, e. g. heparin or acetylsalicylic acid), an inadvertent vasopuncture when administering the local anaesthetic can lead to serious bleeding, and that in general the hemorrhagic tendency is increased (see section "Interactions").

Inadvertant intravascular application must be avoided (see section "Posology and method of administration")

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.

Precautions for use:

Each time a local anaesthetic is used the following drugs/therapy should be available:

- Anti-convulsant medicines (medicines for treating seizures e. g. benzodiazepines or barbiturates), muscle relaxants (drugs which reduce the tension in voluntary muscles), atropine and vasopressors (drugs for treating low blood pressure) or adrenaline 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 monitored after each local anaesthetic injection. Restlessness, anxiety, tinnitus (ringing in the ear), dizziness, blurred vision, tremors (rhythmical and alternating movement), depression, or drowsiness may be early warning signs of central nervous system toxicity (see section "Therapy of overdose").

Patients taking phenothiazines (medicines for treating severe mental disorders)

Phenothiazines 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 (medicines for treating high blood pressure)

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

PREGNANCY AND LACTATION

No clinical experience of the use in pregnant and lactating women is available. Safe use of local anaesthetics during pregnancy has not been established with respect to adverse effects on fetal development. This medicine should only be used in pregnancy when the benefits are considered to outweigh the risks.

The excretion of articaine and its metabolites in human milk is unknown. However, preclinical safety data suggest that the concentration of articaine in breast milk does not reach clinically relevant concentrations. Therefore, nursing mothers should milk and discard the first mother's milk following anaesthesia with articaine.

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 at least 30 minutes after the injection.

INTERACTIONS

- The sympathomimetic effect of adrenaline can be intensified by the simultaneous intake of MAO inhibitors or tricyclic antidepressants (drugs for treating depression) (see section "Contraindications").
- Adrenaline can inhibit insulin release in the pancreas and thus diminish the effect of oral antidiabetics (drugs for treating diabetes mellitus)
- The concomitant administration of non-cardioselective ß-blockers (drugs for treating high blood pressure) can lead to an increase in blood pressure due to the adrenaline in Ubistesin.
- Certain inhalational anaesthetics (agent to abolish sensation), such as halothane, can sensitise the heart to catecholamines and therefore induce arrhythmias following administration of Ubistesin.
- During treatment with blood coagulation inhibitors (drugs which prevent blood clotting), the hemorrhagic tendency is increased (see also section "Special warnings and precautions for use").

POSOLOGY AND METHOD OF ADMINISTRATION

The following dosage instructions apply:

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

For extraction of maxillary teeth, 1.7 ml Ubistesin per tooth suffices in most cases; painful palatal injections can thus be avoided. In the case of serial extractions of neighbouring teeth, a reduction of the injection volume is often possible.

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

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

Vestibular injections of 0.5–1.7 ml Ubistesin 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 20–30 kg, doses of 0.25–1 ml are sufficient; in children weighing 30–45 kg, 0.5–2 ml.
Ubistesin must not be used in children aged below 4 years.

Increased plasma levels of Ubistesin can occur in older patients due to diminished metabolic processes and lower distribution volume. The risk of accumulation of Ubistesin is increased in particular after repeated application (e. g. re-injection). A similar effect can ensue from the reduced general condition of the patient, as well as severely impaired hepatic and renal function (see also section "Special warnings and precautions for use"). A lower dosage range is thus recommended in all such cases (minimum quantity for sufficient anaesthetic depth).

The dose has to be likewise reduced in patients with certain pre-existing diseases (angina pectoris (pain in the center of the chest), arteriosclerosis (hardening of the arteries)) (see also section "Special warnings and precautions for use").

Maximum Recommended Dosage:

Adults:

For healthy adults, the maximum dose is 7 mg/kg body weight articaine (500 mg for a 70 kg patient), equivalent to 12.5 ml Ubistesin.
The maximum dose represents 0.175 ml 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 7 mg articaine/kg (0.175 ml Ubistesin/kg) of body weight.

Ubistesin forte is also available and may be more appropriate for procedures of longer duration and when there is a risk of significant bleeding into the operative field.

Method of administration

For injection/oromucosal use

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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.

THERAPY OF OVERDOSE

Undesirable effects (showing an abnormally high concentration of local anaesthetic in the blood) may appear either immediately, caused by accidential 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 caused by the local anaesthetic ingredient articaine:

Milder central nervous symptoms involve metallic taste, tinnitus (ringing in the ear), dizziness, nausea (sickness), vomiting, restlessness, anxiety, initial increase in respiratory rate (breathing rate).

More severe symptoms are drowsiness, confusion, tremor (rhythmical and alternating movement), muscular twitching, tonic-clonic seizures (convulsion), coma and respiratory paralysis (severe breathing disorders).

Severe cardiovascular (circulatory) episodes are seen in the form of a drop in blood pressure, cardiac impulse conduction disorders, bradycardia (slow heart rate), cardiovascular (circulatory) arrest.

Symptoms caused by adrenaline as a vasoconstrictor:

Cardiovascular (circulatory) symptoms such as heat sensation, sweating, heart racing, migrainelike headache, blood pressure increase, angina pectoris disorders (pain in the center of the chest), tachycardias (fast heart rate), tacharrhythmias (irregularity of pulse with fast heart rate) and cardiovascular (circulatory) arrest.

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

Therapy

If adverse reactions arise the application of the local anaesthetic has to be stopped.

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

UNDESIRABLE EFFECTS

Due to the local anaesthetic ingredient articaine, the following undesirable effects can occur

Cardiovascular disorders

Rare (≥ 0.01 %)

Decrease in heart rate, hypotension (low blood pressure)

Drop in blood pressure, cardiac impulse conduction disorders, bradycardia (slow heart rate), asystolia (cardiac standstill), cardiovascular (circulatory) arrest.

Nervous system disorders

Rare (≥ 0.01 %)

Metallic taste, tinnitus (ringing in the ear), dizziness, nausea (sickness), vomiting, restlessness, anxiety, yawning, shaking, nervousness, nystagmus (tremble of the eyes), logorrhoea (compulsive talking), headache, increase in respiratory rate (breathing rate).

Paresthesias (loss of sensation, burning, tingling) of the lip, tongue, or both.

When these signs appear rapid corrective measures are required to prevent possible worsening: Drowsiness, confusion, tremor (rhythmical and alternating movement), muscle twitching, tonic-clonic seizures (convulsion), coma and respiratory paralysis (severe breathing disorders).

Respiratory disorders

Rare (≥ 0.01 %)

Tachypnea (rapid breathing), then bradypnea (slow breathing), which could lead to apnoea (cessation of breathing).

Allergic reactions

Very rare (< 0.01 %)

One may observe manifestation of hypersensitivity to articaine as rash, pruritus edema (itching swelling), pruritus (itching), and erythema (redness of the skin) as well as nausea (sickness), diarrhea, wheezing or anaphylaxis. Cross reactivity to articaine has been reported in a patient with delayed hypersensitivity to prilocaine.

In general, patients with demonstrated hypersensitivity to articaine or other amides should receive an ester-group local anaesthetic for subsequent procedures.

The administration of large doses of articaine may produce methaemoglobinemia (chemically changed red blood pigment) in patients with subclinical methaemoglobinemia.

Due to the content of adrenaline as a vasoconstrictor admixture, the following undesirable effects can occur

Cardiovascular disorders

Rare (≥ 0.01 %)

Heat sensation, sweating, heart racing, migrainelike headache, blood pressure increase, angina pectoris disorders (pain in the center of the chest), tachycardias (fast heart rate), tacharrhythmias (irregularity of pulse with fast heart rate) and cardiovascular (circulatory) arrest as well as acute oedematous thyroid swelling.

Due to the content of sulphite as excipient, the following undesirable effects can occur

Allergic reactions

Very rare (< 0.01 %)

Allergic reactions or hypersensitivity reactions, particularly in bronchial asthmatics, which are manifested as vomiting, diarrhoea, wheezing, acute asthma attack, clouding of consciousness or shock.

Due to the content of both articaine and adrenaline, the following undesirable effects can occur

Nervous system disorders

2 weeks delayed onset of facial nerve paralysis has been described with articaine/adrenaline, the event still occurs 6 months later.

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

INFORMATION CONCERNING STORAGE AND STABILITY

Keep out of the reach and sight of children.

Do not store above 25°C.

Store in the original package in order to protect from light.

Do not use after the expiry date stated on the bottom of the tin and the cartridges.

DATE OF REVISION OF THE TEXT

12/2014