SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Anestadent 4% w/v and 1:100,000 solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Articaine hydrochloride……...40.00 mg/mL

Adrenaline tartrate

Quantity corresponding to adrenaline……..0.01 mg/mL

Excipient(s) with known effect:

Sodium metabisulphite (E223)…….0.5 mg/mL

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection for dental use.

Sterile, clear and colourless solution for injection with a pH between 2.7 – 4.5 and osmolality of aproximately 267 mOsm/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Local or local-regional anesthesia in dentistry and dental surgical procedures in patients at least 4 years old.

4.2 Posology and method of administration

Posology

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

Adults

The quantity to be injected will be adjusted as a function of the extent of the intervention.

As a general rule, one to three cartridges per session.

The dose should not exceed 7 mg of articaine hydrochloride per kilogram of body weight.

Paediatric population

Articaine hydrochloride/Epinephrine NewLine Pharma should not be used in children aged below 4 years because of safety and efficacy concerns.

The quantity to be injected depends on the age and the weight of the child as well as the type of intervention to be performed.

The maximum dose is 5 mg of articaine hydrochloride (0.125 mL of anaesthetic solution) per kilogram of body weight.

The average dose in mg of articaine hydrochloride that can be administered in children can be calculated as follows:

Weight of the child (in kilograms) x 1.33

Elderly

Reduce to one-half the dose used for adults.

Method of administration

Local or regional intraoral submucosal injection.

The injection rate must not exceed 1 mL of solution per minute

4.3 Contraindications

This medicinal product is contraindicated in the following situations:

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1
- Known allergy or hypersensitivity to other local anaesthetics of the amide type

4.4 Special warnings and precautions for use

Special warnings

This product contains 0.01 mg/mL of adrenaline (epinephrine).

Be aware of a risk of local necrosis in hypertensive or diabetic subjects.

Risk of self-biting under anesthesia: various bite wounds (lips, cheeks, mucosa, and tongue); warn the patient to avoid chewing gum or food for as long as the insensitivity persists.

Precautions for use

This medicinal product should be used with caution in cases of:

- severe alterations of renal and hepatic functions;
- angina pectoris;
- arteriosclerosis (vessel calcification);
- blood coagulation disturbances (e.g. in patients receiving anticoagulants);

- patients with cholinesterase deficiency, as a prolonged and possibly pronounced drug effect can be expected;
- epilepsy.

Due to the presence of adrenaline, precautions and monitoring should be increased in the case of:

- rhythm disorders, except bradycardia;
- severe cardiovascular diseases such as unstable angina, recent myocardial infarction, recent coronary artery bypass surgery, coronary heart disease, congestive heart failure;
- severe arterial hypertension;
- uncontrolled or poorly controlled hypertension;
- hyperthyroidism;
- diabetes mellitus.

In the case of serious liver failure, it may be necessary to reduce the doses of articaine due to the principally hepatic metabolism of local anesthetics with amide function.

This medicinal product contains less than 1 mmol sodium (23 mg) per cartridge, i.e. essentially ‘sodium- free’.

Due to the presence of sodium metabisulphite, it may rarely cause severe hypersensitivity reactions and bronchospasm.

Overdose of the medicinal product should be avoided and two maximal doses of the drug should be administered with a minimum interval of 24 hours.

Although nerve injuries may be rare (see section 4.8), usual precautions for nerve-block anaesthesia should be observed.

Food intake should only commence after the anaesthetic effect has worn off.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations requiring precautions for use

Due to the presence of adrenaline:

- Halogenated volatile anesthetics:

  Serious ventricular rhythm disorders (increase of cardiac reactivity).

- Tricyclic antidepressants (imipramine):

  Paroxysmal hypertension with the possibility of rhythm disorders (inhibition of adrenaline uptake into sympathetic fibers).

- SNRI’s antidepressants (minalcipran, venlafaxine):

  Paroxysmal hypertension with possibility of rhythm disorders (inhibition of adrenaline uptake into sympathetic fibers).

- Nonselective MAOIs (iproniazide):

Increase in the hypertensive effect of adrenaline, most often moderate.

For use only with strict medical supervision

- Selective MAOIs (moclobemide, toloxatone) by extrapolation from non-selective MAOIs:

  Risk of increased hypertensive effect.

  For use only with strict medical supervision.

- Non-selective betablockers:

  The hypertensive effects of adrenaline can be markedly increased in patients taking non-selective beta blockers. There is also an increased risk of bradycardia.

- Guanethidine and related medicinal products (antiglaucoma agents):

  Significant increase in blood pressure (hyper-reactivity linked to sympathetic tone reduction and/or inhibition of adrenaline uptake into sympathetic fibers).

  If the combination cannot be avoided, use smaller doses of sympathomimetics (adrenaline) with precaution.

4.6 Fertility, Pregnancy and lactation

Pregnancy

There are a limited amount of data from the use of articaine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

There are a limited amount of data from the use of adrenalin in pregnant women. Animal studies have shown reproductive toxicity at supratherapeutic doses (see section 5.3).

Articaine hydrochloride/Epinephrine NewLine Pharma may not be used during pregnancy, unless strictly necessary.

Breastfeeding

It is unknown if articaine and adrenaline are excreted in breastmilk. However, at therapeutic doses of Articaine hydrochloride/Epinephrine NewLine Pharma exposure to the infant receiving breastfeeding is expected to be very low. Articaine hydrochloride/Epinephrine NewLine Pharma can be used during breastfeeding.

Fertility

There are no available data on the effect of articaine or adrenaline on human fertility

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

The dentist will evaluate after surgery, the patient ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects may result from overdose, due in particular to accidental intravascular injection or in cases of abnormal absorption, such as in inflamed or highly vascularised tissues.

The following frequencies are used for the description of the occurrence of adverse reactions: 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) not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Undesirable effects due to articaine*:*

Metabolism and nutrition disorders: Rare

Metabolism increase

Nervous system disorders: Rare

Metallic flavour, tinnitus, disorientation, tremors, excitatory reactions, vertigo, midryasis, paraesthesia (of lips, tongue), mandibular spasm and convulsions.

Eye disorders: Rare

During and immediately after anaesthesia rare transient eye disorders may occur (diplopia)

Cardiac disorders: Rare

Bradycardia with myocardial depression, arrhythmia

Vascular disorders: Rare

Hypotension, hypertension

Respiratory, thoracic and mediastinal disorders: Rare

Tachypnea, broncodilatation

Gastrointestinal disorders: Rare

Nausea, vomiting

Skin and subcutaneous tissue disorders: Very rare

Cutaneous rashes, pruritus, urticaria

General disorders and administration site conditions:

Very rare: Allergic reactions (bronchospasm, oedema of the larynx up to cardiorespiratory collapse from anaphylactic shock)

Rare: increase in body temperature

Undesirable effects due to adrenaline:

Cardiac disorders: Rare

Arrhythmia

Vascular disorders: Rare

Hypertension (severe in patients suffering from hypertension and hyperthyroidism)

Gastrointestinal disorders: Rare

Vomiting

General disorders and administration site conditions: Rare

Heat sensation, sweating, headache, anxiety, retrosternal and pharyngeal pain.

Patients with cardiovascular diseases may exhibit exaggerated vasoconstrictor response. Ischemic injury or necrosis may result.

The product contains sodium metabisulphite: this substance may cause allergic-type reactions and severe asthmatic episodes in certain susceptible people and in particular in asthmatic patients.

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

Nervous System disorders:

Very rare (< 1/10,000):

Persistent hypoesthesia and gustatory loss after mandibular or inferior alveolar nerve blocks 2 weeks delayed onset of facial nerve paralysis has been described with articaine/adrenaline, the event still occur 6 months later.

In some cases, an incorrect injection may cause severe ischemia and necrosis. Lesions to nerves, hyposensitivity and alterations of taste, may occur after an incorrect injection or in case of patient with particular conditions.

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

4.9 Overdose

Toxic reactions

CNS excitation: confusion, fear, and tachypnea, increase in blood pressure and face blushing, nausea, vomiting, tremors, spasms, mandibular spasms and convulsions.

CNS depression: vertigo, inability to speak, hearing difficulties, and loss of consciousness, muscular contractions, vascular-motor complications, tonic-clonic seizures, coma, respiratory difficulties, respiratory block and death.

Cardiovascular depression: bradycardia, arrhythmia, fibrillation, hypotension, cardiac arrest, and cyanosis.

Emergency procedures and therapy

At the first sign of adverse reactions administration must be interrupted, the patient placed in horizontal position and the clear passage of the airways ascertained; respiration, pulse and blood pressure should be monitored. Oxygen must be administered or artificial ventilation applied in cases of serious dyspnoea. Heart rate and arterial pressure should be monitored. An intravenous injection of an isotonic solution is also recommended in cases of not severe symptom appearance. Any seizures may be controlled using anti-convulsant medicines (diazepam) endovenously administered followed by oxygen administration. In cases of

circulatory problems and shock, glucocorticoids, as plasmatic mass expander, and human albumin should be intravenously administered. In case of collapse and increasing bradycardias, adrenaline should be immediately administered and heart rateand blood pressure monitored.

Severe tachycardia and arrhythmia require treatment with anti arrhythmic and cardioselective drugs.

Hypertension in hypertonic patients should be treated with peripheral anti-hypertensive drugs.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Local anaesthtics; ATC code: N01BB58

Mechanism of action

Articaine hydrochloride is a local anaesthetic with amide function that interrupts the propagation of nerve pulses along the nerve fiber at the injection site.

The adrenaline (diluted to 1/100,000) that is added to the articaine solution slows the passage of articaine into the general circulation and thus assures the extended maintenance of an active tissue concentration, permitting obtaining an operating field that is relatively devoid of blood.

Anaesthesia is initiated in 2 to 3 minutes. The duration of anaesthesia permitting a surgical intervention is approximately 60 minutes.

5.2 Pharmacokinetic properties

Injected into the oral mucosa, articaine reaches its peak blood concentration approximately 30 minutes after injection.

Articaine is metabolised in approximately 5% to 10% by hepatic cytochrome P-450 isoenzyme systems; 2% is eliminated in unchanged form in the urine. Up to 90% of articaine is rapidly hydrolysed by esterase to its primary inactive metabolite articainic acid which is further metabolised in to articainic acid glucuronide. The elimination half-life of articaine hydrochloride is approximately 110 minutes.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development.

Adrenaline is known to induce teratogenicity in rats and human. There is evidence of congenital malformations and a disrupted uteroplacental blood circulation. These effects are considered not relevant at the exposure with the current indication.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

Sodium metabisulphite

Hydrochloric acid

Sodium hydroxide

Water for injection

6.2 Incompatibilities

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

6.3 Shelf life

18 months

6.4 Special precautions for storage

Store at a temperature below 30ºC.

Do not freeze.

6.5 Nature and contents of container

Cartridge (type I glass) sealed at the base by a grey bromobutyl stopper and at the other end by a bromobutyl disk covered by an aluminum cap.

Box of 50 cartridges of 1.8 mL with self-aspirating stopper

Box of 50 cartridges of 1.8 mL with standard stopper

Box of 50 cartridges of 2.2 mL with self-aspirating stopper

Box of 50 cartridges of 2.2 mL with standard stopper

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

As with any cartridge, the membrane will be disinfected just before use. It will be carefully swabbed:

- either with 70% ethyl alcohol
- or with 90% pure isopropyl alcohol for pharmaceutical use.

The cartridges must never be immersed in any solution whatsoever.

Do not mix the solution for injection in the same syringe with other products.

All opened anaesthetic solution cartridges must not be reused.

7 MARKETING AUTHORISATION HOLDER

DENTSPLY Limited

Building 3, The Heights

Weybridge, Surrey, KT13 0NY

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 04690/0034

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02/10/2018

10 DATE OF REVISION OF THE TEXT

21/06/2019