1 NAME OF THE MEDICINAL PRODUCT

SEPTANEST WITH ADRENALINE 1/100 000, solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution for injection contains:

Articaine hydrochloride	40 mg
Adrenaline	0.0100 mg
(as Adrenaline tartrate	0.0182 mg)

One cartridge of 1.7 ml of solution for injection contains 68 mg of Articaine hydrochloride and 0.0170 mg of Adrenaline.

Excipient(s) with known effect: SEPTANEST WITH ADRENALINE 1/100 000 contains sodium metabisulfite (E223), sodium chloride, disodium edetate, sodium hydroxide.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear and colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

SEPTANEST WITH ADRENALINE 1/100 000 is a local anaesthetic indicated for the local and loco-regional anaesthesia in dental procedures in adults, in adolescents and in children above 4 years of age (or from 20 kg (44 lbs) of body weight).

Articaine hydrochloride 40 mg/ml with adrenaline 0.01 mg/ml is particularly appropriate for procedures of longer duration and when there is a risk of significant bleeding into the operative field.

4.2 Posology and method of administration

For professional use by dentists and stomatologists.

4.2.1 Posology

- *Adults, adolescents and children 4 years and above*

Due to the lack of clinical data, SEPTANEST WITH ADRENALINE 1/100 000 is contra-indicated in paediatric patients under 4 years of age (corresponding to approximately 20 kg).

As occurs with all local anaesthetics, doses vary and depend on the area to be anaesthetised, on the vascularity of tissues, on the number of nerve segments to be blocked, on the individual tolerance (degree of muscular relaxation and condition of the patient) and on the technique and depth of anaesthesia. The lowest dose leading to efficient anaesthesia should be

used. The necessary dosage must be determined on an individual basis.

The number of cartridges corresponding to the maximum dose can be calculated as follows:

Patient weight (kg) x Maximum articaine dose (mg/kg)/ Quantity of articaine per cartridge (mg)

	Maximum articaine dose	**Maximum cartridges of SEPTANEST WITH ADRENALINE 1/100 000 on the basis of 70 kg body weight and above**
Children 20-55kg	5 mg/kg	Not applicable
Adults & adolescents	6.8mg/kg with a maximum of 476 mg	= 7 cartridges of 1.7 ml

Articaine quantity per cartridge:
68 mg for 1.7 ml cartridge

- *Special populations*

Due to lack of clinical data, particular precaution should be used in order to administer the lowest dose leading to efficient anaesthesia in elderly patients over 70 years old and in patients with renal or hepatic impairment.

4.2.2 Method of Administration

Infiltration and perineural use in oral cavity.

The rate of injection should not exceed 1 ml of solution per minute.

4.3 Contraindications

• Hypersensitivity to articaine (or any local anaesthetic agent of the amide type) or to adrenaline or to any of the excipients.

• Children (age below 4 years old).

Due to articaine

• Known plasma cholinesterase deficiency;

• Severe conduction disturbances;

• Poorly controlled epileptic patient.

Due to adrenaline

• Uncontrolled / severe hypertension;

• Severe ischemic heart disease;

• Persistent / refractory tachyarrhythmia;

• Thyrotoxicosis;

• Pheochromocytoma.

4.4 Special warnings and precautions for use

4.4.1 Special warnings

SEPTANEST WITH ADRENALINE 1/100 000 must be used with caution in:

Patients with cardiovascular disorders:

- Peripheral vascular disease;
- Arrhythmias particularly of ventricular origin;
- Heart failure;
- Hypotension.

SEPTANEST WITH ADRENALINE 1/100 000 should be administered with caution in patients with impaired cardiac function since they may be less able to compensate changes due to prolongation of atrio-ventricular conduction.

Epileptic patients:

Because of their convulsive actions, all local anaesthetics should be used very cautiously.

For poorly controlled epileptic patients, see section 4.3.

Patients with hepatic disease:

The lowest dose leading to efficient anaesthesia should be used.

Patients with renal disease:

The lowest dose leading to efficient anaesthesia should be used.

Patients with myasthenia gravis:

The lowest dose leading to efficient anaesthesia should be used.

Patients receiving treatment with antiplatelets / anticoagulants:

The increased risk of severe bleeding following accidental vessel puncture and during oro-maxillo-facial surgery should be considered. International Normalized Ratio (INR) monitoring should be increased in patients taking anticoagulants.

Patients with porphyria:

SEPTANEST WITH ADRENALINE 1/100 000 should be used cautiously.

Patients with uncontrolled diabetes:

SEPTANEST WITH ADRENALINE 1/100 000 should be used cautiously due to the hyperglycemic effect of adrenaline.

Patients with susceptibility of acute angle-closure glaucoma:

SEPTANEST WITH ADRENALINE 1/100 000 should be used cautiously due to the presence of adrenaline.

Elderly patients:

Dosages should be reduced in elderly patients over 70 years old (lack of clinical data).

SEPTANEST WITH ADRENALINE 1/100 000 must be used safely and effectively under appropriate conditions:

Adrenaline impairs the flow of blood in the gums, potentially causing local tissue necrosis. Very rare cases of prolonged or irreversible nerve injury and gustatory loss have been reported after mandibular block analgesia.

The local anaesthetic effects may be reduced when SEPTANEST WITH ADRENALINE 1/100 000 is injected into an inflamed area or into an infected area.

Risk of biting trauma (lips, cheeks, mucosa, and tongue) exists, especially in children; the patient should be told to avoid chewing gum or eating until normal sensation is restored.

SEPTANEST WITH ADRENALINE 1/100 000 contains sodium metabisulfite, a sulfite that may rarely cause hypersensitivity reactions and bronchospasm.

SEPTANEST WITH ADRENALINE 1/100 000 contains sodium metabisulfite, sodium chloride, disodium edetate and sodium hydroxide. SEPTANEST WITH ADRENALINE 1/100 000 contains less than 1 mmol sodium (23 mg) per cartridge, i.e. it is considered as essentially ‘sodium free’.

4.4.2 Precautions for use

Before using SEPTANEST WITH ADRENALINE 1/100 000, it is important:

- to make inquiries into the patient’s diatheses, current therapies and history,
- to maintain verbal contact with the patient,
- to have resuscitative equipment at hand (see section 4.9).

Risk associated with accidental intravascular injection:

Accidental intravascular injection (e.g.: inadvertent intravenous injection into systemic circulation, inadvertent intravenous or intra-arterial injection in the head area and neck area) may be associated with severe adverse reactions, such as convulsions, followed by central nervous system depression or cardiorespiratory depression and coma, progressing ultimately to respiratory arrest, due to the sudden high level of adrenaline and articaine in the systemic circulation.

Thus, to ensure that the needle does not penetrate a blood vessel during injection, aspiration should be performed before the medicinal product is injected. However, the absence of blood in the syringe does not guarantee that intravascular injection has been avoided.

Risk associated with intraneural injection:

Accidental intraneural injection may lead the drug to move in retrograde manner along the nerve.

In order to avoid intraneural injection and to prevent nerve injuries in connection with nerve blockades, the needle should always be slightly withdrawn if electric shock sensation is felt by the patient during injection or if the injection is particularly painful. If needle nerve injuries occur, the neurotoxic effect could be aggravated by articaine’s potential chemical neurotoxicity and by the presence of adrenaline as it may impair the perineural blood supply and prevent articaine local wash-out.

Concomitant use of other medicinal products may require thorough monitoring (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

4.5.1 Due to the presence of articaine

Interactions requiring precautions for use

Other local anaesthetics: Toxicity of local anaesthetics is additive. It is not relevant considering dental anaesthesia doses and blood levels, but it is a concern in children.

The total dose of administered articaine should not exceed the maximum recommended dose.

H2 antihistaminics (cimetidine): Increased serum levels of amide anaesthetics have been reported following concomitant administration of cimetidine.

Sedatives (central nervous system depressants): Reduced doses of SEPTANEST WITH ADRENALINE 1/100 000 should be used due to additive effect.

4.5.2 Due to the presence of adrenaline

Interactions that are not recommended

Postganglionic adrenergic blocking agents (e.g., guanadrel, guanethidine, and rauwolfia alkaloids): Reduced doses of SEPTANEST WITH ADRENALINE 1/100 000 should be used under strict medical supervision followed by careful aspiration due to possible increased response to adrenergic vasoconstrictors: risk of hypertension and other cardiovascular effects.

Interactions requiring precautions for use

Halogenated volatile anaesthetics *(e.g.*: halothane): Reduced doses of SEPTANEST WITH ADRENALINE 1/100 000 should be used due to sensitization of the heart to the arrhythmogenic effects of catecholamines: risk of severe ventricular arrhythmia.

The patient's hemodynamic status should be closely monitored.

Non-selective beta-adrenergic blockers (*e.g.*, propranolol, nadolol): Reduced doses of SEPTANEST WITH ADRENALINE 1/100 000 should be used due to possible increase in blood pressure. Close cardiovascular monitoring is recommended.

(TCAs) Trycyclic antidepressants (*e.g.*, amitriptyline, desipramine, imipramine, nortriptyline, maprotiline, and protriptyline): Dose and rate of administration of SEPTANEST WITH ADRENALINE 1/100 000 should be reduced due to strengthening of adrenaline activity.

Close cardiovascular monitoring is recommended.

(MAO inhibitors) MonoAmine Oxidase inhibitors [both A-selective (*e.g.*, brofaromine, moclobemide, toloxatone) and non-selective (e.g., phenelzine, tranylcypromine, linezolide)]:

Use under strict medical supervision due to possible potentialization of the effects of adrenaline.

(COMT inhibitors) Catechol-O-Methyl Transferase inhibitors (*e.g.*, entacapone, tolcapone):

Arrhythmias, increased heart rate and blood pressure variations may occur.

Cardiovascular monitoring is recommended.

(SSRIs) Selective Serotonin Reuptake Inhibitors (*e.g.*, venlafaxine, milnacipran, sertraline):

Dose and rate of administration of SEPTANEST WITH ADRENALINE 1/100 000 should be reduced due to additive or synergistic effects on blood pressure and heart rate.

Cardiovascular monitoring (preferably by Elecrocardiogram (ECG)) is recommended.

Drugs causing arrhythmias (*e.g.*, antiarrhythmics like digitalis, quinidine): Dose of administration of SEPTANEST WITH ADRENALINE 1/100 000 should be reduced due to additive or synergistic effects on heart rate.

Careful aspiration prior to administration and cardiovascular monitoring (ECG) are recommended.

Ergot-type oxytocic drugs (*e.g*; methysergide, ergotamine, ergonovine): Use SEPTANEST WITH ADRENALINE 1/100 000 under strict medical supervision due to additive or synergistic increases in blood pressure and/or ischemic response.

Sympathomimetic vasopressors (*e.g.*, mainly cocaine but also amphetamines, phenylephrine, pseudoephedrine, oxymetazoline): There is a risk of adrenergic toxicity. If cocaine has been used within 24 hours, the planned dental treatment should be postponed.

Other sympathomimetics (*e.g.*, isoproterenol, levothyroxine, methyldopa, antihistamines (such as chlorpheniramine, diphenhydramine)): Reduced doses of SEPTANEST WITH ADRENALINE 1/100 000 should be used.

Phenothiazines (and other neuroleptics): Use under strict medical supervision and cardiovascular monitoring in case of patients with hypotension due to possible inhibition of adrenaline effect.

4.6 Fertility, pregnancy and lactation

4.6.1 Fertility

No adverse effects on fertility were observed in preclinical studies.

4.6.2 Pregnancy

No clinical studies were performed in pregnant women and no cases of pregnant women treated with injectable solution of articaine and adrenaline combination were reported in literature. Animal studies did not indicate direct or indirect harmful effects with respect to reproductive toxicity. Therefore, as a precautionary measure, it is preferable to avoid the use of SEPTANEST WITH ADRENALINE 1/100 000 during pregnancy.

4.6.3 Breastfeeding

No nursing women were included in the clinical studies with SEPTANEST WITH ADRENALINE 1/100 000. Only literature data concerning lidocaine passage in milk are available showing no risk. However, considering the lack of data for articaine, a risk to the newborns/infants cannot be excluded. Therefore, nursing women are advised not to breastfeed within 4 hours following anaesthesia with SEPTANEST WITH ADRENALINE 1/100 000.

4.7 Effects on ability to drive and use machines

Patients should not leave the dental office within 30 minutes following the dental procedure .

4.8 Undesirable effects

a) Summary of the safety profile

Adverse reactions following administration of SEPTANEST WITH ADRENALINE 1/100 000 are similar to those observed with other local amide anaesthetics combined with vasoconstrictors. These adverse reactions are, in general, dose-related and may result from high plasma levels caused by overdose, rapid absorption or unintended intra-vascular injection. They may also result from hypersensitivity, idiosyncrasy, or diminished tolerance by patient. Nervous system disorders, cardiac disorders and vascular disorders are the most frequently occurring adverse reactions.

Serious adverse reactions are generally systemic. The presence of adrenaline increases SEPTANEST WITH ADRENALINE 1/100 000's safety profile due to its sympathomimetic effects.

b) Tabulated list of adverse reactions

The reported adverse reactions come from clinical trials, spontaneous reporting and literature**.**

The frequencies classification follows the convention: Very Common (≥1/10), Common (≥1/100 - <1/10), Uncommon (≥1/1,000 - <1/100), Rare (≥1/10,000 - <1/1,000), and Very Rare (< 1/10,000). Frequency "Not known": "Not known (cannot be estimated from the available data)".

The seriousness of adverse reactions is classified from 1 (most serious) to 3 (less serious) in the following table.

MedDRA System Organ Class	Frequency	Adverse Reactions
Immune system disorders	Rare	1. Angioedema (Face / tongue / lip / throat / larynx / periorbital oedema) 2. Allergic[1], anaphylactic / anaphylactoid reactions 3. Bronchospasm / asthma Urticaria
Psychiatric disorders	Rare	Nervousness / anxiety
	Not known	Euphoric mood

MedDRA System Organ Class	Frequency	Adverse Reactions (continued)
Nervous system disorders	Common	1. Neuropathy: Neuralgia (Neuropathic pain), Hypoesthesia / numbness (oral and perioral) Dysesthesia (oral and perioral), *including* Dysgeusia (e.g., taste metallic, taste disturbance) Ageusia Allodynia Hyperesthesia Thermohyperesthesia 2. Presyncope, syncope Headache Restlessness / agitation Confusional state, disorientation Dizziness (light headedness) Tremor
	Uncommon	Burning sensation
	Rare	1. Deep CNS depression: Loss of consciousness Coma Convulsion (including tonic clonic seizure) 2. Facial nerve disorder[2](palsy, paralysis and paresis) Speech disorder (e.g., dysarthria, logorrhea) Vertigo Balance disorder (disequilibrium) Somnolence (Drowsiness) Nystagmus
	Very rare	Paresthesia[3] (persistent hypoesthesia and gustatory loss) after mandibular or inferior alveolar nerve blocks.
Eye disorders	Rare	Horner's syndrome (eyelid ptosis, enophthalmos, miosis). Diplopia (paralysis of oculomotor muscles) Mydriasis Ptosis Miosis Enophtalmos Visual impairment (temporary blindness) Vision blurred Accommodation disorder
Ear and labyrinth disorders	Rare	Tinnitus Hyperacusis
Cardiac disorders	Common	Bradycardia (also named Bradyarrhythmia)Tachycardia
	Rare	1. Cardiac arrest Myocardial depression Tachyarrhythmia (including ventricular extrasystoles and ventricular fibrillation)[4] 2. Angina pectoris[5] 3. Palpitations
	Not known	Conduction disorders (atrioventricular block)

MedDRA System Organ Class	Frequency	Adverse Reactions (continued)
Vascular disorders	Common	Hypotension (with possible circulatory collapse) Pallor (local, regional, general)
	Uncommon	Hypertension

	Rare	Hot flush
	Not known	Vasodilatation Vasoconstriction
Respiratory, thoracic and mediastinal disorders	Rare	Apnoea (respiratory arrest) Dyspnoea Hypoxia [7] Hypercapnia [7] Bradypnoea Tachypnoea Yawning
	Not known	1. Respiratory depression, 2. Dysphonia (Hoarseness)
Gastrointestinal disorders	Common	Gingivitis Swelling [6] of tongue, lip, gums
	Uncommon	Stomatitis, glossitis Nausea, vomiting, diarrhoea
	Rare	Gingival / oral mucosal exfoliation (sloughing) / ulceration
	Not known	Dysphagia
Skin and subcutaneous tissue disorders	Uncommon	Rash (eruption) Pruritus
	Not known	Erythema
Musculoskeletal and connective tissue disorders	Uncommon	Neck pain
	Rare	Muscle twitching Chills (shivering)
	Not known	Aggravation of the neuromuscular manifestations in Kearns-Sayre syndrome
General disorders and administration site conditions	Uncommon	Injection site pain
	Rare	Injection site exfoliation / necrosis Fatigue, asthenia (weakness)
	Not known	1. Local swelling 2. Hyperhidrosis Feeling hot Feeling cold

c) Description of selected adverse reactions

[1]Allergic reactions should not be mistaken with syncopal episodes (cardiac palpitations due to adrenaline).

[2]A 2-week delay in the onset of facial paralysis has been described following administration of articaine combined with adrenaline, and the condition was unchanged 6 months later.

[3]These neural pathologies may occur with various symptoms of abnormal sensations. Paresthesia can be defined as transient anaesthesia or altered sensation (tingling or itching considered as partial anaesthesia) well beyond the expected duration of anaesthesia. Most cases of paresthesia reported following dental treatment are transient and resolve within days, weeks or months.

Persistent paresthesia, mostly following nerve blocks in the mandible, is characterized by slow, incomplete, or lack of recovery.

[4]This mostly occurs in patients with underlying cardiac disease or in patients receiving certain drugs (section 4.5).

[5] This mostly occurs in patients with risk factors of ischemic heart disease.

[6] This occurs by accidental biting or chewing of the lips or tongue while the anaesthesia

persists.

[7] Hypoxia and hypercapnia are secondary to respiratory depression and/or to seizure and sustained muscular exertion.

4.9 Overdose

4.9.1 Types of overdose

Local anaesthetic overdose in the largest sense is often used to describe:

- absolute overdose,
- relative overdose such as:
  - inadvertent injection into a blood vessel, or
  - abnormal rapid absorption into the systemic circulation, or
  - delayed metabolism and elimination of SEPTANEST WITH ADRENALINE 1/100 000.

4.9.2 Symptomatology

- *Due to articaine:*

The symptoms are dose-dependent and have progressive severity in the realm of neurological manifestations, followed by vascular toxicity, respiratory toxicity, and finally cardiac toxicity (detailed in section 4.8).

- *Due to adrenaline:*

Overdose of adrenaline may cause cardiovascular effects.

4.9.3 Treatment of overdose

The availability of resuscitation equipment should be ensured before the onset of dental anaesthesia with local anaesthetics.

If acute toxicity is suspected, the injection of SEPTANEST WITH ADRENALINE 1/100 000 must immediately be stopped.

Oxygen should rapidly be administered, if necessary assisted ventilation should be used. Change patient position to supine position if necessary.

In case of cardiac arrest, immediate initiation of cardiopulmonary resuscitation should be performed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Nervous System / Local Anaesthetics / Anaesthetics, local / Amides

ATC-code: N01BB58

Mechanism of action: Articaine, a local amide anaesthetic, reversibly blocks nerve conduction through a well-known mechanism commonly observed with other local amide anaesthetics. This consists in decreasing or preventing the large transient increase in the permeability of excitable membranes to sodium (Na^+) that is normally produced by slight depolarisation of the membrane.

Adrenaline, as vasoconstrictor, acts directly on both α- and β-adrenergic receptors; β-adrenergic effects predominate.

Onset of action: SEPTANEST WITH ADRENALINE 1/100 000 has an onset of 1.5-1.8 min for infiltration and 1.4-3.6 min for nerve block.

Analgesia duration: Pulpal analgesia lasts from 45 to 75 min, and soft-tissue analgesia lasts from 120 to 360 min depending on administered dose.

Paediatric population: No difference was obtained in pharmacodynamic properties.

5.2 Pharmacokinetic properties

- *Articaine*

Absorption: In clinical trials performed in adults, peak plasma concentrations (C_{max}) of articaine were observed 24 min and 48 min following maxillary infiltration of 68 mg and of 204 mg of articaine hydrochloride 40 mg/ml with adrenaline 0.005 mg/ml, reaching respectively, 384.8 ± 164.6 ng/ml and 899.4 ± 363.3 ng/ml. In three published clinical studies describing the pharmacokinetic profile of the combination articaine hydrochloride 40 mg/ml with adrenaline 0.010 or 0.005 mg/ml, T_{max} values were between 10 and 12 minutes, with C_{max} values ranging from 400 to 2100 ng/mL.

In clinical trials performed in children, C_{max} was 1382 ng/ml and T_{max} 7.78 min following infiltration of a dose of 2 mg/kg body weight.

Distribution: In *in vitro* studies, the protein binding of articaine was shown to be independent from the articaine concentration but dependent on the type of protein. High protein binding was observed with human serum albumin (68.5-80.8%), and ∝/β-globulins (62.5-73.4%). Binding to γ-globulin (8.6-23.7%) was much lower.

The volume of distribution in plasma was about 4 l/kg.

Metabolism: All amide-type local anaesthetics are metabolised in the liver microsomes Articaine is additionally subject to hydrolysis of its carboxyl group by unspecific esterases in the tissue and in blood. Since this hydrolysis is very fast, about 90% of articaine is inactivated by this way The mean peak plasma concentrations of articainic acid, the primary metabolite of articaine, were 4-7 fold higher than those of articaine. The results of *in vitro* metabolism study pointed to articainic acid as the major product of cytochrome P450-induced metabolism of articaine.

This primary metabolite is further metabolised to form articainic acid glucuronide.

Excretion: Following dental injection, the plasmatic half-life of articaine was shown c.a. 20 min. Due to its short half-life, articaine can be reinjected within 20 min, if necessary.

In a clinical trial, plasma concentrations of articaine and articainic acid were shown to decrease rapidly following submucosal injection. Very little articaine was detected in plasma from 12 to 24 hours following injection. More than 50% of the dose was eliminated in the urine, 95% as articainic acid, within 8 hours of administration. Within 24 hours,

approximately 57% (68 mg) and 53% (204 mg) of the dose was eliminated in the urine. Renal elimination of unchanged articaine accounted for only about 2% of total elimination.

- *Adrenaline*

Adrenaline is a vasoconstrictor added to articaine to slow down absorption into the systemic circulation and thus prolong maintenance of active articaine tissue concentration. Moreover, it is also able to perform hemostasis during surgical procedure.

5.3 Preclinical safety data

Effects in non-clinical studies were only observed at doses much higher than the maximum human exposure indicating little relevance to clinical use.

General toxicity studies were performed on articaine with adrenaline 0.01 mg/ml or 0.005 mg/ml. Single and repeated 4-week dose studies involving subcutaneous administration in several species indicated that 72 or 25 mg/kg/d respectively, was the maximum tolerated dose, giving a therapeutic ratio of at least 10 for single injection and 3 for repeated administration.

I*n vitro* and *in vivo* tests used to evaluate the genotoxicity of SEPTANEST WITH ADRENALINE 1/100 000 were negative.

No effects on fertility were observed with articaine combined with adrenaline, neither were any direct embryotoxicity or teratogenicity noted with SEPTANEST WITH ADRENALINE 1/100 000. However, as a precautionary measure, it is preferable to avoid the use of SEPTANEST WITH ADRENALINE 1/100 000 during pregnancy.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride,

Sodium metabisulfite (E223),

Disodium edetate,

Sodium hydroxide (for pH-adjustment),

Water for injections.

6.2 Incompatibilities

In the absence of compatibility studies, SEPTANEST WITH ADRENALINE 1/100 000 must not be mixed with any other medicinal products.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 25°C.

In order to protect from light, keep the cartridge in the tightly closed outer carton.

Do not freeze.

6.5 Nature and contents of container

Type I glass cartridge sealed at its base by a mobile type I synthetic rubber plunger and at the top by a type I synthetic rubber seal kept in place by a metal cap.

Cartridges of 1.7 ml.

Box containing 50 cartridges.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived form such medicinal product and other handling of the product

As for any cartridge, the diaphragm should be disinfected prior to use. It should be carefully swabbed:

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

The cartridges should under no circumstance be dipped into any solution whatsoever.

One cartridge can only be used for one single patient during one single session.

No opened cartridge of anaesthetic solution should be reused. If only a part is used, the remainder must be discarded.

Any unused product or waste material should be disposed of in accordance with local requirements.