1. **NAME OF THE MEDICINAL PRODUCT**

Scandinibsa 20 mg/ml + 0.01 mg/ml, solution for injection

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

1 ml of solution for injection contains:

- Mepivacaine hydrochloride 20.0 mg
- Epinephrine tartrate 0.018 mg
  (Epinephrine base equivalent) 0.010 mg

For the full list of excipients, see section 6.1.

3. **PHARMACEUTICAL FORM**

Solution for injection.
Clear, colourless solution.

4. **CLINICAL PARTICULARS**

4.1 Therapeutic indications

Local dental anaesthesia by infiltration and nerve blockade.

4.2 Posology and method of administration

The use of Scandinibsa 20 mg/ml + 0.01 mg/ml in children under 4 years of age is not recommended.

The lowest dose required to achieve the desired anaesthesia must be used. Dosage should be adjusted individually according to the age, weight and health status of each patient.

**Posology:**

The recommended doses and maximum doses for adults and children are listed in the following table:

<table>
<thead>
<tr>
<th></th>
<th>ADULTS</th>
<th>CHILDREN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Child weighing 20 kg</td>
<td>Child weighing 40 kg</td>
</tr>
<tr>
<td><strong>Recommended dose</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in cartridges of 1.8 ml</td>
<td>1 cartridge</td>
<td>¼ cartridge</td>
</tr>
<tr>
<td>in ml of solution</td>
<td>0.5 – 2.</td>
<td>0.5 – 1</td>
</tr>
<tr>
<td>in mg of mepivacaine hydrochloride</td>
<td>10 – 40</td>
<td>10 – 20</td>
</tr>
<tr>
<td><strong>Maximum dose</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in cartridges of 1.8 ml</td>
<td>5.5 cartridges</td>
<td>1.5 cartridges</td>
</tr>
<tr>
<td>in mg/kg</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>in mg of mepivacaine hydrochloride</td>
<td>300 mg</td>
<td>88 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>176 mg</td>
</tr>
</tbody>
</table>
For infiltration and trunk blockade injections into the upper or lower jaw, a dose of 1.8 ml is generally sufficient in adults.

The dose must be reduced in patients with certain underlying diseases (angina pectoris, arteriosclerosis) (see section 4.4 “Special warnings and precautions for use”).

Administration:
Local injection (blockade or infiltration)

For use in dental anaesthesia only.

Injections must be performed slowly and with prior aspiration to prevent fast and accidental intravascular injection, which could lead to toxic effects.

4.3 Contraindications

Hypersensitivity to the drug substances or to any of the excipients.

Due to the mepivacaine content

4.3.1 Known hypersensitivity to amide-type local anaesthetics.
4.3.2 Patients with severe atroventricular conduction defects not compensated by a pacemaker.
4.3.3 Patients with degenerative nerve diseases.
4.3.4 Patients with clotting defects.
4.3.5 Uncontrolled epilepsy.
4.3.6 Acute intermittent porphyria.

Due to the epinephrine content

4.3.7 Heart diseases such as:
   4.3.8 Unstable angina pectoris.
   4.3.9 Recent myocardial infarction.
   4.3.10 Recent coronary artery bypass surgery.
   4.3.11 Refractory arrhythmias and paroxysmal or high-frequency tachycardia, continuous arrhythmia.
   4.3.12 Untreated or uncontrolled severe hypertension.
   4.3.13 Untreated or uncontrolled congestive heart failure.

Due to the sodium metabisulfite content

4.3.14 Allergy or hypersensitivity to sulfite.
4.3.15 Severe bronchial asthma.

4.4 Special warnings and precautions for use

Warnings
The patient should be warned that anaesthesia may increase the risk of damage to the lips, tongue, mucous membrane or soft palate. The intake of food must be avoided until the anaesthesia has worn off.

The use of Scandinibsa 20 mg/ml + 0.01 mg/ml in children under 4 years of age is not recommended.

The injection of local anaesthetics into infected regions must be avoided.
Athletes must be informed that this medicinal product contains an active substance which may produce a positive result in anti-doping control.

The presence of sodium metabisulfite as excipient may cause the onset of allergic-type reactions, including anaphylactic-type reactions and bronchospasm in especially susceptible patients, particularly those with a history of asthma or allergies.

**Precautions**

Before the administration of a local anaesthetic, full resuscitation equipment, including an oxygenation and assisted ventilation system, and the drugs required to treat possible toxic reactions, must be available.

Local dental anaesthetics contain high concentrations of an active substance. This means that fast injection at high pressure may lead to complications, even when only small quantities are administered (see section 4.9). The risk is particularly high in the case of involuntary intravascular injection as the medicinal product injected may be transferred in a retrograde manner. Intra-arterial injection in the head and neck region leads to high concentrations of medicinal product, which reaches the brain to a greater extent than in the case of intravenous injection. Careful aspiration should be performed prior to injection to reduce the risk of intravascular injection.

The preparation should be administered with care, even in the case of dental anaesthesia with low doses, in subjects with diseases such as:
- Patients with partial or total heart block as local anaesthetics may lead to myocardial conduction depression.
- Patients with advanced hepatic disease or severe renal dysfunction.
- Elderly and weakened patients.

It should also be noted that local anaesthetics must be administered with care in patients with severe untreated hypertension, major cardiac disease, anaemia, circulatory impairment or severe cardiovascular disease. Monitoring of patients with blood clotting problems or low anticoagulants (INR monitoring) must be increased.

Scandinibsa 20 mg/ml + 0.01 mg/ml solution for injection contains epinephrine therefore it must be used with care in patients with severe or untreated hypertension, insufficiently treated thyrotoxicosis, ischaemic heart disease, heart block, cerebrovascular impairment, advanced diabetes, narrow-angle glaucoma and any other pathological condition that may worsen the effects of epinephrine.

### 4.5 Interaction with other medicinal products and other forms of interaction

Mepivacaine must be used with care in patients who are also receiving pharmacological agents that present structural similarities to local anaesthetics (for example, class Ib antiarrhythmic agents) as their toxic effects are additive in nature.

Prolonged or permanent treatment with antiarrhythmic agents, psychotroipic drugs or anticonvulsants, and the consumption of alcohol, may reduce sensitivity to anaesthetics. It is sufficient to increase the anaesthetic dose or simply wait for it to act for longer prior to the intervention.

Care must be taken with dosing in the event of simultaneous use of medicinal products that produce CNS depression as they may provoke additive effects.
Local anaesthetics may release heavy metal ions from some disinfectant solutions. Special measures must be taken when using this type of disinfectant prior to administering the anaesthetic. These released ions may provoke local irritation, swelling and oedema.

The administration of heparin, non-steroidal anti-inflammatory agents or plasma substitutes (dextran) may increase the likelihood of haemorrhage after the injection of local anaesthetics.

Epinephrine must be used with care in patients receiving tricyclic antidepressants as it may provoke a severe and prolonged hypertension. Moreover, the frequent use of solutions with epinephrine and ergotamine-type oxytocic drugs may cause severe and persistent hypertension, heart attack and stroke.

Phenothiazines and butyrophenones can reduce or reverse the vasopressor effect of epinephrine.

Solutions containing epinephrine must be used with care in patients subjected to general anaesthesia with inhalational agents, such as halothane, due to the risk of serious cardiac arrhythmias.

Non-selective beta-blockers, such as propranolol, increase the vasopressor effect of epinephrine, which may lead to severe hypertension and bradycardia.

4.6 Fertility, pregnancy and lactation

Pregnancy

Data from a limited number of pregnant women do not indicate adverse reactions of mepivacaine during pregnancy or on the health of the foetus or newborn. No other relevant epidemiological information is available to date. The potential risk for humans is unknown.

Breast-feeding:

Mepivacaine is excreted in breast milk. However, in light of the therapeutic doses of Scandinibsa 20 mg/ml + 0.01 mg/ml solution for injection, no effects on the infant are expected and it may be used during breast-feeding.

4.7 Effects on ability to drive and use machines

The influence of Scandinibsa 20 mg/ml + 0.01 mg/ml solution for injection on the ability to drive and use machines is small to moderate, although it may slightly affect motor response and coordination in a temporary manner depending on the local anaesthetic dose.

4.8 Undesirable effects

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

The adverse reactions strictly attributable to the local anaesthetic are limited. However, the physiological effects of nerve blockade are common, although they vary considerably depending on the type of blockade administered. The effects of an involuntary intravascular injection or overdose may be serious and should be taken into account (see section 4.9. Overdose).
The following adverse reactions can occur as a result of the content of mepivacaine as local anaesthetic:

Rare (1/10,000, <1/1,000):

- Nervous system disorders: Unconsciousness and seizures (in the event of absolute or relative overdose).
- Neurological effects (for example, feeling of numbness, residual paresthesia and other sensory problems) have been observed. It has not been clearly established to what extent these symptoms depend on technical aspects (for example intraneural injection) or the anaesthetic.
- Cardiac disorders: Myocardial depression and cardiac arrest (in patients with absolute or relative overdose).
- General disorders: Allergic reactions (skin rash, erythema, pruritus, oedema of the tongue, mouth, lips or throat) and, in the most severe cases, anaphylactic shock. Methemoglobinaemia

The following adverse reactions can occur as a result of the content of epinephrine as a vasoconstrictor component:

Rare (≥1/10,000, <1/1,000)

- Cardiovascular disorders: Hot sensation, sweating, accelerated pulse, migraine-type headaches, increased blood pressure, angina pectoris disorders, tachycardias, tachyarrhythmias, and cardiac arrest, and oedematous swelling of the thyroids cannot be excluded.

The following adverse reactions can occur as a result of the content of sodium metabisulfite and methyl para-hydroxybenzoate as excipients:

Very rare (<1/10,000)

- Particularly in bronchial asthmatics, allergic or hypersensitivity reactions which are manifested as vomiting, diarrhoea, wheezing, acute asthma attack, clouding of the consciousness or shock may occur.

4.9 Overdose

4.9.1. Toxicity

Toxic adverse reactions may appear at plasma concentrations of 5-6 mg/ml or higher due to an overdose, rapid absorption or accidental intravascular injection, or to a hypersensitivity, idiosyncrasy or reduced tolerance on the part of the patient.

Central nervous system

CNS toxicity occurs gradually with symptoms and reactions that progressively worsen. Initial symptoms include agitation, a feeling of intoxication and numbness of the lips and tongue, paresthesia around the mouth, dizziness, visual and hearing problems and ringing in the ears. If these effects are observed whilst performing the injection they must be considered to be a warning sign and the injection must therefore be stopped immediately. Speech difficulties, muscle stiffness or spasms are more serious symptoms that precede generalised seizures. These symptoms must not be erroneously interpreted as neurotic behaviour. Unconsciousness and epileptic attacks that last from a few seconds up to several minutes may occur. A lack of oxygen and hypercapnia occur during the seizures due to increased muscle activity and lack of ventilation. Respiratory arrest may occur in the most serious cases. Acidosis increases the toxic effects of local anaesthetics.

Recovery depends on metabolism of the local anaesthetic and its distribution outside the central nervous system. This occurs rapidly provided large quantities of the medicinal product are not administered.
Cardiovascular system
Cardiovascular effects generally tend to lead to a more serious situation. A drop in blood pressure, bradycardia, arrhythmia and cardiac arrest may occur as a result of high systemic concentrations of local anaesthetic. These effects are generally preceded by signs of CNS toxicity unless the patient has received general anaesthesia or is heavily sedated with components such as benzodiazepines or barbiturates. However, it should be noted that central blockades themselves often lead to a sympathetic blockade, which produces a drop in blood pressure and, possibly, bradycardia.

Symptoms caused by epinephrine as vasoconstrictor:
Cardiovascular symptoms such as hot sensation, sweating, accelerated heart rate, headaches, increased blood pressure, angina pectoris disorders, tachycardia, tachyarrhythmias and cardiovascular arrest.
The simultaneous occurrence of several complications and adverse reactions may interfere with the clinical picture.

4.9.2. Treatment
If signs of acute systemic toxicity appear, the injection of anaesthetic must be interrupted immediately.

Any seizures that occur must be treated immediately, therefore suitable equipment and drugs must be available. The objectives of treatment are to maintain oxygenation, stop the seizures and maintain circulation.

Administration of oxygen is generally sufficient to treat the symptoms of seizures. Assisted ventilation may be administered if necessary.
If the seizures do not stop spontaneously within 15-20 seconds, an intravenous anticonvulsant must be administered. A dose of 100-150 mg IV thiopentone will stop the seizures rapidly.
Alternatively, a dose of 5-10 mg IV diazepam may be used, although its action is inferior. Suxamethonium will rapidly stop muscle seizures but will require tracheal intubation and controlled ventilation.

If cardiovascular depression is clear (hypotension, bradycardia), 5-10 mg IV ephedrine must be administered, repeating the dose at 2-3 minutes if necessary.

In the event of circulatory arrest, cardiopulmonary resuscitation must be performed immediately. Optimal oxygenation, ventilation and circulatory support, as well as treatment of the acidosis, are of vital importance as hypoxia and acidosis increase the toxicity of local anaesthetics.
Epinephrine (0.1-1.2 mg intravenous or intracardiac) must be administered as soon as possible and the dose repeated if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Local anaesthetics: amides; ATC code: N01BB03.

As is the case with other local anaesthetics, mepivacaine exerts a reversible blockade of impulse propagation along the nerve fibres, thereby preventing the movement of sodium ions through the nerve membrane.
Amide-type local anaesthetics act inside the sodium channels of the nerve membrane.

Local anaesthetic drugs have similar effects on the excitable membranes in the brain and myocardium. If excessive quantities of the drug rapidly reach systemic circulation, signs and symptoms of toxicity appear, mainly in the central nervous system and cardiovascular system.

Dental mepivacaine acts rapidly after infiltration, within around 2-3 minutes. Lower alveolar nerve blockade requires 5 minutes or more to achieve full effect. The duration of the anaesthesia varies according to the individual and the anaesthetic technique used. The mean duration of anaesthesia post-infiltration is 20 minutes. After satisfactory regional anaesthesia, such as lower alveolar nerve blockade, anaesthesia will last for 2 hours or more. This time can be increased by using solutions containing epinephrine.

Epinephrine causes local vasoconstriction, thereby delaying the absorption of mepivacaine. The result is a greater concentration of local anaesthetic at the site of administration over a longer period of time, as well as a reduction in the possible occurrence of systemic adverse side effects.

5.2 Pharmacokinetic properties

Absorption of the local anaesthetic depends on its physicochemical (for example lipid solubility) and pharmacological properties (for example vasodilatory effect) as well as on the vasculature at the injection site.

The bioavailability is 100% at the site of action.

The peak plasma concentration of mepivacaine is reached after approximately 30-60 minutes.

The plasma protein binding of mepivacaine is 60-78% (mainly to alpha-1-acid glycoprotein).

Mepivacaine is distributed throughout all body tissues. The highest concentrations of mepivacaine are found in the liver, lungs, heart and brain.

Mepivacaine crosses the placental barrier by simple diffusion. The maternal/foetal plasma concentration ratio is 0.4-0.8.

The plasma half-life is 2-3 hours in adults and 9 hours in newborns. The elimination of amides depends on blood flow to the liver. The plasma half-life is extended if the patient suffers from a hepatic disorder and/or uraemia.

Metabolism mainly occurs by oxidation in the liver. The metabolites are mainly eliminated in bile and 99% by glucuronidation. They are immediately reabsorbed and eliminated in the urine. The pH of the urine affects metabolite elimination.

Only 3-5% of mepivacaine is eliminated unchanged in adults, and approximately 40% in newborns.

Mepivacaine is excreted in human breast milk, although the quantity eliminated after a therapeutic dose is so small that there is no risk of an effect on the infant.

5.3 Preclinical safety data
Data from non-clinical studies reveal no special hazard for humans based on conventional pharmacological safety, repeated-dose toxicity, genotoxicity, carcinogenic potential and reproductive toxicity studies.

As is the case for other amide-type local anaesthetics, the active substance may produce central nervous system and cardiovascular system reactions at high doses (see section 4.8. Undesirable effects).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium metabisulfite
Methyl para-hydroxybenzoate
Hydrochloric acid (to alter the pH)
Water for injectable preparations

6.2 Incompatibilities

A risk of precipitation exists at a pH above 6.5. This characteristic must be taken into account when adding basic solutions, such as carbonates.

In solutions with epinephrine, mixing with alkaline solutions may cause rapid degradation of the vasoconstrictor.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Keep in the original package to protect it from light.

6.5 Nature and contents of container

Type I neutral colourless glass cartridges
Stopper and rubber discs made from bromobutyl rubber.
The aluminium capsule is made with a bromobutyl double-disc.

Scandinibsa 20 mg/ml + 0.01 mg/ml solution for injection is presented in boxes containing 100 cartridges of 1.8 ml each.

6.6 Special precautions for disposal

Cartridges for single use only.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

INIBSA DENTAL, S.L.U.
Ctra. Sabadell a Granollers, km. 14.5
8 MARKETING AUTHORISATION NUMBER
Reg. no. 56,202

9 DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION
04/06/1984

10 DATE OF REVISION OF THE TEXT
July 2008