1. NAME OF THE MEDICINAL PRODUCT

SCANDINIBSA 30 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution for injection contains:

Mepivacaine hydrochloride	30.0 mg
Methyl para-hydroxybenzoate (E-218)	0.6 mg

One cartridge (1.8 ml) contains:

Mepivacaine hydrochloride	54.0 mg
Methyl para-hydroxybenzoate (E-218)	1.08 mg

Each 1.8 ml cartridge contains: 4.25 mg of sodium

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

SCANDINIBSA 30 mg/ml is indicated for local dental anaesthesia (by infiltration and nerve blockade) in adults and children aged 4 years or older.

4.2 Posology and method of administration

Posology:
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.

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

		ADULTS	**CHILDREN**	
			Child of 20 kg	Child of 40 kg
Recommended dose	in cartridges of 1.8 ml	1 cartridge	¼ cartridge	½ cartridge
	In ml of solution	0.5-2	0.5-1	
	in mg of mepivacaine hydrochloride	15-60	15-30	
Maximum dose	in cartridges of 1.8 ml	5.5 cartridges	1.5 cartridges	3 cartridges

	in mg/kg	5	5

	in mg of mepivacaine hydrochloride	300 mg	88 mg	176 mg

For infiltration and trunk blockade injections into the upper or lower jaw, a dose of 54 mg of mepivacaine hydrochloride (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”).

Paediatric population:
The use of SCANDINIBSA 30 mg/ml in children younger than 4 years of age is not recommended due to the unsuitability of this anaesthetic technique prior to this age.

Method of administration:
Local injection into the oral mucosa.
ONLY FOR USE IN DENTAL ANAESTHESIA.

To prevent intravascular injection, an aspiration control in at least two planes (rotation of the needle by 180º) must always be carried out, although a negative aspiration result cannot rule out an involuntary and unnoticed intravascular injection.

For single use only Previously opened cartridges must not be used in other patients. Any unused solution must be disposed of.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Due to its mepivacaine content, Scandinibsa 30 mg/ml should not be used in patients with:
- A known hypersensitivity to amide-type local anaesthetics.
- Severe atrioventricular conduction defects not compensated by a pacemaker.
- Degenerative nerve disease.
- Clotting defects.
- Uncontrolled epilepsy.
- Acute intermittent porphyria.

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 30 mg/ml in children younger than 4 years of age is not recommended due to the unsuitability of this anaesthetic technique before this age.

The injection of local anaesthetics into infected regions must be avoided.

Precautions for use

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 the 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.

In the case of intraneural injection, there is a risk that the medicinal product may be transferred via the nerve in a retrograde manner due to the high pressure. To avoid intraneural injection and prevent nerve damage related to nerve blockade, the needle should be removed slowly if paresthesia occurs during the 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.

Mepivacaine use requires an appointment to determine the medical history and concomitant medication and to perform a challenge injection of 5% to 10% of the dose in the event of allergic risk.

This medicine contains methyl para-hydroxybenzoate (E-218), which may produce allergic reactions (possibly delayed) and, on occasions, bronchospasm.

This medicine also contains 4.25 mg of sodium per cartridge. This may be harmful for patients with sodium-poor diets.

Paediatric population

People accompanying small children must be warned that, due to the prolonged insensitivity of soft tissue, there is a risk that the child may accidentally bite him- or herself.

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, psychotropic drugs or anticonvulsants, and the consumption of alcohol, may reduce the 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-inflammatories or plasma substitutes (dextran) may increase the likelihood of haemorrhage after the injection of local anaesthetics.

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 human breast milk. However, in light of the therapeutic doses of SCANDINIBSA 30 mg/ml, 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 30 mg/ml 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

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*).

Nervous system disorders:

Rare (≥1/10,000 to <1/1,000)

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:

Rare (≥1/10,000 to <1/1,000)

Myocardial depression and cardiac arrest (in patients with absolute or relative overdose).

General disorders and administration site conditions: *Rare:*

(≥1/10,000 to <1/1,000)

Allergic reactions: skin rash, erythema, pruritus, oedema of the tongue, mouth lips or throat and, in the most severe cases, anaphylactic shock.

Methemoglobinaemia

Very rare

(<1/10,000):

In bronchial asthmatics, and due to the methyl para-hydroxybenzoate (E-218) content, allergic or hypersensitivity reactions, which manifest as vomiting, diarrhoea, wheezing, acute asthma attack, clouding of the consciousness or shock, may occur.

4.9 Overdose

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.

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.

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 vascularity 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 69-78% (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 lover. 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

Methyl para-hydroxybenzoate (E-218)
Sodium chloride
Sodium hydroxide (to adjust the pH)
Water for injection

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.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

No special storage conditions required.

6.5 Nature and contents of container

Cartridges of neutral colourless glass (type I).
Stopper and rubber discs made from bromobutyl rubber.
The aluminium cap is manufactured with a double bromobutyl disc.

Pack containing 1 1.8 ml cartridge with flat plunger for self-aspiration.
Pack containing 1 1.8 ml cartridge with cavity plunger for manual aspiration.
Pack containing 100 1.8 ml cartridges with flat plunger for self-aspiration.
Pack containing 100 1.8 ml cartridges with cavity plunger for manual aspiration.

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

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11/2012