1. NAME OF THE MEDICINAL PRODUCT

Scandinibsa 20 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution contains:

Mepivacaine hydrochloride 20.0 mg/ml

For the 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

Local anaesthesia by infiltration, central and peripheral nerve block, regional intravenous anaesthesia and epidural anaesthesia for therapeutic and diagnostic purposes.

4.2 Posology and method of administration

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:**
In general, high concentrations of the drug are required to achieve the complete block of all nerve fibres in long nerves. In short nerves, or when nerve block is minor, lower concentrations of drug are required. The volume of drug administered will affect the extent and depth of anaesthesia.

Experience to date suggests that administration of 100 mg of drug over a period of 24 hours is well tolerated in the majority of adults.

In children, the dose must be calculated according to weight, with a maximum dose of 5 mg/kg.

Administration of mepivacaine in newborns is not recommended.

The following table lists the recommended doses in adults for the most commonly used anaesthetic techniques. There are important individual variations as regards the onset and duration of action.
<table>
<thead>
<tr>
<th>Type of block</th>
<th>Concentration (mg)</th>
<th>Dosing (ml)</th>
<th>Onset (min.)</th>
<th>Duration (h)</th>
<th>Indications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local infiltration</td>
<td>10</td>
<td>1.0</td>
<td>≤40</td>
<td>≤400</td>
<td>1 – 2</td>
<td>2 – 3 Surgery</td>
</tr>
<tr>
<td>Digital block</td>
<td>10</td>
<td>1.0</td>
<td>1 – 5</td>
<td>10 – 50</td>
<td>2 – 5</td>
<td>1.5 – 2 Surgery</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Surgery Post-operative analgesia broken ribs</td>
</tr>
<tr>
<td>Intercostal</td>
<td>10</td>
<td>1.0</td>
<td>2 – 5</td>
<td>20 – 50</td>
<td>3 – 5</td>
<td>1 – 2 Surgery Post-operative analgesia broken ribs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-operative analgesia broken ribs</td>
</tr>
<tr>
<td>Paracervical</td>
<td>10</td>
<td>1.0</td>
<td>10</td>
<td>100</td>
<td>3 – 5</td>
<td>1 – 1.5 Surgery Dilatation of the cervix</td>
</tr>
<tr>
<td>Intra-articular block</td>
<td>10</td>
<td>1.0</td>
<td>≤40</td>
<td>≤400</td>
<td>5 – 10</td>
<td>Arthroscopy Surgical</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Surgery</td>
</tr>
<tr>
<td>Retrobulbar</td>
<td>20</td>
<td>2.0</td>
<td>4</td>
<td>80</td>
<td>3 – 5</td>
<td>1.5 – 2 Eye surgery</td>
</tr>
<tr>
<td>Peribulbar</td>
<td>10</td>
<td>1.0</td>
<td>10 – 15</td>
<td>100 – 150</td>
<td>3 – 5</td>
<td>1.5 – 2 Eye surgery</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See section 4.4. Precautionary measures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Not recommended during childbirth</td>
</tr>
<tr>
<td>Brachial plexus: Axillary</td>
<td>10</td>
<td>1.0</td>
<td>40 – 50</td>
<td>400 – 500</td>
<td>15 – 30</td>
<td>1.5 – 2 Surgery</td>
</tr>
<tr>
<td>Interscalene subclavicular and</td>
<td>10</td>
<td>1.0</td>
<td>30 – 40</td>
<td>300 – 400</td>
<td>15 – 30</td>
<td>1.5 – 2 Surgery</td>
</tr>
<tr>
<td>subclavian perivascular</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sciatic</td>
<td>20</td>
<td>2.0</td>
<td>15 – 20</td>
<td>300 – 400</td>
<td>15 – 30</td>
<td>2 – 3 Surgery</td>
</tr>
<tr>
<td>3 in 1</td>
<td>10</td>
<td>1.0</td>
<td>30 – 40</td>
<td>300 – 400</td>
<td>15 – 30</td>
<td>1.5 – 2 Surgery</td>
</tr>
<tr>
<td>Femoral, obturator and lateral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cutaneous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbar epidural</td>
<td>20</td>
<td>2.0</td>
<td>15 – 25</td>
<td>300 – 500</td>
<td>15 – 20</td>
<td>1.5 – 2 Surgery</td>
</tr>
<tr>
<td>Thoracic epidural</td>
<td>20</td>
<td>2.0</td>
<td>10 – 15</td>
<td>200 – 300</td>
<td>10 – 20</td>
<td>1.5 – 2 Surgery</td>
</tr>
<tr>
<td>Caudal epidural</td>
<td>10</td>
<td>1.0</td>
<td>20 – 30</td>
<td>200 – 300</td>
<td>15 – 30</td>
<td>1 – 1.5 Surgery and analgesia</td>
</tr>
<tr>
<td>(children)</td>
<td>20</td>
<td>2.0</td>
<td>15 – 25</td>
<td>300 – 500</td>
<td>15 – 30</td>
<td>1.5 – 2 Surgery</td>
</tr>
<tr>
<td>Caudal epidural</td>
<td>10</td>
<td>1.0</td>
<td>0.5 ml/kg</td>
<td>5 mg/kg</td>
<td>10 – 15</td>
<td>1 – 2 Surgery</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
Administration:
Local injection (block or infiltration)

SCANDINIBSA must be administered with care to prevent acute toxicity reaction due to inadvertent intravascular injection. In all cases, an aspiration must be performed prior to and during the injection to prevent intravascular injection.

The local anaesthetic must not be administered into infected regions.

The main dose must be administered slowly, at a rate of up to 100-200 mg/min, or in dose increases, maintaining constant verbal contact with the patient. If symptoms of toxicity are observed, administration must be stopped immediately. Accidental intravascular injection can be detected by a temporary increase in heart rate.

For a more prolonged effect, the anaesthetic drug can be injected via a permanent catheter. This is a common technique in epidural anaesthesia, and can also be used in brachial plexus anaesthesia and interpleural anaesthesia.

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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Due to the mepivacaine content:
- Known hypersensitivity to amide-type local anaesthetics.
- Patients with severe atrioventricular conduction defects not compensated by a pacemaker.
- Patients with degenerative nerve diseases.
- Patients with clotting defects.
- Uncontrolled epilepsy.
- Acute intermittent porphyria.

4.4 Special warnings and precautions for use

Warnings

Administration during childbirth is not recommended as mepivacaine readily crosses the placental barrier and neonatal metabolism is slow, thus increasing the toxic potential for the foetus and newborn.

The use of Scandinibsa 20 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.

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.
Regional or local anaesthetic processes, except those of a minor nature, must always be performed by suitably trained professionals in areas with immediate access to resuscitation equipment and medications. Specialists must have received appropriate training in such procedures and must be familiar with the diagnosis and treatment of side effects, systemic toxicity and other complications (see section 4.9. Overdose).

When major blocks are performed, a catheter must be inserted prior to injecting the anaesthetic.

Some local anaesthetic procedures may be associated with serious adverse reactions irrespective of the anaesthetic drug used:
- Central nerve block may cause cardiovascular depression, especially in the presence of hypovolaemia. Epidural anaesthesia must be used with care in patients with weak cardiovascular function.
- Retrobulbar injections may occasionally reach the cranial subarachnoid space, causing temporary blindness, cardiovascular collapse, apnoea, seizures, etc. These must be diagnosed and treated rapidly.
- Retro- and peribulbar injections of local anaesthetics carry a small risk of permanent dysfunction of the eye muscle. The main causes include trauma and/or local toxicity on the muscles and/or nerves. The severity of these tissue reactions is related to the degree of trauma, the concentration of local anaesthetic and the duration of exposure of the tissue to the local anaesthetic. Therefore, and as is the case for other local anaesthetics, the lowest effective dose must be used.
- If the anaesthetic is administered in regions of the head and neck, it must be considered that an inadvertent intravascular injection, which may cause serious adverse reactions even at low doses, may occur.
- Paracervical block may occasionally cause foetal bradycardia/tachycardia, therefore foetal heart rate must be monitored.
- When prolonged blocks are used, as in the case of repeated administrations, the risk of reaching a toxic plasma concentration or inducing localised neuronal deterioration must be considered.
- Epidural anaesthesia may result in hypotension and bradycardia. This risk can be reduced by circulatory preload with colloidal or crystalloidal solutions, or by injection of a vasoconstrictor such as ephedrine at a dose of 20-40 mg i.m. Hypotension must be treated immediately with ephedrine at a dose of 5-10 mg intravenously, repeating the dose if necessary.

Some patients require special care to reduce the side-effects:
- 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.
Regional anaesthesia is often indicated in these patients. Attempts must be made to optimise the state of the patient prior to administering a general anaesthesia prior to performing a block of major nerves.

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.

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 Pregnancy and breast-feeding

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.

The administration of mepivacaine during childbirth is not recommended (see section 4.4. Special warnings and precautions for use).

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

4.7 Effects on ability to drive and use machines

The influence of Scandinibsa 20 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

Adverse reactions to local anaesthetics are rare (≥1/10,000 to <1/1,000), except in the case of overdose or inadvertent intravascular injection. Such reactions must be differentiated from the physiological effects of the nerve block itself, such as decreased blood pressure and bradycardia during epidural anaesthesia.
The effects of overdose and accidental intravascular injection may be serious (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 to <1/1000)

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 accidental intravascular injection) or the anaesthetic.

Medical and surgical procedures: Depending on the regional anaesthetic technique used, and irrespective of the type of anaesthetic, nerve trauma, neuropathy, occlusion of the anterior spinal artery and arachnoiditis may occur.

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

General disorders: Allergic reactions to amide-type local anaesthetics (skin rash, erythema, pruritus, oedema of the tongue, mouth, lips or throat) and, in the most severe cases, anaphylactic shock. Methemoglobinemia.

4.9 Overdose

4.9.1. Toxicity

In the case of accidental intravascular injection, the toxic effect becomes clear within 1 to 3 minutes, whereas in the event of overdose the peak plasma concentration may not be reached for up to 20-30 minutes, depending on the site of injection, such that the signs of toxicity are delayed. Toxic reactions mainly affect the central nervous system and cardiovascular system.

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.

Recuperation depends on metabolism of the local anaesthetic and its distribution outside the central nervous system. Metabolisation is rapid provided large quantities of the medicinal product are not injected.

Cardiovascular system

Cardiovascular effects generally tend to lead to a more serious situation. A 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 decrease in blood pressure and, on occasions, bradycardia.

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 block 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.

Central nervous system toxicity (see section 4.9. Overdose) normally precedes the cardiovascular effects as it occurs at lower plasma concentrations. The direct effects of local anaesthetics on the heart include slow conduction, negative inotropism and, occasionally, cardiac arrest. The indirect cardiovascular effects (hypotension, bradycardia) may occur after epidural or spinal administration, depending on the extent of concomitant sympathetic block.
5.2 Pharmacokinetic properties

The rate of absorption depends on the dose, route of administration and vascularisation of the injection site. The highest plasma concentrations are achieved with intercostal block (approx. 1.6 µg/ml per 100 mg injected).

Epidural and brachial plexus block lead to plasma concentrations of 0.75 - 1.0 µg/ml.

Mepivacaine exhibits biphasic absorption after epidural injection. The maximum concentration is reached at 15-20 minutes. The steady-state volume of distribution is 84 litres.

The bioavailability is 100% at the site of action.

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 of 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 by 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 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 hydroxide (to adjust 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.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

No special storage conditions required.

6.5 Nature and contents of container

Vial of type I neutral glass, hydrolytic resistance.

Presentations:

Pack containing 1 vial or 100 vials of 2 ml.
Pack containing 1 vial or 100 vials of 10 ml.

6.6 Special precautions for disposal

Cartridges for single use only.
Any unused medicinal product or material that has been in contact with it should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Inibsa Hospital S.L.U.
Ctra. Sabadell a Granollers km 14,5
08185 Lliçà de Vall – Barcelona
Spain

8. Marketing Authorisation Number(s)

37.725

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

08/05/1962

10. DATE OF REVISION OF THE TEXT

July 2008