SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Brand Name: NURABUCAIN
Bupivacaine Hydrochloride in Dextrose Injection USP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Bupivacaine Hydrochloride USP
Eq. to Anhydrous Bupivacaine……. 5.0 mg
Dextrose Monohydrate USP……80 mg
Water for injection USP……. Q.S.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nurabucain injection is indicated in adults and children of all ages for intrathecal (subarachnoid) spinal anaesthesia for surgery (urological and lower limb surgery lasting 2–3 hours, abdominal surgery lasting 45–60 minutes).

4.2 Posology and method of administration

Adults and children above 12 years of age

The doses recommended below should be regarded as a guide for use in the average adult. The figures reflect the expected average dose range needed. Standard textbooks should be consulted for factors affecting specific block techniques and for individual patient requirements. The clinician's experience and knowledge of the patient's physical status are of importance in calculating the required dose. The lowest dose required for adequate anaesthesia should be used. Individual variations in onset and duration occur, and the extent of the spread of anaesthesia may be difficult to predict, but will be affected by the volume of the drug used, especially with the isobaric (plain) solution.

Dosage recommendations

Intrathecal anaesthesia for surgery:
2-4 ml (10-20 mg bupivacaine hydrochloride).
The dose should be reduced in the elderly and in patients in the late stages of pregnancy, see Section 4.4.

Neonates, infants and children up to 40 kg

Nurabucain Heavy may be used in children.

One of the differences between small children and adults is a relatively high CSF volume in infants and neonates, requiring a relatively larger dose/kg to produce the same level of block as compared to adults.
Paediatric regional anaesthesia procedures should be performed by qualified clinicians who are familiar with this population and the techniques.
The doses in the table should be regarded as guidelines for use in paediatric patients. Individual variations occur. Standard textbooks should be consulted for factors affecting specific block technique and for individual patient requirements. The lowest dose required for adequate anaesthesia should be used.

Dosage recommendations in neonates, infants and children

Body weight (kg)	**Dose (mg/kg)**
<5	0.40-0.50 mg/kg
5 to 15	0.30-0.40 mg/kg
15 to 40	0.25-0.30 mg/kg

The spread of anaesthesia obtained with Nurabucain Heavy depends on several factors including the volume of solution and the position of the patient during and following the injection.

When injected at the L3–L4 intervertebral space, with the patient in the sitting position, 3 ml of Nurabucain Heavy spreads to the T7–T10 spinal segments. With the patient receiving the injection in the horizontal position and then turned supine, the blockade spreads to T4–T7 spinal segments. It should be understood that the level of spinal anaesthesia achieved with any local anaesthetic can be unpredictable in a given patient.

The recommended site of injection is below L3.
The effects of injections of Nurabucain Heavy exceeding 4 ml have not yet been studied and such volumes can therefore not be recommended.

Method of administration
Route of administration: For intrathecal injection.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Hypersensitivity to local anaesthetics of the amide type.
Intrathecal anaesthesia, regardless of the local anaesthetic used, has its own contraindications, which include:
• Active disease of the central nervous system such as meningitis, poliomyelitis, intracranial haemorrhage, sub-acute combined degeneration of the cord due to pernicious anaemia and cerebral and spinal tumours.
• Spinal stenosis and active disease (e.g. spondylitis, tuberculosis, tumour) or recent trauma (e.g. fracture) in the vertebral column.
• Septicaemia.
• Pyogenic infection of the skin at or adjacent to the site of lumbar puncture.
• Cardiogenic or hypovolaemic shock.
• Coagulation disorders or ongoing anticoagulation treatment.

4.4 Special warnings and precautions for use

Intrathecal anaesthesia should only be undertaken by clinicians with the necessary knowledge and experience.

Regional anaesthetic procedures should always be performed in a properly equipped and staffed area. Resuscitative equipment and drugs should be immediately available and the anaesthetist should remain in constant attendance.

Intravenous access, e.g. an i.v. infusion, should be in place before starting the intrathecal anaesthesia. The clinician responsible should take the necessary precautions to avoid intravascular injection and be appropriately trained and familiar with the diagnosis and treatment of side effects, systemic toxicity and other complications. If signs of acute systemic toxicity or total spinal block appear, injection of the local anaesthetic should be stopped immediately.

Like all local anaesthetic drugs, bupivacaine may cause acute toxicity effects on the central nervous and cardiovascular systems, if utilised for local anaesthetic procedures resulting in high blood concentrations of the drug. This is especially the case after unintentional intravascular administration or injection into highly vascular areas.

Ventricular arrhythmia, ventricular fibrillation, sudden cardiovascular collapse and death have been reported in connection with high systemic concentrations of bupivacaine. Should cardiac arrest occur, a successful outcome may require prolonged resuscitative efforts. High systemic concentrations are not expected with doses normally used for intrathecal anaesthesia.

There is an increased risk of high or total spinal blockade, resulting in cardiovascular and respiratory depression, in the elderly and in patients in the late stages of pregnancy. The dose should therefore be reduced in these patients.

Intrathecal anaesthesia can cause hypotension and bradycardia. The risk of such effects can be reduced, e.g., by injecting a vasopressor. If hypotension develops it should be treated promptly with a sympathomimetic intravenously, repeated as necessary. Severe hypotension may result from hypovolaemia due to haemorrhage or dehydration, or aorto-caval occlusion in patients with massive ascites, large abdominal tumours or late pregnancy. Marked hypotension should be avoided in patients with cardiac decompensation.

Patients with hypovolaemia due to any cause can develop sudden and severe hypotension during intrathecal anaesthesia.

Intrathecal anaesthesia can cause intercostal paralysis and patients with pleural effusions may suffer respiratory embarrassment. Septicaemia can increase the risk of intraspinal abscess formation in the postoperative period.

Neurological injury is a rare consequence of intrathecal anaesthesia and may result in paraesthesia, anaesthesia, motor weakness and paralysis. Occasionally these are permanent. Before treatment is instituted, consideration should be taken if the benefits outweigh the possible risks for the patient.

Patients in poor general condition due to ageing or other compromising factors such as partial or complete heart conduction block, advanced liver or renal dysfunction require special attention, although regional anaesthesia may be the optimal choice for surgery in these patients.

Patients treated with anti-arrhythmic drugs class III (e.g. amiodarone) should be kept under close surveillance and ECG monitoring considered, since cardiac effects may be additive.

4.5 Interaction with other medicinal products and other forms of interaction

Bupivacaine should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics, e.g. certain anti-arrhythmics, such as lidocaine and mexiletine, since the systemic toxic effects are additive.

Specific interaction studies with bupivacaine and anti-arrhythmic drugs class III (e.g. amiodarone) have not been performed, but caution is advised.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no evidence of untoward effects in human pregnancy. In large doses, there is evidence of decreased pup survival in rats and an embryological effect in rabbits if Nurabucain is administered in pregnancy. Nurabucain should not therefore be given in early pregnancy unless the benefits are considered to outweigh the risks.
It should be noted that the dose should be reduced in patients in the late stages of pregnancy.

Breast-feeding

Bupivacaine enters the mother's milk, but in such small quantities that there is generally no risk of affecting the child at therapeutic dose levels.

4.7 Effects on ability to drive and use machines

Nurabucain Heavy has minor influence on the ability to drive and use machines. Besides the direct anaesthetic effect, local anaesthetics may have a very mild effect on mental function and co-ordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness.

4.8 Undesirable effects

4.8.1 General

Tabulated list of adverse reactions

The adverse reaction profile for Nurabucain Heavy is similar to those for other long acting local anaesthetics used for intrathecal anaesthesia.
Frequencies are defined as 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) or not known (cannot be estimated from the available data).
Table of Adverse Drug Reactions

System Organ Class	Frequency Classification	Adverse Drug Reaction
Immune system disorders	Rare	Allergic reactions, anaphylactic shock
Nervous system disorders	Common	Postdural puncture headache
	Uncommon	Paraesthesia, paresis, dysaesthesia
	Rare	Total unintentional spinal block, paraplegia, paralysis, neuropathy, arachnoiditis
Cardiac disorders	Very Common	Hypotension, bradycardia
	Rare	Cardiac arrest
Respiratory, thoracic and mediastinal disorders	Rare	Respiratory depression
Gastrointestinal disorders	Very Common	Nausea
	Common	Vomiting
Musculoskeletal and connective tissue disorders	Uncommon	Muscle weakness, back pain
Renal and urinary disorders	Common	Urinary retention, urinary incontinence

Adverse reactions caused by the drug *per se* are difficult to distinguish from the physiological effects of the nerve block (e.g. decrease in blood pressure, bradycardia, temporary urinary retention), events caused directly (e.g. spinal haematoma) or indirectly (e.g. meningitis, epidural abcess) by needle puncture or events associated to cerebrospinal leakage (e.g. postdural puncture headache).

4.8.2 Acute systemic toxicity

Nurabucain Heavy, used as recommended, is not likely to cause blood levels high enough to cause systemic toxicity. However, if other local anaesthetics are concomitantly administered, toxic effects are additive and may cause systemic toxic reactions.

Systemic toxicity is rarely associated with spinal anaesthesia but might occur after accidental intravascular injection. Systemic adverse reactions are characterised by numbness of the tongue, light-headedness, dizziness and tremors, followed by convulsions and cardiovascular disorders.

4.8.3 Treatment of acute systemic toxicity

No treatment is required for milder symptoms of systemic toxicity but if convulsions occur then it is important to ensure adequate oxygenation and to arrest the convulsions if they last more than 15–30 seconds. Oxygen should be given by face mask and the respiration assisted or controlled if necessary. Convulsions can be arrested by injection of thiopental 100–150 mg intravenously or with diazepam 5–10 mg intravenously. Alternatively, succinylcholine 50–100 mg intravenously may be given but only if the clinician has the ability to perform endotracheal intubation and to manage a totally paralysed patient.

High or total spinal blockade causing respiratory paralysis should be treated by ensuring and maintaining a patent airway and giving oxygen by assisted or controlled ventilation.

Hypotension should be treated by the use of vasopressors, e.g. ephedrine 10–15 mg intravenously and repeated until the desired level of arterial pressure is reached. Intravenous fluids, both electrolytes and colloids, given rapidly can also reverse hypotension.

Paediatric population
Adverse drug reactions in children are similar to those in adults, however, in children, early signs of local anaesthetic toxicity may be difficult to detect in cases where the block is given during sedation or general anaesthesia.

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 to **TMDA**

4.9 Overdose
Nurabucain Heavy, used as recommended, is not likely to cause blood levels high enough to cause systemic toxicity. However, if other local anaesthetics are concomitantly administered, toxic effects are additive and may cause systemic toxic reactions.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group (ATC code): N01B B01

Bupivacaine is a long acting local anaesthetic agent of the amide type.
Moderate muscular relaxation of lower extremities.
Motor blockade of the abdominal muscles.
Nurabucain Heavy is hyperbaric and its initial spread in the intrathecal space is affected by gravity.

5.2 Pharmacokinetic properties

Rapid onset of action and long duration i.e. T_{10}–T_{12} segments – duration 2–3 hours.

Muscular relaxation of lower extremities lasts 2–2.5 hours.

Blockade of the abdominal muscles lasts 45–60 minutes. The duration of motor blockade does not exceed duration of analgesia.

In children the pharmacokinetics are similar to that in adults.

5.3 Preclinical safety data
Bupivacaine hydrochloride is a well-established active ingredient.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Dextrose monohydrate
Water for injection

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months from the date of manufacturing.

6.4 Special precautions for storage
Store below 30 ºC.

6.5 Nature and contents of container
4 ml clear and colourless liquid is filled in 5 ml Amber coloured Ampoule with snapp-off ring. Such 10 ampoules packed in tray pack in a Printed carton along with the insert.

6.6 Special precautions for disposal and other handling
The solution should be used immediately after opening of the ampoule. Any remaining solution should be discarded. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER
FARBE FIRMA
Plot no: 1508, G.I.D.C., Ankleswar
(Gujarat) 393 002, India.

8. MARKETING AUTHORISATION NUMBER(S)
TAN 22 HM 0438

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07th October, 2022

10. DATE OF REVISION OF THE TEXT