PROFESSIONAL INFORMATION

SCHEDULING STATUS **S4**

1 NAME OF THE MEDICINE

MACAINE HCl 0,5 % SPINAL INJECTION WITH DEXTROSE, spinal injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 4 mL contains bupivacaine hydrochloride 20 mg (5 mg/mL)

Contains sugar: Dextrose anhydrous 290,8 mg (72,7 mg/mL) (equivalent to dextrose monohydrate 320 mg (80 mg/mL)).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Spinal injection

Clear, colourless, solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Spinal anaesthesia for surgery (e.g. urological and lower limb surgery lasting 2 to 3 hours and abdominal surgery lasting 45 to 60 minutes).

4.2 Posology and method of administration

Posology

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The following dose should be regarded as a guide for use in the average adult:

2 mL to 3 mL to 4 mL (10 mg to 15 mg to 20 mg) bupivacaine hydrochloride.

The spread of anaesthesia obtained with MACAINE HCl 0,5 % SPINAL INJECTION WITH DEXTROSE is dependent upon several factors, the most important being volume of solution injected and the age and positioning of the patient.

The difference in spread between a 10 mg and 20 mg dose is approximately two segments. The larger dose gives a half to 1 hour longer duration of anaesthesia in the lumbar segments and a longer lasting motor blockade.

The effects of spinal injections of MACAINE HCl 0,5 % SPINAL INJECTION WITH DEXTROSE exceeding 20 mg have not yet been studied and such volume can therefore not be recommended.

Method of administration

Before administration of the medicine, make sure that resuscitative equipment, such as equipment to maintain a free airway, oxygenation and circulation, is immediately available.

When injected into the sub-arachnoid space via the L_3/L_4 interspace with the patient kept in the sitting position, 3 mL of MACAINE HCl 0,5 % SPINAL INJECTION WITH DEXTROSE spreads to between the T_7 and T_{10} segments.

If the patient is in the supine horizontal position the blockade spreads to between the T_4 and T_7 segment.

4.3 Contraindications

- Hypersensitivity to bupivacaine or to local anaesthetics of the amide type or to any of the excipients listed in section 6.1
- Bupivacaine HCl is not recommended for use in paracervical block in obstetrics
- 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

Intravenous access, e.g. an IV infusion, should be in place before starting the intrathecal anaesthesia. The healthcare provider 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, see sections 4.8 and 4.9.

Like all local anaesthetic medicines, 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 medicine. This is especially the case after unintentional intravascular administration or injection into highly vascular areas.

Spinal anaesthetics should be used with caution in patients with impaired cardiovascular function such as severe disturbances of cardiac rhythm, shock, heart block or congestive heart failure.
There should be careful and constant monitoring of cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness after local anaesthetic injection.

In addition, ventricular dysrhythmia, ventricular fibrillation, dose-related convulsions, cardiovascular collapse and death may result from diminished tolerance, high systemic concentrations of bupivacaine and rapid absorption from the injection site. 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 aortocaval 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.

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 antidysrhythmic class III medicines such as amiodarone should be kept under close surveillance and ECG monitoring considered, since cardiac effects may be additive (see section 4.5)

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

Bupivacaine should be used with caution in patients receiving other local anaesthetics or medicines structurally related to amide-type local anaesthetics, e.g. certain antidysrhythmics, such as lidocaine (lignocaine) and mexiletine, since the systemic toxic effects are additive. Specific interaction studies with bupivacaine and antidysrhythmic medicines class III (e.g. amiodarone) have not been performed, but caution is advised (see section 4.4)

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy, other than in labour, has not yet been established.

MACAINE HCl 0,5 % SPINAL INJECTION WITH DEXTROSE should therefore not be given in early pregnancy.

It should be noted that the dose should be reduced in patients in the late stages of pregnancy (see section 4.4).

Breastfeeding

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.

Fertility

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No data on male and female fertility is available.

4.7 Effects on ability to drive and use machines

MACAINE HCl 0,5 % SPINAL INJECTION WITH DEXTROSE 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

a. Summary of the safety profile

The adverse reaction profile for MACAINE HCl 0,5 % SPINAL INJECTION WITH DEXTROSE is similar to those for other long-acting local anaesthetics used for intrathecal anaesthesia.

b. Tabulated list of adverse reactions

System organ class	**Frequency**	**Adverse reaction**
Immune system disorders	Rare	Allergic type reactions, anaphylactic shock
Nervous system disorders	Common	Postdural puncture headache
	Uncommon	Paraesthesia, paresis, dysaesthesia

	Rare	Total unintentional spinal block, paraplegia, paralysis, neuropathy, arachnoiditis
	Frequency not known	Impaired perineal sensation and sexual function, persistent anaesthesia, loss of sphincter control, septic meningitis, meningismus, shivering, cranial nerve palsies due to traction on nerves (from loss of cerebrospinal fluid)
Cardiac disorders	Very common	Hypotension, bradycardia, myocardial depression
	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
Pregnancy, puerperium and perinatal conditions	Uncommon	Slowing of labour, increased incidence of forceps delivery

Acute systemic toxicity

MACAINE HCl 0,5 % SPINAL INJECTION WITH DEXTROSE, 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 nausea, vertigo, numbness of the tongue, light-headedness, dizziness, blurred vision and tremors, followed by drowsiness, convulsions unconsciousness and possibly respiratory arrest.

c. Paediatric population

Adverse 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.

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Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc-org) found on SAHPRA website.

For reporting of side effects directly to the Holder of the Certificate of Registration, contact +27 11 635 0134 or email Adcock.aereports@adcock.com

4.9 Overdose

Treatment of extensive spinal blockade consists of assuring and maintaining a patent airway and supporting ventilation using oxygen, if necessary, by assisted or controlled ventilation.

Should circulatory depression occur, a vasopressor, preferably one with inotropic activity, e.g. ephedrine 15 mg to 30 mg, should be given intravenously.

In the case of inadvertent intravascular injection resulting in convulsions, this should be treated rapidly by intravenous injection e.g. thiopentone 100 mg to 200 mg or diazepam 5 mg to 10 mg.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A.4 Local anaesthetics

Pharmacotherapeutic group and ATC code: Anaesthetics, local; amides.

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ATC code: N01BB01.

Bupivacaine is a long-acting local anaesthetic of the amide type that provides moderate muscular relaxation of the lower extremities and motor blockade of the abdominal muscles.

Pharmacodynamic effects

Bupivacaine is hyperbaric and its initial spread in the intrathecal space is affected by gravity.

5.2 Pharmacokinetic properties

The onset of action is 10 to 15 minutes and the duration of analgesia in the T_{10} to T_{12} segments is 2 to 3 hours. Muscular relaxation of the lower extremities lasts 2 to 2½ hours. The motor blockade of the abdominal muscles lasts 45 to 60 minutes. The duration of motor blockade is shorter than the duration of sensory blockade.

Paediatric population

In children the pharmacokinetics are similar to that in adults.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextrose anhydrous (as monohydrate)

Sodium hydroxide (for pH adjustment)

Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25 °C

6.5 Nature and contents of container

Clear colourless solution of 4 mL packed in a 5 mL Type I clear one-point cut (OPC) glass closed ampoule in packs of 10.

The ampoules are placed in an outer cardboard carton.

6.6 Special precautions for disposal and other handling

The solution must not be stored in such a way that it can be influenced by metals, e.g. needles or metal parts of syringes, as dissolved metal ions may cause swelling at the site of the injection.

The solution should be used immediately after opening of the ampoule. Any remaining solution should be discarded.

7 HOLDER OF CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER

U/4/91

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 29 November 1988

10 DATE OF REVISION OF THE TEXT

27 October 2025

Namibia: NS2 90/4/00135

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