APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

LIDOCAINE HCl 1 % (VIALS) FRESENIUS solution for injection

LIDOCAINE HCl 2 % (VIALS) FRESENIUS solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

LIDOCAINE HCl 1 % (VIALS) FRESENIUS: Each 1 ml contains lidocaine (lignocaine) hydrochloride monohydrate equivalent to 10 mg lidocaine (lignocaine) hydrochloride anhydrous.

LIDOCAINE HCl 2 % (VIALS) FRESENIUS: Each 1 ml contains lidocaine (lignocaine) hydrochloride monohydrate equivalent to 20 mg lidocaine (lignocaine) hydrochloride anhydrous.

Preservative: Methyl hydroxybenzoate 0,1 % *m/v*.

Excipients with known effect

Each 1 ml of **LIDOCAINE HCl 1 % (VIALS) FRESENIUS** contains 2,7 mg of sodium.

Each 1 ml of **LIDOCAINE HCl 2 % (VIALS) FRESENIUS** contains 1,8 mg of sodium.

Sugar free.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

A clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS is used as a local anaesthetic in infiltration, field block and nerve block. As a local anaesthetic it has an action of intermediate duration which can be increased by adding adrenaline (epinephrine).

4.2 Posology and method of administration

Posology

As local anaesthetic the dose is dependent of the area to be anaesthetised and it is given subcutaneously or intramuscularly:

1. Infiltration anaesthesia - a 0,5 to 1,0 % solution is used.
2. Field block anaesthesia - as for infiltration anaesthesia.
3. Nerve block anaesthesia - depending upon which nerves or plexuses, the type of fibres - a 1 to 2 % solution is used.
4. Epidural anaesthesia - determined by the segmental level of anaesthesia required. The volume of anaesthetic required is determined by which nerve fibres are to be blocked, what level of anaesthesia is required and whether adrenaline is used. The addition of adrenaline 1:200 000 is often used to increase the duration of anaesthesia.

The maximum 24-hour dose is 300 mg of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**.

Method of Administration

It is recommended that a needle not larger than 21 gauge is used to reduce fragmentation of

the rubber stopper.

4.3 Contraindications

- Contraindicated in patients that are hypersensitive to lidocaine (lignocaine) hydrochloride or other amide type local anaesthetics or to any of the excipients listed in 6.1.
- **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** should not be given to patients with:
  - Hypovolaemia
  - Complete heart block or other conduction disturbances
  - Bradycardia
  - Cardiac decompensation or hypotension unrelated to treatable tachydysrhythmias
  - Myasthenia gravis
  - Porphyria.

4.4 Special warnings and precautions for use

Should not be given intravenously.

Doses should be reduced in elderly and debilitated patients and in children.

LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS should be used with caution in patients with epilepsy, myasthenia gravis, cardiac conduction disturbances (see section 4.3), congestive heart failure, bradycardia, severe shock, impaired respiratory function or impaired renal function with a creatinine clearance of less than 10 ml/minute. Lidocaine (lignocaine) is metabolised in the liver, and it should be used with caution in patients with impaired hepatic function. Lower doses should be used in congestive cardiac failure and following cardiac surgery.

Hypokalaemia, hypoxia and disorders of acid-base balance should be corrected before treatment with **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS.**

Facilities for resuscitation should be available when administering **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**.

The effect of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** may be reduced if the injection is made into an inflamed or infected area.

Intra-articular administration of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** may cause chondrotoxicity.

Certain local anaesthetic procedures may be associated with serious adverse reactions, regardless of the local anaesthetic medicine used.

- Central nerve blocks may cause cardiovascular depression, especially in the presence of hypovolaemia, and therefore epidural anaesthesia should be used with caution in patients with impaired cardiovascular function.
- Blood pressure should be monitored during spinal anaesthesia. Epidural anaesthesia may lead to hypotension and bradycardia. This risk can be reduced by preloading the circulation with crystalloidal or colloidal solutions. Hypotension should be treated promptly.
- Paracervical block can sometimes cause foetal bradycardia or tachycardia, and careful monitoring of the foetal heart rate is necessary.
- Injections in the head and neck regions may be made inadvertently into an artery, causing cerebral symptoms even at low doses.
- Retrobulbar injections may rarely reach the cranial subarachnoid space, causing serious/severe reactions, including cardiovascular collapse, apnoea, convulsions and temporary blindness.
- Retro- and peribulbar injections of local anaesthetics carry a low risk of persistent ocular motor dysfunction. The primary causes include trauma and/or local toxic effects on muscles and/or nerves.

- The severity of such tissue reactions is related to the degree of trauma, the concentration of the local anaesthetic and the duration of exposure of the tissue to the local anaesthetic. For this reason, as with all local anaesthetics, the lowest effective concentration and dose of local anaesthetic should be used.
- **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** may increase creatinine phosphokinase concentrations which can interfere with the diagnosis of acute myocardial infarction**. LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** is considered to be unsafe in patients with porphyria.
- **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** is not recommended for use in neonates. The optimum serum concentration of lidocaine (lignocaine) required to avoid toxicity, such as convulsions and cardiac dysrhythmias, in this age group is not known.

4.5 Interaction with other medicines and other forms of interaction

Effects of LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS on other medicines

LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS should be used with caution in patients receiving other local anaesthetics or medicines structurally related to amide-type local anaesthetics (e.g., antidysrhythmic medicine, such as mexiletine), since the systemic toxic effects are additive. Specific interaction studies with lidocaine (lignocaine) and class III antidysrhythmic medicines (e.g., amiodarone) have not been performed, but caution is advised.

There may be an increased risk of enhanced and prolonged neuromuscular blockade in patients treated concurrently with muscle relaxants (e.g., suxamethonium).

Effects of other medicines on LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS

The clearance of lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS,** may be reduced by beta-adrenoceptor blocking medicines (e.g., propranolol) and by cimetidine, requiring a reduction in the dosage of **LIDOCAINE HCl 1 % AND 2 %**

(VIALS) FRESENIUS. Increase in serum levels of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** may also occur with antiviral medicine (e.g., amprenavir, atazanavir, darunavir, lopinavir).

There may be an increased risk of ventricular dysrhythmia in patients treated concurrently with antipsychotics which prolong or may prolong the QT interval (e.g., pimozide, sertindole, olanzapine, quetiapine, zotepine), or 5HT3 antagonists (e.g., tropisetron, dolasetron).

While adrenaline (epinephrine) when used in conjunction with **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** might decrease vascular absorption, it greatly increases the danger of ventricular tachycardia and fibrillation if accidentally injected intravenously.

Cardiovascular collapse has been reported following the use of bupivacaine in patients on treatment with verapamil and timolol; lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**, is closely related to bupivacaine.

Concomitant use of quinupristin/dalfopristin should be avoided.

Hypokalaemia produced by acetazolamide, loop diuretics and thiazides antagonise the effect of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**, if administered concomitantly (see section 4.4).

Inhibition of CYP1A2 by fluvoxamine considerably reduces elimination of lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** and increases the risk of lidocaine (lignocaine) toxicity. Concomitant use of both fluvoxamine and a CYP3A4 inhibitor such as erythromycin can further increase concentration of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**. Because lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**, possesses a narrow therapeutic window, doses of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** may need to be adjusted accordingly. Conversely, reduced serum concentrations of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** may result from medicines that may stimulate the hepatic metabolism of lidocaine (lignocaine) (e.g., phenytoin, oral HRT).

Narcotics are probably proconvulsant and this would support the evidence that lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**, reduces the seizure threshold to fentanyl in man.

Opioid-antiemetic combination sometimes used for sedation in children could reduce the convulsant threshold to lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** and increase the CNS depressant effect.

Lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**, is markedly bound to α-l-acid glycoprotein (AAG). AAG concentrations may be reduced by oestrogens leading to a higher free fraction of lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**, in women than in men and the free fraction is further increased during pregnancy and in women taking oral contraceptives or HRT.

4.6 Fertility, pregnancy and lactation

Pregnancy

LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS crosses the placenta and blood-brain barrier and should not be administered during early pregnancy.

Foetal intoxication has occurred following the use of lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS,** in labour (see section 4.8).

Lidocaine (lignocaine) given by epidural or paracervical block, especially in large doses, or by local perineal infiltration prior to delivery crosses rapidly into the foetal circulation. Elevated lidocaine (lignocaine) levels may persist in the newborn for at least 48 hours after delivery. Foetal bradycardia or neonatal bradycardia, hypotonia or respiratory depression may occur.

Breastfeeding

LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS is distributed into breast milk.

Small amounts of lidocaine (lignocaine) are secreted into breast milk and the possibility of an allergic reaction in the infant, albeit remote, should be borne in mind when using lidocaine (lignocaine) in nursing mothers.

4.7 Effects on ability to drive and use machines

When outpatient anaesthesia affects areas of the body involved in driving or operating machinery, patients should be advised to avoid these activities until normal function is fully restored.

4.8 Undesirable effects

a) Summary of the safety profile

In common with other local anaesthetics, adverse reactions to **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** are rare and are usually the result of raised plasma concentrations due to accidental intravascular injection, excessive dosage or rapid absorption from highly vascular areas, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Systemic toxicity mainly involves the central nervous system and/or the cardiovascular system (see section 4.9).

Following regional blockade as when **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** is injected intrathecally or extradurally, hypotension, hypoventilation, Horner's syndrome and hypoglycaemia may be seen. The degree of these effects will depend on the dose and the height of the block. Urinary retention may occur following sacral or lumbar epidural block. It should not outlast the duration of the block. Apnoea and hemiparesis may occur following stellate ganglion block. The probable cause is a direct injection of lidocaine (lignocaine) into the vertebral or carotid arteries.

b) Tabulated summary of adverse reactions

MedDRA system organ class	**Adverse reactions**
Blood and the lymphatic system disorders	Methaemoglobinaemia.
Immune system disorders	Hypersensitivity reactions (allergic or anaphylactoid reactions, anaphylactic shock) – see also Skin and subcutaneous tissue disorders. Skin testing for allergy to lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** is not considered to be reliable.
Nervous system disorders	Neurological signs of systemic toxicity include yawning, restlessness, excitement, nervousness, dizziness or light-headedness, nervousness, tremor, circumoral paraesthesia, tongue numbness, convulsions, coma. Nervous system reactions may be excitatory and or depressant. Signs of CNS stimulation may be brief, or may not occur at all, so that the first signs of toxicity may be confusion and drowsiness, followed by respiratory failure and coma. Neurological complications of spinal anaesthesia include transient neurological symptoms such as pain of the lower back, buttock and legs. These symptoms usually develop within twenty-four hours of anaesthesia and resolve within a few days. Isolated cases of arachnoiditis or cauda equina syndrome, with persistent paraesthesia, bowel and urinary dysfunction, or lower limb paralysis have been reported following spinal anaesthesia with lidocaine (lignocaine) and other similar medicines. The

MedDRA system organ class	**Adverse reactions**
	majority of cases have been associated with hyperbaric concentrations of lidocaine (lignocaine), as in **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**, or prolonged spinal infusion.
Eye disorders	Blurred vision, diplopia and transient amaurosis may be signs of lidocaine (lignocaine) toxicity. Bilateral amaurosis may also be a consequence of accidental injection of the optic nerve sheath during ocular procedures. Orbital inflammation and diplopia have been reported following retro- or peribulbar anaesthesia (see section 4.4).
Ear and labyrinth disorders	Tinnitus, hyperacusis.
Cardiac disorders	Cardiovascular reactions are depressant and may manifest as, bradycardia, myocardial depression, cardiac dysrhythmias and possibly cardiac arrest or circulatory collapse. Isolated cases of bradycardia and cardiac arrest have also been reported.
Vascular disorders	Pallor, sweating, hypotension. Hypotension may accompany spinal and epidural anaesthesia.
Respiratory, thoracic and mediastinal disorders	Dyspnoea, bronchospasm, respiratory depression, respiratory arrest.
Gastrointestinal disorders	Nausea, vomiting.

MedDRA system organ class	Adverse reactions
Skin and subcutaneous tissue disorders	Rash, urticaria, oedema (including angioedema, face oedema).
General disorders and administration site conditions	Lassitude and amnesia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS** is important. It allows continued monitoring of the benefit/risk balance of **LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS**. Health care providers are asked to report any suspected adverse reactions via the **Adverse Drug Reaction Reporting Form**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

Health care providers are asked to report any suspected adverse reactions to the Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com, and to the relevant medicine's regulatory authority in the country where the product is marketed.

4.9 Overdose

See symptoms mentioned under section 4.8.

Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A4 Local anaesthetcs

Pharmacotherapeutic group: Anaesthetics, local, Amides

ATC code: N01BB02

Lidocaine (lignocaine) has local anaesthetic action (it blocks conduction of nerve impulses by decreasing or preventing the large transient increase in permeability of the cell membrane to sodium ions) with a rapid onset and intermediate duration of action when injected.

5.2 Pharmacokinetic properties

Absorption

Lidocaine (lignocaine) is absorbed from injection sites including muscle and its rate of absorption is determined by factors such as the site of administration and the tissue vascularity. Except for intravascular administration, the highest blood levels occur following intercostal nerve block and the lowest after subcutaneous administration.

Distribution

Lidocaine (lignocaine) is bound to plasma proteins, including alpha-1-acid- glycoprotein. Lidocaine (lignocaine) crosses the blood-brain and placental barriers.

Biotransformation

Lidocaine (lignocaine) is metabolised in the liver and about 90 % of a given dose undergoes *N*-dealkylation to form monoethylglycinexylidide and glycinexylidide, both of which may contribute to the therapeutic and toxic effects of lidocaine (lignocaine). Further metabolism occurs and metabolites are excreted in the urine with less than 10 % of unchanged lidocaine (lignocaine).

Elimination

The elimination half life of lidocaine (lignocaine) following an intravenous bolus injection is one to two hours, but this may be prolonged in patients with hepatic dysfunction.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl hydroxybenzoate

Sodium chloride

Sodium hydroxide

Water for injection

6.2 Incompatibilities

LIDOCAINE HCl 1 % AND 2 % (VIALS) FRESENIUS has been reported to be incompatible in solution with amphotericin, sulfadiazine, methohexital sodium, cefazolin sodium and phenytoin sodium.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Store at or below 30 °C.

6.5 Nature and contents of container

LIDOCAINE HCl 1 % (VIALS) FRESENIUS is a clear, colourless solution packed in 5 or 20 ml clear glass vials (Type 1) sealed with chlorobutyl rubber stopper with green aluminium cap.

LIDOCAINE HCl 2 % (VIALS) FRESENIUS is a clear, colourless solution packed in 20 ml clear glass vial (Type 1) sealed with chlorobutyl rubber stopper with gold aluminium cap.

Pack size: 10 vials packed in polystyrene containers.

6.6 Special precautions for disposal and other handling

Any unused medicine should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten 6020

Gqeberha

South Africa

8 REGISTRATION NUMBERS

LIDOCAINE HCl 1 % (VIALS) FRESENIUS: G2781 (Act 101/1965)

LIDOCAINE HCl 2 % (VIALS) FRESENIUS: G2782 (Act 101/1965)

9 DATE OF FIRST AUTHORISATION

Not applicable.

10 DATE OF REVISION OF THE TEXT

07 July 2023