1 LIDOCAINE-CLARIS (solution for infusion)
Lidocaine-Claris 1% w/v solution for injection.

Lidocaine-Claris 2% w/v solution for injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Active ingredient
Lidocaine hydrochloride monohydrate 10.66mg/mL (= Lidocaine hydrochloride 10.0mg/mL).
Lidocaine hydrochloride monohydrate 21.32mg/mL (= Lidocaine hydrochloride 20.0mg/mL).

For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM
Solution for injection.

Appearance
Lidocaine-Claris is a clear, colourless, particle-free, sterile, isotonic, pH adjusted solution of Lidocaine Hydrochloride Ph Eur conforming to Lidocaine Injection BP.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Lidocaine solutions are indicated for the production of local or regional anaesthesia by the following techniques: local infiltration; minor or major nerve blocks; epidural block; arthroscopy; intravenous regional anaesthesia.

4.2 Dose and method of administration
Adults and children above 12 years
The following table is a guide to dosage for the more commonly used techniques 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 (refer to section 4.4). Individual variations in onset and duration occur.

<table>
<thead>
<tr>
<th>Type of block</th>
<th>Concentration (mg/ml)</th>
<th>Dose (mL)</th>
<th>Dose (mg)</th>
<th>Onset (min)</th>
<th>Duration of effect (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical anaesthesia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbar epidural administration [1]</td>
<td>20</td>
<td>15 to 25</td>
<td>300 to 500</td>
<td>15 to 20</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td>Thoracic epidural administration [1]</td>
<td>15</td>
<td>10 to 15</td>
<td>150 to 225</td>
<td>10 to 20</td>
<td>1 to 1.5</td>
</tr>
<tr>
<td>Caudal epidural block [1]</td>
<td>20</td>
<td>10 to 15</td>
<td>200 to 300</td>
<td>10 to 20</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>20 to 30</td>
<td>200 to 300</td>
<td>15 to 30</td>
<td>1 to 1.5</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>15 to 25</td>
<td>300 to 500</td>
<td>15 to 30</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td>Type of block</td>
<td>Concentration (mg/ml)</td>
<td>Dose (mL)</td>
<td>(mg)</td>
<td>Onset (min)</td>
<td>Duration of effect (h)</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------------</td>
<td>-----------</td>
<td>------</td>
<td>-------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>IV regional (Bier’s block)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) upper limb [2]</td>
<td>5</td>
<td>40</td>
<td>200</td>
<td>10 to 15</td>
<td>until tourniquet release</td>
</tr>
<tr>
<td>b) lower limb [2]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. thigh tourniquet</td>
<td>5</td>
<td>40</td>
<td>200</td>
<td>10 to 15</td>
<td>until tourniquet release</td>
</tr>
<tr>
<td>ii. calf tourniquet</td>
<td>5</td>
<td>≤60</td>
<td>≤300</td>
<td>5 to 10</td>
<td>30 to 60 minutes after washout</td>
</tr>
<tr>
<td>Intra-articular block [3]</td>
<td>5</td>
<td>≤60</td>
<td>≤300</td>
<td>5 to 10</td>
<td>30 to 60 minutes after washout</td>
</tr>
<tr>
<td>Field block (eg. minor nerve blocks and infiltration)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infiltration</td>
<td>5</td>
<td>≤80</td>
<td>≤400</td>
<td>1 to 2</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td>Digital block</td>
<td>10</td>
<td>≤40</td>
<td>≤400</td>
<td>1 to 2</td>
<td>2 to 3</td>
</tr>
<tr>
<td>Intercostals (per nerve)</td>
<td>10</td>
<td>2 to 5</td>
<td>20 to 50</td>
<td>3 to 5</td>
<td>1 to 2</td>
</tr>
<tr>
<td>[Maximal number of nerves blocked at same time should be ≤8]</td>
<td>15</td>
<td>2 to 4</td>
<td>30 to 60</td>
<td>3 to 5</td>
<td>2 to 3</td>
</tr>
<tr>
<td>Retrobulbar</td>
<td>20</td>
<td>4</td>
<td>80</td>
<td>1.5 to 2</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td>Peribulbar</td>
<td>10</td>
<td>10 to 15</td>
<td>100 to 150</td>
<td>1.5 to 2</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td>Pudendal (each side)</td>
<td>10</td>
<td>10</td>
<td>100</td>
<td>5 to 10</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td>Major nerve block</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paracervical (each side)</td>
<td>10</td>
<td>10</td>
<td>100</td>
<td>3 to 5</td>
<td>1 to 1.5</td>
</tr>
<tr>
<td>Brachial plexus: axillary</td>
<td>10</td>
<td>40 to 50</td>
<td>400 to 500</td>
<td>15 to 30</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>30 to 50</td>
<td>450 to 600</td>
<td>15 to 30</td>
<td>1.5 to 3</td>
</tr>
<tr>
<td>Supraclavicular, interscalene and subclavien perivascular</td>
<td>10</td>
<td>30 to 40</td>
<td>300 to 400</td>
<td>15 to 30</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>20 to 30</td>
<td>300 to 450</td>
<td>15 to 30</td>
<td>1.5 to 3</td>
</tr>
<tr>
<td>Sciatic</td>
<td>15</td>
<td>15 to 20</td>
<td>225 to 300</td>
<td>15 to 30</td>
<td>2 to 3</td>
</tr>
<tr>
<td>3 in 1 (femoral, obturator and lateral cutaneous)</td>
<td>10</td>
<td>30 to 40</td>
<td>300 to 400</td>
<td>15 to 30</td>
<td>1.5 to 2</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>30</td>
<td>450</td>
<td>15 to 30</td>
<td>2 to 3</td>
</tr>
</tbody>
</table>

Remarks:
1) Dose includes test dose
2) Do not deflate tourniquet within 20 min of injection
3) There have been post marketing reports of chondrolysis in patients receiving post-operative intra-articular continuous infusion of local anaesthetics. Lidocaine is not approved for this indication (refer to section 4.4). ≤ = up to
In general, surgical anaesthesia (eg. epidural administration) requires the use of the higher concentrations and doses. When a less intense block is required, the use of a lower concentration is indicated. The volume of drug used will affect the extent and spread of anaesthesia.

In order to avoid intravascular injection, aspiration should be repeated prior to and during administration of the main dose, which should be injected slowly or in incremental doses, at a rate of 100 to 200mg/min, while closely observing the patient’s vital functions and maintaining verbal contact. When an epidural dose is to be injected, a preceding test dose of 3 to 5mL short-acting local anaesthetic, containing adrenaline is recommended. An inadvertent intravascular injection may be recognized by a temporary increase in heart rate and an accidental intrathecal injection by signs of a spinal block. If toxic symptoms occur, the injection should be stopped immediately.

| Table 2 Dosage recommendations in children aged 1 to 12 years old (without adrenaline) |
|---------------------------------|-----------------|-------------|-------------|-------------|-----------------|
| Type of block                   | Concentration (mg/ml) | Volume (mL) | Dose (mg/kg) | Onset (min) | Duration of effect (h) |
| Caudal epidural                | 10               | 0.5         | 5           | 10 to 15    | 1 to 1.5         |

Consider both age and weight for calculation of dosages.

The doses in Table 2 should be regarded as guidelines for use in paediatrics. Individual variations occur. In children with a high body weight a gradual reduction of the dosage is often necessary and should be based on the ideal body weight. Standard textbooks should be consulted for factors affecting specific block techniques and for individual patient requirements.

4.3 Contraindications

- Known hypersensitivity to local anaesthetics of the amide type.
- Complete heart block.
- Hypovolaemia.

4.4 Special warnings and precautions for use

General

Lidocaine should be administered by persons with resuscitative skills and equipment. Resuscitation equipment must be available at all times. When performing major blocks or using large doses, an IV cannula should be inserted before the local anaesthetic is injected. Clinicians should have received adequate and appropriate training in the procedure to be performed and should be familiar with the diagnosis and treatment of side effects, systemic toxicity or other complications (refer to Overdosage).

Lidocaine should be used with caution in patients with myasthenia gravis, epilepsy, congestive heart failure, bradycardia or respiratory depression, including where agents are known to interact with lidocaine either to increase its availability or additive effects e.g. phenytoin or prolong its elimination e.g. hepatic or end renal insufficiency where the metabolites of lidocaine may accumulate.

Patients being treated with anti-arrhythmic drugs class III (eg. amiodarone) should be under close surveillance and ECG monitoring considered, since cardiac effects may be additive (refer to section 4.5).

There have been post-marketing reports of chondrolysis in patients receiving postoperative intra-articular continuous infusion of local anaesthetics. The majority of reported cases of chondrolysis have involved the shoulder joint. Due to multiple contributing factors and inconsistency in the
scientific literature regarding mechanism of action, causality has not been established. Intra-articular continuous infusion is not an approved indication.

Intramuscular lidocaine may increase creatinine phosphokinase concentrations which can interfere with the diagnosis of acute myocardial infarction. Lidocaine has been shown to be porphyrinogenic in animals and should be avoided in persons suffering from porphyria.

The effect of lidocaine may be reduced if it is injected into inflamed or infected areas.

Hypokalaemia, hypoxia and disorder of acid-base balance should be corrected before treatment with intravenous lidocaine begins.

Lidocaine solution for injection is not recommended for use in neonates. The optimum serum concentration of lidocaine required to avoid toxicity, such as convulsions and cardiac arrhythmias, in this age group is not known.

Dosage reduction may be required in patients presenting impaired hepatic function, cardiac failure or during prolonged administration to patients with renal failure.

**Risks of certain procedures**

Certain local anaesthetic procedures may be associated with serious adverse reactions, regardless of local anaesthetic drug 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.

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 (refer to section 4.6).

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 local anaesthetic. For this reason, as with all local anaesthetic, the lowest effective concentration and dose of local anaesthetic should be used.
4.5 Interaction with other medicines and other forms of interaction

Lidocaine toxicity is enhanced, by the co-administration of cimetidine and propranolol requiring a reduction in the dosage of lidocaine. Both drugs decrease hepatic blood flow. Also, cimetidine depresses microsomal activity. Ranitidine produces a small reduction in lidocaine clearance. Potentially toxic plasma concentrations may occur when lidocaine is given in repeated high doses over a long time period. However, such interactions should be of no clinical importance following short term treatment with lidocaine at recommended doses. Increase in serum levels of lidocaine may also occur with anti-viral agents (e.g. amprenavir, atazanavir, darunavir, lopinavir).

Hypokalaemia caused by diuretics may antagonize the action of lidocaine if administered concomitantly (refer to section 4.4).

Lidocaine should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics (e.g. anti-arrhythmics, such as mexiletine and tocainide), since the systemic toxic effects are additive. Specific interaction studies with lidocaine and class III antiarrhythmic drugs (e.g. amiodarone) have not been performed, but caution is advised.

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

Concomitant use of quinupristin/dalfopristin may increase lidocaine levels with a subsequent increased risk of ventricular arrhythmias and therefore should be avoided.

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

Cardiovascular collapse has been reported following the use of bupivacaine in patients on treatment with verapamil and timolol; lidocaine is structurally related to bupivacaine.

Dopamine and 5 hydroxytryptamine reduce the convulsant threshold to lidocaine.

Narcotics are probably proconvulsants and this would support the evidence that lidocaine reduces the seizure threshold to fentanyl in man.

Opioid-antiemetic combination sometimes used for sedation in children could reduce the convulsant threshold to lidocaine and increase the CNS depressant effect.

While adrenaline when used in conjunction with lidocaine might decrease vascular absorption, it greatly increases the danger of ventricular tachycardia and fibrillation if accidentally injected intravenously.

4.6 Fertility, pregnancy and lactation

Fertility

No fertility data are available.
Pregnancy (Category A)
Category A refers to medicines which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

It is reasonable to assume that a large number of pregnant women and women of child-bearing age have been given lidocaine. No specific disturbances to the reproductive process have so far been reported, e.g. no increased incidence of malformations.

Lidocaine readily crosses the placental barrier after epidural or intravenous administration to the mother. The ratio of umbilical to maternal venous concentration is 0.5 to 0.6. The foetus appears to be capable of metabolising lidocaine at term. The elimination half-life in the newborn of the drug received in utero is about three hours, compared with 100 minutes in the adult. Elevated lidocaine levels may persist in the newborn for at least 48 hours after delivery. Foetal bradycardia or tachycardia, neonatal bradycardia, hypotonia or respiratory depression may occur. Foetal adverse effects due to local anaesthetics, such as foetal bradycardia, seem to be most apparent in paracervical block anaesthesia. Such effects may be due to high concentrations of anaesthetic reaching the foetus.

Breast feeding
Small amounts of lidocaine 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 in nursing mothers.

4.7 Effects on ability to drive and use machines
This medicine is likely to have mild to moderate effects on the ability to drive or operate machinery. Besides the direct anaesthetic effect, local anaesthetics may have a very mild effect on mental function and coordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness.

Major motor nerve block occurs e.g. brachial plexus, epidural, spinal block may result in a loss of sensation resulting from nerve block to areas of muscle co-ordination or balance. Advice is that for general anaesthesia as sedative/hypnotic drugs are often used during nerve blockade.

4.8 Undesirable effects
The adverse reaction profile of lidocaine is similar to those of other amide local anaesthetics. Adverse reactions caused by the drug per se are difficult to distinguish from the physiological effects of the nerve block (eg. decrease in blood pressure, bradycardia), events caused directly (eg. nerve trauma) or indirectly (eg. epidural abscess) by the needle puncture.

Adverse reactions that are usually dose related include nervousness, blurred vision, dizziness, bradycardia, hypotension, tremor, nausea, vomiting, drowsiness, speech disturbances, perioral numbness, muscle twitching, confusion, vertigo or tinnitus, psychosis, seizures and respiratory depression. Others include metallic taste, rash, sinus arrest, atrioventricular block, urticaria and anaphylactoid reactions.
Table of adverse drug reactions

Common (from 1 in 100 to 1 in 10)
Vascular disorders: hypotension, hypertension Gastrointestinal disorders: nausea, vomiting
Nervous system disorders: paraesthesia, dizziness Cardiac disorders: bradycardia.

Uncommon (from 1 in 1,000 to 1 in 100)
Nervous system disorders: signs and symptoms of CNS toxicity (convulsions, paraesthesia circumoral, numbness of the tongue, hyperacusis, visual disturbances, tremor, tinnitus, dysarthria, CNS depression).

Rare (below 1 in 1,000)
Cardiac disorders: cardiac arrest, cardiac arrhythmias.


Nervous system disorders: neuropathy, peripheral nerve injury, arachnoiditis Eye disorders: diplopia.

Acute systemic toxicity
Systemic toxic reactions primarily involve the central nervous system (CNS) and the cardiovascular system (CVS). Such reactions are caused by high blood concentrations of a local anaesthetic, which may appear due to (accidental) intravascular injection, overdose or exceptionally rapid absorption from highly vascularised areas (refer to section 4.9). CNS reactions are similar for all amide local anaesthetics, while cardiac reactions are more dependent on the drug, both quantitatively and qualitatively. Signs of toxicity in the central nervous system generally precede cardiovascular toxic effects, unless the patient is receiving a general anaesthetic or is heavily sedated with drugs such as benzodiazepine or barbiturate.

Central nervous system toxicity is a graded response with symptoms and signs of escalating severity. The first symptoms are usually, circumoral paraesthesia, numbness of the tongue, light-headedness, hyperacusis, tinnitus and visual disturbances. Dysarthria, muscular twitching or tremors are more serious and precede the onset of generalized convulsions. These signs must not be mistaken for a neurotic behaviour. Unconsciousness and grand mal convulsions may follow which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly following convulsions due to the increased muscular activity, together with the interference with respiration and possible loss of functional airways. In severe cases apnoea may occur. Acidosis, hyperkalaemia, hypocalcaemia and hypoxia increase and extend the toxic effects of local anaesthetics.

Recovery is due to redistribution of the local anaesthetic drug from the central nervous system and subsequent metabolism and excretion. Recovery may be rapid unless large amounts of the drug have been injected.

Cardiovascular system toxicity may be seen in severe cases and is generally preceded by signs of toxicity in the central nervous system. In patients under heavy sedation or receiving a general anaesthetic, prodromal CNS symptoms may be absent. Hypotension, bradycardia, arrhythmia and even cardiac arrest may occur as a result of high systemic concentrations of local anaesthetics, but in rare cases cardiac arrest has occurred without prodromal CNS effects.
In children, early signs of local anaesthetic toxicity may be difficult to detect in cases where the block is given during general anaesthesia.

**Treatment**
If signs of acute systemic toxicity appear, injection of the local anaesthetic should be stopped immediately and CNS symptoms (convulsion, CNS depression) must be promptly treated with appropriate airway/respiratory support and the administration of anticonvulsant drugs.

If circulatory arrest should occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance.

If cardiovascular depression occurs (hypotension, bradycardia), appropriate treatment with intravenous fluids, vasopressor, chronotropic and or inotropic agents should be considered. Children should be given doses commensurate with age and weight.

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continuing monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphv.otago.ac.nz/reporting/

**4.9 Overdose**
Accidental intravascular injections of local anaesthetics may cause immediate (within seconds to a few minutes) systemic toxic reactions. In the event of overdose, systemic toxicity appears later (15 to 60 minutes after injection) due to the slower increase in local anaesthetic blood concentration.

**Signs and symptoms**
Central nervous system toxicity presents with symptoms of increasing severity. Patients may present initially with circumoral paraesthesia, numbness of the tongue, light-headedness, hyperacusis and tinnitus. Visual disturbance and muscular tremors or muscle twitching are more serious and precede the onset of generalised convulsions. These signs must not be mistaken for neurotic behaviour. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercapnia occur rapidly following convulsions due to increased muscular activity, together with the interference with normal respiration and loss of the airway. In severe cases, apnoea may occur. Acidosis increases the toxic effects of local anaesthetics.

Effects on the cardiovascular system may be seen in severe cases. Hypotension, bradycardia, arrhythmia and cardiac arrest may occur as a result of high systemic concentrations, with potentially fatal outcome.

Recovery occurs as a consequence of redistribution of the local anaesthetic drug from the central nervous system and metabolism and may be rapid unless large amounts of the drug have been injected.

**Treatment**
If signs of acute systemic toxicity appear, injection of the anaesthetic should be stopped immediately.

Treatment will be required if convulsions and CNS depression occurs. The objectives of treatment are to maintain oxygenation, stop the convulsions and support the circulation. A patent airway should be established and oxygen should be administered, together with assisted ventilation (mask and bag) if necessary. The circulation should be maintained with infusions of plasma or intravenous fluids. Where further supportive treatment of circulatory depression is required, use of a vasopressor agent
may be considered although this involves a risk of CNS excitation. Convulsions may be controlled by the intravenous administration of diazepam or thiopentone sodium, bearing in mind that anti-convulsant drugs may also depress respiration and the circulation. Prolonged convulsions may jeopardize the patient’s ventilation and oxygenation and early endotracheal intubation should be considered. If cardiac arrest should occur, standard cardiopulmonary resuscitation procedures should be instituted. Continual optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance.

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine.

For advice on the management of overdose please contact the National Poisons Centre on phone number: 0800 764 766 [0800 POISON] in New Zealand (or 131126 in Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group and ATC code
N01BB02: member of N01BB - amides, a subset of N01B – anaesthetics, local.

Actions
Lidocaine is used to provide anaesthesia by reversible nerve blockade at various sites in the body and in the control of dysrhythmias. It has a rapid onset of action (about one minute following intravenous injection and fifteen minutes following intramuscular injection) and rapidly spreads through the surrounding tissues. The effect lasts about ten to twenty minutes and about sixty to ninety minutes following intravenous and intramuscular injection respectively.

5.2 Pharmacokinetic properties
The concentration of lidocaine in the blood will be determined by its rate of absorption from the site of injection, the rate of tissue distribution and the rate of metabolism and excretion.

Absorption
The systemic absorption of lidocaine is determined by the site of injection, the dosage and its pharmacological profile. The maximum blood concentration occurs following intercostal nerve blockade followed in order of decreasing concentration, the lumbar epidural space, brachial plexus site and subcutaneous tissue. The total dose injected regardless of the site is the primary determinant of the absorption rate and blood levels achieved. There is a linear relationship between the amount of lidocaine injected and the resultant peak anaesthetic blood levels.

The lipid solubility and vasodilator activity will also influence its rate of absorption. This is seen in the epidural space where lidocaine is absorbed more rapidly than prilocaine. Lidocaine shows complete and biphasic absorption from the epidural space with half-lives of the two phases in the order of 9.3min and 82min respectively. The slow absorption is the rate-limiting factor in the elimination of lidocaine, which explains why the apparent terminal half-life is longer after epidural administration. Absorption of lidocaine from the subarachnoid space is monophasic with an absorption half-life of 71 min.

Distribution
Lidocaine is distributed throughout the total body water and the volume of distribution at steady state is 91 litres. Lidocaine is 65% protein-bound (mainly to alpha-1-acid glycoprotein) in plasma.

Lidocaine is distributed less rapidly than prilocaine (an amide drug of similar potency and duration of action) but equally as with mepivacaine. Its distribution is throughout all body tissues. In general, the
more highly perfused organs will show higher concentrations of lidocaine. The highest percentage of this drug will be found in skeletal muscle. This is because of the mass of muscle rather than a particular affinity.

Lidocaine readily crosses the placenta and equilibrium with regard to the unbound concentration is rapidly reached. The degree of plasma protein binding in the foetus is less than in the mother, which results in lower total plasma concentrations in the foetus.

Lidocaine is excreted in breast milk, but in such small quantities that there is no risk of affecting the child with therapeutic doses.

**Biotransformation**
Lidocaine undergoes enzymatic degradation primarily in the liver. Some degradation may take in tissues other than liver. The main pathway involves oxidative de-ethylation to monoethylglycine-xylidide (MEGX), glycinexylidide (GX), followed by subsequent hydrolysis to 2,6-xylidine and 4-hydroxy-2,6-xylidine. MEGX has a convulsant activity similar to that of lidocaine and a somewhat longer half-life. GX lacks convulsant activity and has a half-life of about 10h. The N-dealkylation to MEGX, is considered to be mediated by both CYP1A2 and CYP3A4.

The metabolite 2,6-xylidine is converted to 4-hydroxy-2,6-xylidine by CYP2A6 and the latter is the major urinary metabolite in man. Only 3% of lidocaine is excreted unchanged. About 70% appears in the urine as 4-hydroxy-2,6-xylidine.

**Elimination**
Lidocaine has a total plasma clearance of 0.95 litres/min, a terminal half-life of 1.6h and an estimated hepatic extraction ratio of 0.65. Its rate of clearance from the blood can be described by a two or three compartment model. There is a rapid disappearance (alpha) phase which is believed to be related to uptake by rapidly equilibrating tissues (i.e. tissues with a high vascular perfusion). The slower phase is related to distribution, to slowly equilibrating tissues (Betaphase) and to its metabolism and excretion (Gamma phase).

The renal clearance is inversely related to its protein binding affinity and the pH of the urine. This suggests by the latter that excretion of lidocaine occurs by non-ionic diffusion.

**Special patient groups**
The terminal half-life in neonates (3.2h) is approximately twice that of adults, whereas clearance is similar (10.2mL/min kg).

5.3 Preclinical safety data
No preclinical safety data are available.

**6 PHARMACEUTICAL PARTICULARS**

6.1 List of excipients
Sodium chloride
Sodium hydroxide [Sodium content is 2.75mg/mL (0.119 mmol/mL)]
Hydrochloric acid
Nitrogen
Water for injections (pH adjusted from 5.0 to 7.0).

This preparation does not contain antioxidants or antimicrobial agents.
6.2 Incompatibilities
Lidocaine has been found to be incompatible when mixed with amphotericin, methohexitone and glyceryl trinitrate. It is not advisable to mix lidocaine with other agents.

6.3 Shelf life
48 months from date of manufacture.

6.4 Special precautions for storage

Unopened container
Store at or below 25°C. Do not refrigerate or freeze.

Opened container
Use immediately. Discard any residue.

6.5 Nature and contents of container
There are six presentations in two concentrations and three ampoule or vial sizes:

10mg/ml (1%)
Lidocaine Hydrochloride Ph Eur 20mg in 2mL, 50mg in 5mL and 200mg in 20mL.

20 mg/ml (2%)
Lidocaine Hydrochloride Ph Eur 40mg in 2mL, 100mg in 5mL and 400mg in 20mL.

Primary packaging materials
Vial stopper is composed entirely of siliconised synthetic bromobutyl rubber.

Package quantities
2mL and 5mL ampoules – packs of 25 ampoules.
20mL vials – single vial packs or pack of 5 vials.

*Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Compatibility
Lidocaine-Claris injection is compatible with the following sterile diluents: 0.9% w/v sodium chloride injection; 5% w/v glucose intravenous infusion; sodium chloride intravenous infusion with glucose intravenous infusion; Lactated Ringer’s (Hartmann’s) solution. Solutions prepared in these diluents are stable for up to 48 hours.

Disposal
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE
Prescription only medicine.
8 SPONSOR

LIDOCAINE-CLARIS is distributed in New Zealand by:
Baxter Healthcare Ltd
33 Vestey Drive
Mt Wellington
Auckland 1060.

Phone (09) 574 2400.

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:
27 September 2012.

10 DATE OF REVISION OF THE TEXT

6 September 2018.

SUMMARY TABLE OF CHANGES

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<tr>
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<th>Summary of new information</th>
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<tr>
<td>ALL</td>
<td>Data sheet converted to SPC format.</td>
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<td>Sponsor details updated.</td>
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Please refer to the Medsafe website (www.medsafe.govt.nz) for most recent data sheet.