Lidocaine hydrochloride  
Antiarrhythmic agent  
Single-dose syringe

**Composition**
Each single-dose syringe contains: 5 ml of Lidocaine hydrochloride anhydrous 20 mg/ml, sodium chloride 30 mg, sodium hydroxide q.s. to pH 6.9, water for injection to 5 ml.

**Pharmaceutical form**
XYLOCARD 2% (20 mg/ml) single-dose syringe contains a sterile solution without any preservative. The disposable syringe is specially designed to ensure injection of the right quantity, so that overdosage can be prevented, and also to avoid risk of confusion with other preparations for cardiological use. The single-dose syringe is designed for the doses (50-100 mg) given by intravenous injection. The syringe has a Luer fitting.

**Therapeutic indications**
Cardiac arrhythmias: Prophylaxis and treatment of ventricular tachyarrhythmias, especially in connection with myocardial infarction, mechanical irritation of the myocardium during cardiac surgery or diagnostic procedures (e.g. heart catheterisation and angiography), digitalis intoxication and intoxication with tricyclic antidepressants. Facilitation of defibrillation of ventricular fibrillation and prevention of recurrence.

Status epilepticus:

**Posology and method of administration**
The dosage is individual.

When high doses are used and the patients myocardial function is impaired, combination with other drugs which reduce the excitability of cardiac muscle requires caution.

Lidocaine treatment may aggravate arrhythmias. The potassium concentration should be normalised before lidocaine treatment is started.

In patients with bradycardia complicated by ventricular tachyarrhythmia, lidocaine may have to be combined with atropine or atropine-like drugs or pacemaker treatment.

Cardiac arrhythmia: Therapeutic plasma concentration range 1.5-6 µg/ml (6.5-26 µmol/l).

Adults: In the treatment of ventricular arrhythmias, an intravenous injection should be given initially, followed by an intravenous infusion.

Normal dose: ½-1 disposable syringe, 2% (20 mg/ml) = 50-100 mg of lidocaine hydrochloride. This normal dose corresponds to 1 mg/kg body weight per injection. The intravenous injection should be given at a rate of 25-50 mg/minute. An effect is usually evident within 1-2 minutes and it usually persists for 15-20 minutes. If no effect is observed after the first injection, the injection may be repeated once or twice at 5-10 minutes intervals. Not more than 200-300 mg should be given during one hour.

Children: Initial dose: 0.5-1.0 mg/kg body weight given as an intravenous injection at a rate of 0.5-1.0 mg/kg/minute.
Normal dose 2 mg/kg body weight; may be increased to 4 mg/kg body weight if required. For continued treatment Xylocard may be given by intravenous infusion, see Xylocard 20% (200 mg/ml) sterile solution (disposable syringe for preparation of i.v. infusions).

Notes:
1. The treatment of status epilepticus with intravenous lidocaine is most appropriate for cases of grand mal and Jackson attacks, when reduction of the level of consciousness is undesirable.
2. Since the onset of action of lidocaine is very rapid, this treatment is also suitable for cases in which it is desired to stop an attack quickly.

Impaired renal function
There is a risk of accumulation of metabolites if the renal function is impaired. Caution should be observed during repeated treatment with lidocaine in patients with impaired renal function.

Impaired hepatic function
Liver disease means a risk of accumulation of lidocaine. Caution should be observed during repeated treatment with lidocaine in patients with impaired hepatic function.

Elderly
A reduction in dosage may be necessary for elderly patients, particularly those with compromised cardiovascular and/or hepatic function and/or prolonged infusion. Elderly patients should be given reduced doses corresponding to their age and physical status.

Contraindications
Known hypersensitivity to lidocaine (extremely rare).
Known hypersensitivity to other local anaesthetics of the amide type, such as prilocaine, mepivacaine or bupivacaine.
Second or third degree AV-block in the absence of pacemaker.

Special warnings and precautions for use
ECG-monitoring should be instituted when lidocaine is administered as an intravenous infusion. Caution should be observed in patients with cardiac decompensation and hypotension or posterior diaphragmatic infarction with a tendency towards heart block.

Lidocaine should be administered with caution to patients with bradycardia, untreated first-degree AV-block with bifascicular block or hypokalaemia. Severely impaired liver or kidney function may mean a risk of accumulation and toxic reactions as lidocaine is mainly metabolised in the liver and the metabolites are excreted by the kidneys. Caution should be observed during repeated treatment with lidocaine in patients with these functional disorders. Through their lower enzyme capacity, neonates are at risk of methaemoglobinaemia. Methaemoglobinaemia can become clinically overt (cyanosis), and treatment with methylene blue may be considered necessary.

Interactions
It is possible to explain observed drug-drug interactions or even in certain cases predict the potential for drug-drug interactions based on the site of metabolism/excretion or other pharmacologic effects of a drug. Lidocaine is completely metabolised.

Potential for influence of lidocaine on the plasma levels/effect of other drugs
Lidocaine is metabolised by cytochrome P4503A4 (CYP3A4) and thus has the potential to inhibit the metabolism of other drugs metabolised by this enzyme, resulting in increased plasma levels of these. This has so far not been reported for any CYP3A substrate.

Potential for influence of other drugs on the plasma levels/effect of lidocaine
Concomitant treatment with drugs that are substrates, inhibitors, or inducers of CYP3A4 has the potential to influence the metabolism and hence the plasma levels and effect of lidocaine. Concomitant administration with the substrate amiodarone has resulted in increased plasma levels of lidocaine resulting in toxic effects. During concomitant administration with carbamazepine, phenobarbitone, and phenytoin which are inducers of CYP3A4, decreased plasma levels of lidocaine have been reported. Primidone has also been reported to induce the metabolism of lidocaine. Furthermore, the plasma levels of lidocaine have been reported to increase, resulting in toxic effects,
during concomitant administration with cimeti
dine, which has an unspecific inhibitory effect on CYP (including CYP3A4) mediated metabolism. Concomitant treatment with metoprolol, nadolol, and propranolol have also been reported to increase the plasma levels of lidocaine resulting in toxic effects.

**Pregnancy and lactation**
It is reasonable to assume that Lidocaine has been used, mainly as a local anaesthesia, by a large number of pregnant women and women of child-bearing age. No specific disturbances to the reproductive process have so far been reported, e.g. an increased incidence of malformations or direct or indirect harmful effects on the fetus.

Enters breast milk but is not likely to affect the infant when therapeutic doses are used.

**Effects on ability to drive and use machines**
Not applicable.

**Undesirable effects**
Most frequent are adverse reactions from the central and peripheral nervous system. They occur in 5-10% of the patients and are mostly dose-related.

Central and peripheral nervous system: Dizziness, paraesthesia and drowsiness. Rarely persistent dizziness, tinnitus, confusion, blurred vision, tremor, convulsions, loss of consciousness and respiratory depression.

Cardiovascular: Rarely hypotension and bradycardia, which may lead to cardiac arrest. Arrhythmias including ventricular tachycardia/ventricular fibrillation.

Blood and lymphatic system disorders: Very rarely neonatal methaemoglobinaemia.

**Overdose**

**Symptoms**
The most serious effects of lidocaine intoxication are on the CNS and cardiovascular system and overdosage can result in severe hypotension, asystole, apnoea, seizures, coma, respiratory arrest, and death.

**Treatment**
The administration of Xylocard should be discontinued immediately. Adequate ventilation should be ensured by checking that the airways are free and administering oxygen.

Hypotension may be counteracted by giving sympathicomimetic drugs (e.g. adrenaline). Adrenergic agents of both ß-adrenoceptor stimulating (e.g. metaraminol) and ß-adrenoceptor stimulating type (e.g. isoprenaline) are generally effective.

The bradycardia may be treated with parasympatholytic agents (e.g. atropine).

Convulsions may be treated with small doses of a short-acting barbiturate (e.g. methohexital 50-120 mg i.v. or diazepam 10-15 mg i.v.).

**Pharmacodynamic properties**
Lidocaine is the model class 1 B substance according to Vaughan Williams and Harrison. Lidocaine blocks the sodium channels in the cell membranes of the heart and reduces the rate of the rise of the action potential and hence the conduction velocity in, above all, the His-Purkinje system and in the atrial ventricular musculature. The automaticity and excitability are also reduced by lidocaine. The duration of the action potential (APD) and the effective refractory period (ERP) are reduced but the ratio ERP/APD is increased. The sinus node and AV-node are not influenced by therapeutic plasma concentrations of lidocaine.

The electrophysiological effects of lidocaine are strongly dependent on the extracellular potassium concentration (probably secondary to the change of the resting potential of the cells) and may be almost completely blocked by hypokalaemia. The effects are also frequency-dependent and are negligible at normal or low heart rates but pronounced at high rates. The effect of lidocaine may therefore be enhanced during tachyarrhythmias in connection with acute myocardial ischaemia, when leakage of potassium to the extracellular space occurs.

Lidocaine does not normally cause changes in the ECG. The QT-time is sometimes somewhat shortened.

In animal experiments, high doses of lidocaine have caused a negative inotropic effect. However, at therapeutic plasma concentrations, the risk of provocation of heart failure is small.

In the recommended doses, lidocaine is practically lacking in hypotensive and vasodilating effects.
Pharmacokinetic properties
Absorption and distribution
Treatment with lidocaine is easily managed, owing to rapid distribution, metabolism and excretion. During the first half-hour after an intravenous injection, the plasma concentration falls with a half-life of 10-15 minutes (alpha-phase), owing to the rapid distribution to different body tissues, including the heart. The therapeutic plasma concentration range is 1.5-6 µg/ml (6.5-26 µmol/l). The plasma protein binding is about 70%. The apparent distribution volume is approximately 1 l/kg.

Metabolism and elimination
Lidocaine is mainly metabolised by the liver (70-90%) through cytochrome P4503A4 (CYP 3A4). The metabolites have a weaker antiarrhythmic action and are excreted by the kidneys. The half-life in the elimination phase (ß-phase) is 90-120 minutes. Less than 10% of the dose of lidocaine is excreted unchanged in the urine. There is a risk of accumulation of metabolites if the renal function is impaired. Heart failure and liver disease also mean a risk of accumulation of lidocaine. During continuous infusion, steady-state conditions are not reached until after 6-8 hours. In order to reach an adequate plasma concentration rapidly and maintain a therapeutic concentration, one or more intravenous injections must be given initially.

Pharmaceutical particulars
List of excipients
Sodium chloride
Sodium hydroxide
Water for injection

Incompatibilities
Not applicable.

Shelf life
Please see outer pack.

Special precautions for storage
Do not store above 25°C. Do not freeze.

Pack size
Please see outer pack.

Instructions for the use of the syringe:
1. Place the rear end of the glass cartridge against a firm, horizontal surface. DO NOT remove the needle cover.
2. Support the syringe with one hand and press downwards, on the needle cover flange, until the rubber membrane of the cartridge is penetrated.
3. Unscrew the needle cover and assemble it to the cartridge.
4. Check that rubber piston runs freely by gently drawing it backwards a few millimetres.

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