PRESCRIBING INFORMATION

Cathejell®

Lidocaine hydrochloride jelly, USP

20 mg / g (2% w / w)

Topical anesthetic

Sterile

Pharmazeutische Fabrik MONTAVIT Ges.m.b.H.
Absam, Austria 6067
www.montavit.com/en

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BioSyent Pharma Inc.
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Table of Contents

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Non-medicinal Ingredients
Topical	Jelly in collapsible syringe 20 mg / g (2% w / w); When fully compressed, each syringe expresses approximately 10 g (9.4 mL), 200 mg of lidocaine hydrochloride	Glycerol, hydrochloric acid, hydroxyethylcellulose, sodium hydroxide, and water for injection

INDICATIONS AND CLINICAL USE

Adults (>18 years of age):

Cathejell® (lidocaine hydrochloride) is indicated as a surface anesthesia and lubrication for:

- The male and female urethra during cystoscopy, catheterization, exploration by sound, and other endourethral operations;
- Nasal and pharyngeal cavities in endoscopic procedures such as gastroscopy and bronchoscopy;
- Proctoscopy and rectoscopy;
- Tracheal intubation;
- Symptomatic treatment of pain in connection with cystitis and urethritis.

Geriatrics (>65 years of age):

Elderly patients should be given reduced doses commensurate with their age and physical condition (see DOSAGE AND ADMINISTRATION, Special Populations).

Pediatrics (<18 years of age):

Children should be given reduced doses commensurate with their age, weight and physical condition (see DOSAGE AND ADMINISTRATION, Special Populations).

Lidocaine should be used with caution in children younger than two years of age as there are insufficient data to support the safety and efficacy of this product in this patient population at this time (see WARNINGS AND PRECAUTIONS, Special Populations).

CONTRAINDICATIONS

Cathejell® (lidocaine hydrochloride) is contraindicated in:

- Patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components in the formulation (see DOSAGE FORMS, COMPOSITION, AND PACKAGING).
- Patients with congenital or idiopathic methemoglobinemia.
- Infants who require treatment with methemoglobin-inducing agents, e.g., sulfonamides, and are 12 months of age or younger (see DRUG INTERACTIONS).

WARNINGS AND PRECAUTIONS

General

EXCESSIVE DOSAGE, OR SHORT INTERVALS BETWEEN DOSES, CAN RESULT IN HIGH PLASMA LEVELS OF LIDOCAINE OR ITS METABOLITES AND SERIOUS ADVERSE EFFECTS. Absorption from the mucous membranes is variable but is especially high from the bronchial tree. Such applications may therefore result in rapidly rising or excessive plasma concentrations, with an increased risk for toxic symptoms, such as convulsions. PATIENTS SHOULD BE INSTRUCTED TO STRICTLY ADHERE TO THE RECOMMENDED DOSAGE. This is especially important in children where doses vary with weight. The management of serious adverse reactions may require the use of resuscitative equipment, oxygen, and other resuscitative drugs (see OVERDOSAGE).

The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Tolerance to elevated blood levels varies with the status of the patient.

Lidocaine should be used with caution in patients with sepsis and/or traumatized mucosa at the area of application, since under such conditions there is the potential for rapid systemic absorption.

When using Cathejell® in younger children, especially infants under the age of 3 months, care must be taken to ensure that the caregiver understands the need to limit the dose and area of application, and to prevent accidental ingestion (see DOSAGE AND ADMINISTRATION). Children should be closely observed during and after use of the lidocaine jelly, as they are at greater risk than adults for serious adverse events (e.g., methemoglobinemia).

In patients under general anesthesia who are paralyzed, higher plasma concentrations may occur than in spontaneously breathing patients. Unparalyzed patients are more likely to swallow a large proportion of the dose, which then undergoes considerable first-pass hepatic metabolism following absorption from the gut.

Avoid contact with eyes.

Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. It has been shown that the use of amide

local anesthetics in malignant hyperthermia patients is safe. However, there is no guarantee that neural blockade will prevent the development of malignant hyperthermia during surgery. It is also difficult to predict the need for supplemental general anesthesia. Therefore, a standard protocol for the management of malignant hyperthermia should be available.

When used for endotracheal tube lubrication, care should be taken to avoid introduction of the jelly into the lumen of the tube. If allowed into the inner lumen, the jelly may dry on the inner surface leaving a residue which tends to clump with flexion, narrowing the lumen. There have been rare reports in which this residue has caused the lumen to occlude. Similarly, do not use the jelly to lubricate the endotracheal stylettes.

When topical anesthetics are used in the mouth, the patient should be aware that the production of topical anesthesia may impair swallowing and thus enhance the danger of aspiration. Numbness of the tongue or buccal mucosa may enhance the danger of unintentional biting trauma. Food or chewing gum should not be taken while the mouth or throat area is anesthetized (see also Part III: CONSUMER INFORMATION).

Cathejell® is ineffective when applied to intact skin.

Lidocaine has been shown to be porphyrinogenic in animal models. Cathejell® should only be prescribed to patients with acute porphyria on strong or urgent indications, when they can be closely monitored. Appropriate precautions should be taken for all porphyria patients.

Cardiovascular

Lidocaine should be used with caution in patients with bradycardia or impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by amide-type local anesthetics.

Lidocaine should be used with caution in patients in severe shock.

Hematology

Methemoglobinemia: Excessive dosage, or short intervals between doses, can result in sufficient high plasma levels of lidocaine or its metabolites to trigger methemoglobinemia. Patients should be instructed to strictly adhere to the recommended dosage. This is especially important in children where doses vary with weight. The management of methemoglobinemia should follow the established standard of care (see OVERDOSAGE).

Hepatic

Because amide-type local anesthetics such as lidocaine are metabolized by the liver, these drugs, especially repeated doses, should be used cautiously in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at greater risk of developing toxic plasma concentrations.

Neurologic

Epilepsy:

The risk of central nervous system side effects when using lidocaine in patients with epilepsy is very low, provided that the dose recommendations are followed (see DOSAGE AND ADMISTRATION).

Locomotion and Coordination:

Topical lidocaine formulations generally result in low plasma concentrations because of a low degree of systemic absorption. However, depending on the dose, local anesthetics 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.

Renal

Lidocaine is metabolized primarily by the liver to monoethylglycinexylidine (MEGX, which has some CNS activity) and then further to metabolites glycinexylidine (GX) and 2,6-dimethylaniline (see ACTION AND CLINICAL PHARMACOLOGY). Only a small fraction (2%) of lidocaine is excreted unchanged in the urine. The pharmacokinetics of lidocaine and its main metabolite were not altered significantly in hemodialysis patients (n=4) who received an intravenous dose of lidocaine. Therefore, renal impairment is not expected to significantly affect the pharmacokinetics of lidocaine when Cathejell® is used for short treatment durations, according to dosage instructions (see DOSAGE AND ADMINISTRATION). Caution is recommended when lidocaine is used in patients with severely impaired renal function because lidocaine metabolites may accumulate during long term treatment (see DOSAGE AND ADMINISTRATION).

Sensitivity

Lidocaine should be used with caution in persons with known drug sensitivities.

Cathejell® is contraindicated in patients with known hypersensitivities to local anesthetics of the amide type and to other components in the formulation.

Special Populations

Debilitated patients, acutely ill patients, and patients with sepsis should be given reduced doses commensurate with their age, weight, and physical condition because they may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses.

Cathejell® is contraindicated in patients with congenital or idiopathic methemoglobinemia and in infants 12 months of age or younger who require treatment with methemoglobin-inducing agents (see CONTRAINDICATIONS). Caution is advised for patients with glucose-6-phosphate dehydrogenase deficiency who are more susceptible to drug-induced methemoglobinemia (see CONTRAINDICATIONS).

Pregnant Women:

There are no adequate and well-controlled studies in pregnant women on the effect of lidocaine on the developing fetus.

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. However, care should be given during early pregnancy when maximum organogenesis takes place.

Labour and Delivery:
Lidocaine is not contraindicated in labour and delivery. Should Cathejell® be used concomitantly with other products containing lidocaine during labour and delivery, the total dose contributed by all formulations must be kept in mind.

Nursing Women:
Lidocaine and its metabolites are excreted in the breast milk. At therapeutic doses, the quantities of lidocaine and its metabolites in breast milk are small and generally are not expected to be a risk for the infant.

Pediatrics:
Children should be given reduced doses commensurate with their age, weight, and physical condition because they may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses (see DOSAGE AND ADMINISTRATION).

Cathejell® is contraindicated for infants (12 months of age or younger) who require treatment with methemoglobin-inducing drugs (see CONTRAINDICATIONS).

Cathejell® should be used with caution in children under the age of 2 as there are insufficient data to support the safety and efficacy of this product in this patient population at this time.

Children should be closely observed during and after use of topical anesthetics, as they are at greater risk than adults for serious adverse events (e.g., methemoglobinemia).

When using Cathejell® in younger children, care must be taken to ensure that the caregiver understands the need to limit the dose and area of application, and to prevent accidental ingestion (see DOSAGE AND ADMINISTRATION).

Cathejell® should not be applied to the genital mucosa of children or infants due to insufficient data on absorption.

Geriatrics:
Elderly patients may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses and may require dose reductions.

ADVERSE REACTIONS

Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide local anesthetic agents. These adverse experiences are, in general, dose-related and may result from high plasma levels caused by

overdosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy, or diminished tolerance on the part of the patient.

An increased incidence of postoperative sore throat has been reported following endotracheal tube lubrication with lidocaine jelly.

Serious adverse experiences are generally systemic in nature. The following types are those most commonly reported:

Central Nervous System

CNS manifestations are excitatory and/or depressant and may be characterized by the following signs and symptoms of escalating severity: circumoral paresthesia, light-headedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, hyperacusis, tinnitus, blurred vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression, and arrest. The excitatory manifestations (e.g., twitching, tremors, convulsions) may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.

Drowsiness following the administration of lidocaine is usually an early sign of a high lidocaine plasma level and may occur as a consequence of rapid absorption.

Cardiovascular System

Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, arrhythmia, and cardiovascular collapse, which may lead to cardiac arrest.

Allergic

Allergic reactions are characterized by cutaneous lesions, urticaria, edema or, in the most severe instances, anaphylactic shock. Allergic reactions of the amide type are rare (<0.1%) and may occur as a result of sensitivity either to the local anesthetic agent or to other components in the formulation (see DOSAGE FORMS, COMPOSITION, AND PACKAGING).

DRUG INTERACTIONS

Overview

Lidocaine is mainly metabolized in the liver by CYP1A2 and CYP3A4 to its two major metabolites, monoethylglycinexylidine (MEGX) and glycinexylidine (GX), both of which are pharmacologically active. Lidocaine has a high hepatic extraction ratio. Only a small fraction (2%) of lidocaine is excreted unchanged in the urine. The hepatic clearance of lidocaine is expected to depend largely on blood flow.

Strong inhibitors of CYP1A2, such as fluvoxamine, given concomitantly with lidocaine, can cause a metabolic interaction leading to an increased lidocaine plasma concentration. Therefore, prolonged administration of lidocaine should be avoided in patients treated with strong inhibitors of CYP1A2, such as fluvoxamine. When co-administered with intravenous lidocaine, two strong inhibitors of CYP3A4, erythromycin

and itraconazole, have each been shown to have a modest effect on the pharmacokinetics of intravenous lidocaine. Other drugs such as propranolol and cimetidine have been reported to reduce intravenous lidocaine clearance, probably through effects on hepatic blood flow and/or metabolism.

When lidocaine is used topically, plasma concentrations are of importance for safety reasons (see WARNINGS AND PRECAUTIONS, General; ADVERSE REACTIONS). However, with the low systemic exposure and short duration of topical application, the abovementioned metabolic drug-drug interactions are not expected to be of clinical significance when Cathejell® is used according to dosage recommendations.

Clinically relevant pharmacodynamic drug interactions may occur with lidocaine and other local anesthetics or structurally related drugs, and Class I and Class III antiarrhythmic drugs due to additive effects.

Co-administration of Cathejell® and other methemoglobin-inducing agents to patients 12 months of age or younger may result in clinical signs of methemoglobinemia (see CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, DRUG INTERACTIONS, ADVERSE REACTIONS).

Drug-Drug Interactions

Local anesthetics and agents structurally related to amide-type local anesthetics:
Lidocaine should be used with caution in patients receiving other local anesthetics or agents structurally related to amide-type local anesthetics (e.g., antiarrhythmics such as mexiletine), since the toxic effects are additive.

Antiarryhythmic Drugs:
Class I Antiarrhythmic drugs
Class I antiarrhythmic drugs (such as mexiletine) should be used with caution since toxic effects are additive and potentially synergistic.

Class III Antiarrhythmic drugs
Caution is advised when using Class III antiarrhythmic drugs concomitantly with lidocaine due to potential pharmacodynamic or pharmacokinetic interactions with lidocaine, or both. A drug interaction study has shown that the plasma concentration of lidocaine may be increased following administration of a therapeutic dose of intravenous lidocaine to patients treated with amiodarone (n=6). Case reports have described toxicity in patients treated concomitantly with lidocaine and amiodarone. Patients treated with Class III antiarrhythmic drugs (e.g., amiodarone) should be kept under close surveillance and ECG monitoring should be considered, since cardiac effects of these drugs and lidocaine may be additive.

Strong Inhibitors of CYP1A2 and CYP3A4:
Cytochrome CYP1A2 and CYP3A4 are involved in the formation of the pharmacologically active lidocaine metabolite MEGX.

Fluvoxamine
Strong inhibitors of CYP1A2, such as fluvoxamine, given during prolonged administration of lidocaine to areas with a high extent of systemic absorption (e.g.,

mucous membranes) can cause a metabolic interaction leading to an increased lidocaine plasma concentration. The plasma clearance of a single intravenous dose of lidocaine was reduced by 41% to 60% during co-administration of fluvoxamine, a selective and potent CYP1A2 inhibitor, to healthy volunteers.

Erythromycin and Itraconazole
Erythromycin and itraconazole, which are strong inhibitors of CYP3A4, have been shown to reduce clearance of lidocaine by 9% to 18%, following a single intravenous dose of lidocaine to healthy volunteers.

During combined co-administration with fluvoxamine and erythromycin the plasma clearance of lidocaine was reduced by 53%.

β-blockers and Cimetidine:
Following a single intravenous dose of lidocaine, administered to healthy volunteers, the clearance of lidocaine has been reported to be reduced up to 47% when co-administered with propranolol and up to 30% when co-administered with cimetidine. Reduced clearance of lidocaine when co-administered with these drugs is probably due to reduced liver blood flow and/or inhibition of microsomal liver enzymes. The potential for clinically significant interactions with these drugs should be considered during long-term treatment with high doses of lidocaine.

Methemoglobinemia
Cathejell® may induce the formation of methemoglobin and result in overt clinical signs of methemoglobinemia in patients treated concomitantly with Cathejell® and other methemoglobin-inducing agents, including but not limited to sulfonamides, acetanilid, aniline dyes, benzocaine, chloroquine, dapsone, naphthalene, nitrates and nitrites, nitrofurantoin, nitroglycerin, nitroprusside, pamaquine, para-aminosalicylic acid, phenacetin, phenobarbital, phenytoin, primaquine and quinine (see CONTRAINDICATIONS and OVERDOSAGE).

Acetaminophen has been shown to induce methemoglobin formation in vitro and in animals. In humans, methemoglobin formation is very rare at therapeutic doses and overdoses of acetaminophen.

Drug-Food Interactions
Interactions of lidocaine with food have not been established.

Drug-Herb Interactions
Interactions of lidocaine with herbal products have not been established.

Drug-Laboratory Tests Interactions
Interactions of lidocaine with laboratory tests have not been established.

Drug-Lifestyle Interactions
Interactions of lidocaine with lifestyle have not been established.

DOSAGE AND ADMINISTRATION

General Dosing Considerations

When Cathejell® (lidocaine hydrochloride) is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Cathejell® in the pre-filled syringe is preservative-free, latex free, and intended for single use only.

The absorption of lidocaine jelly from the nasopharynx is usually lower than with other lidocaine products. Blood concentrations of lidocaine after instillation of the jelly in the intact urethra and bladder in doses up to 800 mg are fairly low and below toxic levels.

Special Populations

Lidocaine should also be used with caution in patients with epilepsy, impaired cardiac conduction, bradycardia, impaired hepatic, or renal function and in severe shock (see WARNINGS AND PRECAUTIONS).

Debilitated patients, elderly patients, acutely ill patients, patients with sepsis, and children should be given reduced doses commensurate with their age, weight and physical condition (see WARNINGS AND PRECAUTIONS).

Cathejell® should be used with caution in children under the age of 2 as there is insufficient data to support the safety and efficacy of this product in this patient population at this time (see WARNINGS AND PRECAUTIONS).

Recommended Dose and Dosage Adjustment

When fully compressed, each 13.3 g syringe will express approximately 10 g (9.4 mL) of Cathejell® (200 mg of lidocaine hydrochloride). The amount expressed may vary with the technique used.

Urethral Anesthesia:

Surface Anesthesia of the Male Adult Urethra

For adequate analgesia in males, 20 g (400 mg lidocaine hydrochloride) of jelly (2 syringes) is usually required. The jelly is instilled slowly until the patient has a feeling of tension, approximately 10 g (200 mg lidocaine hydrochloride) of jelly (1 syringe). A penile clamp is then applied for several minutes at the corona, after which another 10 g (200 mg lidocaine hydrochloride) of jelly (1 syringe) is instilled.

When anesthesia is especially important (e.g., during sounding or cystoscopy), a larger quantity of jelly (e.g., 30–40 g, i.e., 600-800 mg lidocaine hydrochloride) (3–4 syringes) may be instilled in 3–4 portions and allowed to act for 10–12 minutes before insertion of the instrument. The jelly instilled into the bladder is also effective for procedures in this region.

To anesthetize only the anterior male urethra (e.g., for catheterization), small volumes (e.g. 5–10 g, i.e., 100–200 mg lidocaine hydrochloride) (½ to 1 syringe) are usually adequate for lubrication.

For Surface Anesthesia of the Female Adult Urethra
Instill 5-10 g (100-200 mg lidocaine hydrochloride) of jelly (½ to 1 syringe) in small portions to fill the whole urethra. If desired, some jelly may be deposited on the orifice and covered with a cotton swab. In order to obtain adequate anesthesia, several minutes should be allowed prior to performing urological procedures.

Endoscopy:
The instillation of 10–20 g (200–400 mg lidocaine hydrochloride) of jelly (1–2 syringes) is recommended for adequate analgesia and a small amount may be applied to the lubricating instrument. When combined with other lidocaine products (e.g., for bronchoscopy), the total dose of lidocaine hydrochloride should not exceed 400 mg (20 g of jelly) (2 syringes).

Proctoscopy and Rectoscopy:
Up to 20 g (400 mg lidocaine hydrochloride) of jelly (2 syringes) can be used for anal and rectal procedures. The total dose of lidocaine hydrochloride should not exceed 400 mg (20 g of jelly) (2 syringes).

Lubrication for Endotracheal Intubation:
Apply approximately 2 g of jelly to the external surface of the endotracheal tube just prior to insertion. Care should be taken to avoid introducing the product into the lumen of the tube (see WARNINGS AND PRECAUTIONS). Do not use the jelly to lubricate endotracheal stylettes. It is also recommended that the use of endotracheal tubes with dried jelly on the external surface be avoided for lack of lubricating effect.

Maximum Dosage
Adults:
The dose of Cathejell® depends on the application site. A safe dose for oral use is 400 mg lidocaine hydrochloride (20 g of jelly) (2 syringes). A safe dose for use in the urethra and bladder is 800 mg lidocaine hydrochloride (40 g of jelly) (4 syringes). A maximum single dosage for Cathejell® is not established. No more than four doses should be given during a 24-hour period.

Children (Under 12 Years):
It is difficult to recommend a maximum dose of any drug for children since this varies as a function of age and weight. The maximum amount per dose should not exceed 6 mg lidocaine hydrochloride per kg of body weight or 3 g Cathejell® per 10 kg body weight. No more than four doses should be given during a 24-hour period.

For children over 12 years of age doses should be commensurate with weight and physical condition.

Children should be closely observed during and after use of topical anesthetics, as they are at greater risk than adults for serious adverse events (e.g., methemoglobinemia).

OVERDOSAGE

For management of suspected drug overdose,
contact your regional Poison Control Centre

Acute systemic toxicity from local anesthetics is generally related to high plasma levels encountered during therapeutic use of local anesthetics and originates mainly in the central nervous and the cardiovascular systems (see ADVERSE REACTIONS and WARNINGS AND PRECAUTIONS). It should be kept in mind that clinically relevant pharmacodynamic drug interactions (i.e., toxic effects) may occur with lidocaine and other local anesthetics or structurally related drugs, and Class I and Class III antiarrhythmic drugs due to additive effects (see DRUG INTERACTIONS).

Symptoms

Central Nervous System Toxicity:

This is a graded response, with symptoms and signs of escalating severity. The first symptoms are circumoral paresthesia, numbness of the tongue, light-headedness, hyperacusis, and tinnitus. Visual disturbance and muscular tremors are more serious and precede the onset of generalized convulsions. 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 normal respiration. In severe cases apnea may occur. Acidosis, hyperkalemia, hypocalcemia, and hypoxia increase and extend the toxic effects of local anesthetics.

Recovery is due to redistribution and metabolism of the local anesthetic drug. Recovery may be rapid unless large amounts of the drug have been administered.

Cardiovascular Effects:

The effects may be seen in cases with high systemic concentrations. Severe hypotension, bradycardia, arrhythmia, and cardiovascular collapse may be the result in such cases. Cardiovascular toxic effects are generally preceded by signs of toxicity in the central nervous system unless the patient is receiving a general anesthetic or is heavily sedated with drugs such as a benzodiazepine or barbiturate.

Methemoglobinemia

Rare cases of methemoglobinemia have been reported.

Mild methemoglobinemia is characterized by tissue cyanosis, a bluish-grey or brownish discoloration of the skin, especially around the lips and nail beds, which is not reversed by breathing 100% oxygen. Clinical signs may also include pallor and marbleization.

Severe methemoglobinemia (MetHb concentrations above approximately 25%) is associated with signs of hypoxemia, ie. dyspnea, tachycardia and depression of consciousness.

Drug-induced methemoglobinemia may occur with the use of drugs including but not limited to amino-amide, sulfonamides, acetanilid, aniline dyes, benzocaine, lidocaine, chloroquine, dapsone, naphthalene, nitrates and nitrites, nitrofurantoin, nitroglycerin,

nitroprusside, pamaquine, para-aminosalicylic acid, phenacetin, phenobarbital, phenytoin, primaquine and quinine.

Acetaminophen has been shown to induce methemoglobin formation *in vitro* and in animals. In humans, methemoglobin formation is very rare at therapeutic doses and overdoses of acetaminophen.

Treatment

The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic administration. At the first sign of change, oxygen should be administered.

The first step in the management of systemic toxic reactions consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. This may prevent convulsions if they have not already occurred.

If convulsions occur, the objective of the treatment is to maintain ventilation and oxygenation and support circulation. Oxygen must be given, and ventilation assisted if necessary (mask and bag or tracheal intubation). Should convulsions not stop spontaneously after 15–20 seconds, an anticonvulsant should be given intravenous (i.v.) to facilitate adequate ventilation and oxygenation. Thiopental sodium 1–3 mg / kg body weight (bw) i.v. is the first choice. Alternatively, diazepam 0.1 mg / kg bw i.v. may be used, although its action will be slow. Prolonged convulsions may jeopardise the patient's ventilation and oxygenation. If so, injection of a muscle relaxant (e.g., succinylcholine 1 mg / kg bw) will facilitate ventilation and oxygenation can be controlled. Early endotracheal intubation is required when succinylcholine is used to control motor seizure activity.

If cardiovascular depression is evident (hypotension, bradycardia), ephedrine 5–10 mg i.v. should be given and may be repeated, if necessary, after 2–3 minutes.

Should circulatory arrest occur, immediate cardiopulmonary resuscitation should be instituted. Continual oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance since hypoxia and acidosis will increase the systemic toxicity of local anesthetics. Epinephrine (0.1–0.2 mg as intravenous or intracardial injections) should be given as soon as possible and repeated, if necessary.

Children should be given doses of epinephrine commensurate with their age and weight.

In neonates, methemoglobin concentrations of up to 5 - 6% are not considered to be of clinical significance, with treatment of symptomatic methemoglobinemia not typically necessary unless methemoglobin concentrations are above 25 - 30%. However, the severity of clinical symptoms should be the primary consideration in the decision to initiate treatment, rather than the level of methemoglobin. Most patients recovered spontaneously after removal of the jelly. Methemoglobinemia may be treated with a slow intravenous injection of methylene blue. It has been reported in published literature

that methylene blue should be used cautiously as a treatment for methemoglobinemia in patients with glucose-6-phosphate dehydrogenase deficiency because it may not be effective for these patients and may cause hemolytic anemia.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anesthetic action. Local anesthetics of the amide type are thought to act within the sodium channels of the nerve membrane.

Pharmacodynamics

Onset of Action

Anesthesia is achieved within 5 minutes, depending on the area of application. Duration of anesthesia is approximately 20–30 minutes. Cathejell® (lidocaine hydrochloride) is ineffective when applied to intact skin.

Hemodynamics

Lidocaine, like other local anesthetics, may also have effects on excitable membranes in the brain and myocardium. If excessive amounts of drug reach systemic circulation rapidly, symptoms and signs of toxicity will appear, emanating from the central nervous and cardiovascular systems.

Central nervous system toxicity (see OVERDOSAGE) usually precedes the cardiovascular effects since it occurs at lower plasma concentrations. Direct effects of local anesthetics on the heart include slow conduction, negative inotropism, and eventually cardiac arrest.

Pharmacokinetics

Absorption:

The rate and extent of absorption depends upon concentration and total dose administered, the specific site of application and duration of exposure. In general, the rate of absorption of local anesthetic agents following topical application to wound surfaces and mucous membranes is high and occurs most rapidly after intratracheal and bronchial administration. The absorption of lidocaine jelly from the nasopharynx is usually lower than with other lidocaine products. Blood concentrations of lidocaine after instillation of the jelly in the intact urethra and bladder in doses up to 800 mg are fairly low and below toxic levels. Lidocaine is also well absorbed from the gastrointestinal tract, although little intact drug may appear in the circulation because of biotransformation in the liver.

Distribution:

Lidocaine has a total plasma clearance of 0.95 L / min and a volume of distribution at steady state of 91 L.

Lidocaine readily crosses the placenta, and equilibrium in regard to free, unbound drug will be reached. Because the degree of plasma protein binding in the fetus is less than

in the mother, the total plasma concentration will be greater in the mother, but the free concentrations will be the same.

The plasma binding of lidocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to 4 µg of free base per mL, 60% to 80% of lidocaine is protein bound. Binding is also dependent on the plasma concentration of the alpha-1-acid glycoprotein. Lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion.

Metabolism:
Lidocaine is metabolized rapidly by the liver, and its metabolites and the unchanged drug are excreted by the kidneys. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. Only 2% of lidocaine is excreted unchanged. Most of it is metabolized first to monoethylglycinexylidide (MEGX) and then to glycinexylidide (GX) and 2,6-dimethylaniline. Up to 70% appears in the urine as 4-hydroxy-2,6-dimethylaniline. The pharmacological/toxicological actions of MEGX and GX are similar to, but less potent than those of lidocaine. GX has a longer half-life (about 10 h) than lidocaine and may accumulate during long-term administration.

Excretion:
Lidocaine has an elimination half-life of 1.6 h and an estimated hepatic extraction ratio of 0.65. The clearance of lidocaine is almost entirely due to liver metabolism and depends both on liver blood flow and the activity of metabolizing enzymes. Approximately 90% of the lidocaine administrated intravenously is excreted in the form of various metabolites, and less than 10% is excreted unchanged in the urine. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-dimethylaniline, accounting for about 70% to 80% of the dose excreted in the urine.

The elimination half-life of lidocaine following an intravenous bolus injection is typically 1.5 to 2 hours. The elimination half-life in neonates (3.2 hours) is approximately twice that of adults. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites.

Special Populations and Conditions
Acidosis increases the systemic toxicity of lidocaine while the use of CNS depressants may increase the levels of lidocaine required to produce overt CNS effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 µg free base per mL.

Carcinogenesis and Mutagenesis
Genotoxicity tests with lidocaine showed no evidence of mutagenic potential. A metabolite of lidocaine, 2,6-dimethylaniline, showed weak evidence of activity in some genotoxicity tests. A chronic oral toxicity study of the metabolite 2,6-dimethylaniline (0, 14, 45, 135 mg / kg) administered and fed to rats showed that there was a significantly greater incidence of nasal cavity tumors in male and female animals that had daily oral exposure to the highest dose of 2,6-dimethylaniline for 2 years. The lowest tumour-inducing dose tested in animals (135 mg / kg) corresponds to approximately 50 times the amount of 2,6-dimethylaniline to which a 50 kg subject

would be exposed to following the application of 20 g of lidocaine jelly 2% for 24 hours on the mucosa, assuming the highest theoretical extent of absorption of 100% and 80% conversion to 2,6-dimethylaniline. Based on a yearly exposure (once daily dosing with 2,6-dimethylaniline in animals and 5 treatment sessions with 20 g lidocaine jelly 2% in humans), the safety margins would be approximately 3400 times when comparing the exposure in animals to man.

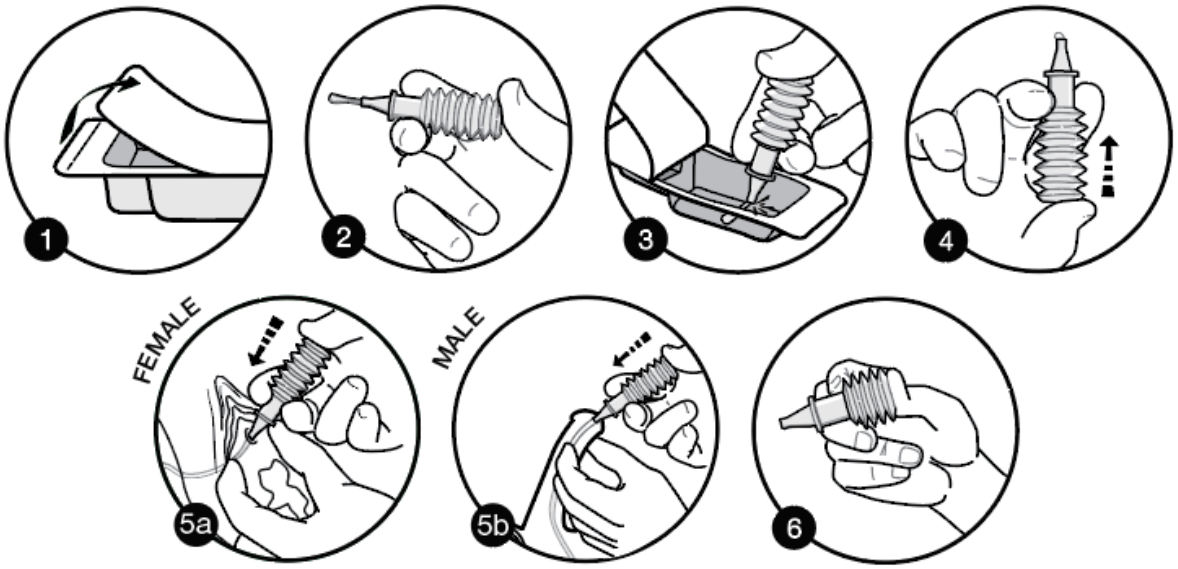
STORAGE AND STABILITY

Store between 15° C–30° C.

SPECIAL HANDLING INSTRUCTIONS

Administration

1. Peel off the paper cover from the transparent blister pack (see image 1).
2. Inspect mixture visually for clarity, particulate matter, precipitation, discolouration, and leakage prior to administration (see image 2).
3. Break off the applicator tip using a vigorous downward stroke in the bottom of the sterile blister pack (see image 3).
4. Remove the applicator tip completely. Release one drop of jelly to coat the nozzle for easier insertion (see image 4).
5. Instill by applying slight but steady pressure to the collapsible syringe (see images 5a and 5b).
6. While removing the syringe, keep the syringe compressed to avoid suction of the instilled jelly (see image 6).



For further assistance, questions or concerns please contact BioSyent Pharma Inc. (cathejell@biosyent.com or 1.888.439.0013) or Pharmazeutische Fabrik MONTAVIT Ges.m.b.H. (pharma@montavit.com).

DOSAGE FORMS, COMPOSITION, AND PACKAGING

Dosage Forms

Cathejell® (lidocaine hydrochloride) is a clear to almost clear, slightly coloured jelly.

When fully compressed, each 13.3 g syringe will express approximately 10 g (9.4 mL) of Cathejell® (200 mg of lidocaine hydrochloride).

Composition

Medicinal ingredients:

Cathejell® contains 20 mg / g (2% w / w) lidocaine hydrochloride.

Non-medicinal ingredients:

Glycerol, hydrochloric acid, hydroxyethylcellulose, sodium hydroxide, and water for injection.

Cathejell® is preservative free, latex free, and is intended for single use only.

Packaging

Cathejell® is available in polypropylene collapsible syringes (accordion-type syringes) with applicator cone. Packaging sizes include 1 x 13.3 g, 5 x 13.3 g, and 25 x 13.3 g.

Cathejell®

2% (w / w)
Lidocaine hydrochloride jelly, USP

PART III: CONSUMER INFORMATION

This leaflet is part of the "Prescribing Information" published when Cathejell® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Cathejell®. Contact your doctor or pharmacist if you have any questions about the drug.

Before using Cathejell®, read this leaflet carefully. Please keep this leaflet to refer to until you have used up all your Cathejell®.

This medicine has been prescribed for you personally and you should not pass it on to others; it may harm them, even if their symptoms are the same as yours.

ABOUT THIS MEDICATION

What the Medication is Used for
Cathejell® is used to produce a temporary loss of feeling or numbness of the skin in adults and children 2 years of age and older, and can be used:

- Before certain types of examinations done by your doctor;
- To help relieve the pain from inflammation of the urinary bladder and the urethra.

What it Does
Cathejell® is a topical anesthetic that contains the drug lidocaine which produces a temporary loss of sensation or numbness on the area where it is applied. Cathejell® should start to work within 5 to 15 minutes after you apply it. The effect usually lasts 20 to 30 minutes.

When it Should Not be Used
Do not use Cathejell®:

- If you are allergic to lidocaine, any other "-caine" type anesthetics (e.g., bupivacaine, ropivacaine, mepivacaine) or any of the non-medicinal ingredients in the product (see **Non-Medicinal Ingredients**);
- If you have a blood disorder called methemoglobinemia;
- In infants (12 months of age or younger) who are taking medicines that may cause methemoglobinemia (see **INTERACTIONS WITH THIS MEDICATION**).

What the Medicinal Ingredient Is
Lidocaine hydrochloride.

Non-Medicinal Ingredients
Glycerol, hydrochloric acid, hydroxyethylcellulose, sodium hydroxide, and water for injection.

Tell your doctor if you think you may be sensitive to any of the above ingredients.

What Dosage Forms it Comes In
Cathejell® is available as a single use syringe containing 20 milligrams of lidocaine hydrochloride in each gram of jelly (2% w / w).

WARNINGS AND PRECAUTIONS

Before you use Cathejell®, tell your doctor or pharmacist:

- About all health problems you have now or have had in the past;
- About other medicines you take, including ones you can buy without a prescription;
- If you are taking other medicines such as drugs used to treat irregular heart activity (anti-arrhythmics);
- If you have ever had a bad, unusual, or allergic reaction to Cathejell® or any other medicines ending with "caine";
- If you think you may be allergic or sensitive to any ingredients in Cathejell® (see above);
- If there is an infection, skin rash, cut or wound at or near the area you want to apply Cathejell®;
- If you have a skin condition that is severe or that covers a large area;
- If you have a severe heart, kidney, or liver disease (see **PROPER USE OF THIS MEDICATION**);
- If you have epilepsy (there is very low risk if used as per **PROPER USE OF THIS MEDICATION**);
- If you or someone in your family has been diagnosed with porphyria;
- If you are experiencing severe shock;
- If you are pregnant, plan to become pregnant, or are breastfeeding;
- If you have a condition called glucose-6-phosphate dehydrogenase deficiency because you are at increased risk for methemoglobinemia.

Use in children: Younger children, especially those under the age of 3 months, are at greater risk for serious side effects than adults. You should:

- Tell your child's doctor if you will be using Cathejell® in a child who is less than 2 years of age;
- Always follow the doctor's instructions for using Cathejell®, especially in young children and infants;
- Be careful not to use more Cathejell® than instructed by your child's doctor. Limit the dose and area of application, especially in infants less than 3 months of age;
- Monitor your child closely during and after you use Cathejell® on them.

Do not use Cathejell® on the genitals of children or infants.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist about any other drugs you take, including:

- Drugs you can buy without a prescription;
- Anti-arrhythmic drugs for heart problems (e.g. mexiletine, amiodarone) (see **PROPER USE OF THIS MEDICATION**);
- Other anesthetics (see **PROPER USE OF THIS MEDICATION**);
- Propranolol for heart problems or cimetidine for gastrointestinal problems, if you are going to use high doses of Cathejell® for a long time;
- Fluvoxamine, for depression, if you are going to use high doses of Cathejell® for a long time.
- Other medicines which may cause methemoglobinemia, including: amino-amide, sulfonamides, acetanilid, aniline dyes, benzocaine (or other "-caine" type anesthetics), chloroquine, dapsone, naphthalene, nitrates or nitrites, nitrofurantoin, nitroglycerin, nitroprusside, pamaquine, para-aminosalicylic acid, phenacetin, phenobarbital, phenytoin, primaquine, quinine and acetaminophen.

Please inform your doctor/dentist/pharmacist if you are taking or have recently taken any other medicines, even those that can be bought without a prescription. Usage of such medicines at the same time may increase the risk of serious side effects.

PROPER USE OF THIS MEDICATION

When fully compressed, each 13.3 g syringe will express approximately 10 g (9.4 mL) of Cathejell® (200 mg of lidocaine hydrochloride). The amount expressed may vary with the technique used.

Usual Dose
If this medicine is recommended by your doctor, be sure to follow the directions for use that have been given. If you are treating yourself, such as for the treatment of pain caused by inflammation of the urethra or urinary bladder, or for self catheterization, follow the directions below and your doctor's or pharmacist's instructions for how to apply the jelly. Check with your doctor or pharmacist if you have any questions about your directions.

The following are general guidelines for the maximum amount of Cathejell® that should be used without a doctor's advice. These guidelines apply only to otherwise healthy people. If you have a special skin or other condition that requires a doctor's supervision; ask your doctor about the maximum amount of jelly that you should use.

Do not use more Cathejell®, more often, or for a longer period of time than either your doctor ordered or than these package directions suggest as this may cause unwanted side effects (see **SIDE EFFECTS AND WHAT TO DO ABOUT THEM**).

If possible, clean the affected area well before each application of jelly. Use the smallest amount of jelly needed to control your symptoms. Avoid contact with your eyes.

Conditions where dose adjustments may be required:

- Elderly patients;
- Acutely ill patients;
- Patients with severe liver disease;
- Patients with severe kidney disease;
- Patients also treated with other anesthetics or certain antiarrhythmic drugs (such as amiodarone or mexiletine).

Dose for Adults
The dose of the jelly depends on the application site. For oral use of Cathejell®, a dose of 20 g jelly (2 syringes) is usually safe. For use in the urethra (i.e., before insertion of urinary catheters or urinary procedures), 5 to 20 g jelly (½ to 2 syringes) is usually enough. A safe dose for use in the urethra and bladder is 40 g jelly (4 syringes).

No more than four doses should be given during a 24-hour period.

Dose for Children Under 12 Years of Age
Your child's doctor will tell you how much Cathejell® to use and how often to use it. The dose will depend on your child's:

- Age;
- Weight;
- Medical condition(s) and any medicines they are taking.

No more than 3 g of jelly per 10 kilograms of the child's weight should be used per dose. For a 10 kg child, the dose should be no more than ⅓ of the syringe.
No more than four doses should be given during a 24-hour period.

For use in children under 2 years of age, consult a doctor.

If you have any questions about how to measure the above amounts, be sure to ask your pharmacist.

If you are treating yourself and your condition does not seem to improve within three to five days, check with your doctor about continuing to use Cathejell®.

Instructions for Cathejell® Use

1. Peel off the paper cover from the transparent blister pack (see image 1).

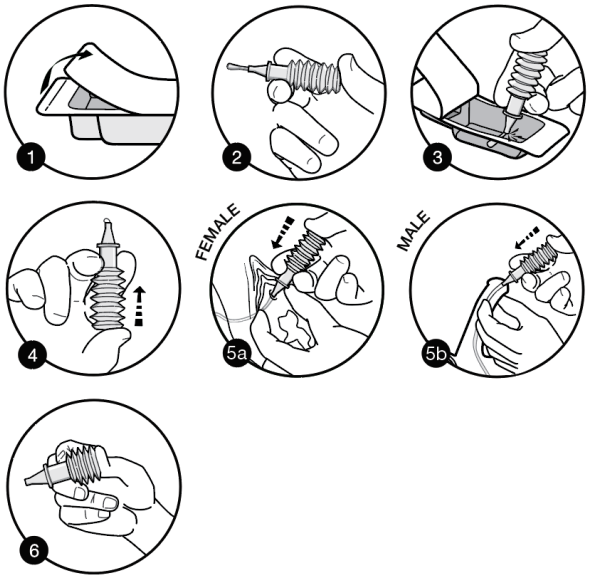
2. Inspect mixture visually for clarity, particulate matter, precipitation, discolouration, and leakage prior to administration (see image 2).

3. Break off the applicator tip by using a vigorous downward stroke in the bottom of the sterile blister pack (see image 3).

4. Remove the applicator tip completely. Release one drop of jelly to coat the nozzle for easier insertion (see image 4).

5. Instill by applying slight but steady pressure to the collapsible syringe (see images 5a and 5b).

6. While removing the syringe, keep the syringe compressed to avoid suction of the instilled jelly (see image 6).



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SYMPTOMS AND TREATMENT OF OVERDOSAGE

For management of suspected drug overdose, contact your regional Poison Control Centre.

Early signs of overdosage are numbness of the lips and around the mouth, light-headedness, dizziness, and sometimes blurred vision. In the event of a serious overdosage, trembling, seizures, or unconsciousness may occur. If the early signs of overdosage are noticed and no further Cathejell® is given, the risk of serious adverse effects occurring rapidly decreases. If you think you or anyone else is experiencing any of the above signs, telephone your doctor or go to the nearest hospital right away.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like any medication, Cathejell® may cause side effects in some people.

Avoid eating or chewing gum when Cathejell® is used in the mouth or throat since numbness in these areas may interfere with swallowing and could potentially cause choking. Numbness of the tongue or gums may also increase the danger of injury due to biting. Avoid exposure to extreme hot or cold temperatures (e.g. food, drink) until complete sensation has returned.

Avoid contact with the eyes because numbness in the eyes may prevent you from noticing if you get something in your eye. With the recommended doses, Cathejell® has no effect on the ability to drive and use machines.

Medicines affect different people in different ways. Just because side effects have occurred in some patients, does not mean that you will get them. If any side effects bother you, or if you experience any unusual effects while you are using Cathejell®, stop using it and check with your doctor or pharmacist as soon as possible.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

SYMPTOM/EFFECT	Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
	Only if severe	In all cases	
COMMON **Allergic reaction such as:** redness, itching or swelling of your skin, hives, burning, stinging, or any other skin problems, swelling of the neck area, or any difficulty with breathing, not present before using this medicine		■	
RARE **Overdose such as:** drowsiness, numbness of your tongue, light-headedness, ringing in your ears, blurred vision, vomiting, dizziness, unusually slow heartbeat, fainting, nervousness, unusual sweating, trembling or seizures			■
RARE **Methemoglobinemia:** brownish or bluish-grey skin especially around lips and nails, paleness, skin marbelling, shortness of breath, abnormally fast heartbeat, loss of consciousness			■

This is not a complete list of side effects. For any unexpected effects while taking Cathejell®, contact your doctor or pharmacist.
The above side effects are extremely rare, but can occur when too much Cathejell® is used at one time

and when large amounts are used over a long period of time. Consult your doctor immediately if any of these symptoms appear.

HOW TO STORE IT

Keep Cathejell® well out of sight and reach of children when not in use.

Keep Cathejell® at room temperature. Do not keep Cathejell® in the bathroom medicine cabinet or other warm, moist places. Store in the original package.

Do not use Cathejell® after the expiry date marked on the package.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail, or by fax
- Calling toll-free 1.866.234.2345

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

Important Note: This leaflet alerts you to some of the times you should call your doctor. Other situations which cannot be predicted may arise. Nothing about this leaflet should stop you from calling your doctor with any questions or concerns you have about using Cathejell®.

If you want more information about Cathejell®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada websitehttps://health-products.canada.ca/dpd-bdpp/index-eng.jsp, the manufacturer's website www.Cathejell.ca, or by calling 1-888-439-0013.

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Pharmazeutische Fabrik MONTAVIT Ges.m.b.H.
Absam, Austria6067

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