**Composition**
Active constituents:
1 g Xyloproct ointment contains: Lidocaine base 50 mg, Hydrocortisone acetate 2.5 mg
1 Xyloproct suppository contains: Lidocaine base 60 mg, Hydrocortisone acetate 5 mg

**Pharmaceutical form**
Xyloproct ointment/suppository is a white to slightly yellowish ointment/suppository. Lidocaine is the anaesthetic substance and hydrocortisone acetate has an antiinflammatory effect.

**Therapeutic indications**
Xyloproct is intended for the treatment of pain, itching and discomfort arising from irritated anorectal tissues e.g. haemorrhoids, pruritus ani, proctitis, milder forms of anal fissures, postoperative pain relief.

Xyloproct suppositories should be used in preference to ointment for the treatment of proctitis or internal haemorrhoids

**Posology and method of administration**
As with any local anaesthetic, the safety and effectiveness of lidocaine depend on the proper dosage, the correct technique, adequate precautions and readiness for emergencies.

The following dosage recommendations should be regarded as a guide. The clinician's experience and knowledge of the patient's physical status are of importance in calculating the required dose.

Debilitated or elderly patients and children should be given doses commensurate with their age, weight and physical condition.

External use: Apply the ointment several times a day in a thin layer to the affected area.

Intrarectal use, suppository: Insert one suppository morning and night and after each defecation. If defecation is painful, apply a few minutes before. The suppository is inserted just inside the anus.

Intrarectal use, ointment: Apply the ointment with the special applicator. Cleanse the applicator thoroughly after use.

A daily dose of 5 suppositories or 6 g of ointment is well within safety limits. The duration of treatment may vary between ten days and three weeks. If the treatment is prolonged, a free interval can be recommended, especially if it is suspected that irritation due to lidocaine or hydrocortisone has occurred. If the local irritation disappears after the cessation of treatment, the possibility of sensitivity to lidocaine or hydrocortisone can be investigated by a patch test, for example.

**Contraindications**
Known hypersensitivity to local anaesthetics of the amide type or to other components of the product. For infections caused by viruses, bacteria, pathogenic fungi or parasites, topical glucocorticoids should not be used without concomitant causal therapy.

**Special warnings and precautions for use**
Excessive dosage of lidocaine or short intervals between doses, may result in high plasma levels of lidocaine and serious adverse effects. Patients should be instructed to strictly adhere to recommended dosage.

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

When applying Xyloproct ointment to the rectum by means of the special applicator, care should be taken to avoid the introduction of an excessive amount. Following rectal application the systemic availability is relatively high and large doses may result in central nervous system reactions.

Xyloproct should not be used until an adequate proctologic examination is completed to exclude malignant processes.
Prolonged and excessive use of hydrocortisone use may produce systemic corticosteroid effects or local effects such as skin atrophy. With the recommended dosage systemic effects of hydrocortisone are unlikely. If irritation or rectal bleeding develops, treatment with Xyloproct should be discontinued, the patient examined and appropriate therapy instituted.

**Interactions**

With large doses of lidocaine, consideration should be given to the risk of additional systemic toxicity in patients receiving other local anaesthetics or agents structurally related to local anaesthetics. Specific interaction studies with lidocaine and anti-arrhythmic drugs class III (eg, amiodarone) have not been performed, but caution when treating patients is advised (see also section Special warnings and precautions for use).

**Pregnancy and lactation**

**Pregnancy**

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

**Lactation**

Lidocaine and hydrocortisone acetate are excreted into breast milk in small amounts. Any effect on the nursing infant seems unlikely at therapeutic doses of Xyloproct.

**Effects on ability to drive and use machines**

Depending on the dose 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. With the recommended doses of Xyloproct adverse effects on the CNS are unlikely.

**Undesirable effects**

**Allergic reactions**

Allergic reactions (in the most severe instances anaphylactic shock) to local anaesthetics of the amide type are rare.

**Local reactions**

Contact sensitivity to lidocaine has been reported after perianal use. Contact sensitivity may also occur after the use of topical hydrocortisone. Following treatment with potent topical corticosteroids, skin atrophy may occur. This has not been reported to occur after the use of hydrocortisone. The risk of undesirable local effects increases with increasing strength of the corticosteroids and the duration of treatment. Improper use may mask or worsen bacterial, parasitic, fungal or viral infections. Hydrocortisone belongs to the group of corticosteroids that is least likely to produce side effects.

**Overdose**

Lidocaine can cause acute toxic effects if high systemic levels occur due to rapid absorption or over-dosage. With the recommended doses of Xyloproct, toxic effects have not been reported. However, should systemic toxicity occur, the signs are anticipated to be similar in nature to those following the administration of local anaesthetics by other routes.

Local anaesthetic toxicity is manifested by symptoms of nervous system excitation and, in severe cases, central nervous and cardiovascular depression. Severe neurological symptoms (convulsions, CNS depression) must be treated symptomatically by respiratory support and the administration of anti-convulsive drugs.

**Pharmacodynamic properties**

Pharmacotherapeutic group: Local anaesthetic, ATC code C05A A01

Xyloproct is a combination of lidocaine and hydrocortisone for anorectal use. Lidocaine is a local anaesthetic that produces topical anaesthesia of the anorectal tissues. Hydrocortisone is a mild corticosteroid with anti-inflammatory activity. Lidocaine, like other local anaesthetics, causes a reversible blockade of impulse propagation along nerve fibres by preventing the inward movement of sodium ions through the nerve membrane. Local anaesthetics of the amide type are thought to act within the sodium channels of the nerve membrane.
Local anaesthetic drugs may also have similar effects on excitable membranes in the brain and myocardium. If excessive amounts of drug reach the systemic circulation rapidly, symptoms and signs of toxicity will appear, emanating mainly from the central nervous and cardiovascular systems.

Central nervous system toxicity usually precedes the cardiovascular effects as it occurs at lower plasma concentrations. Direct effects of local anaesthetics on the heart include slow conduction, negative inotropism and eventually cardiac arrest.

Hydrocortisone is produced in the adrenal cortex and is a steroid with principal pharmacological actions upon gluconeogenesis, glycogen deposition, protein and calcium metabolism, together with inhibition of corticotrophin secretion and anti-inflammatory activity.

The adverse effects of corticosteroids are nearly always due to their use in excess of normal physiological requirements.

**Pharmacokinetic properties**

Lidocaine is absorbed following topical administration to mucous membranes, its rate and extent of absorption being dependent upon concentration and total dose administered, the specific site of application, and duration of exposure. In general, the rate of absorption of local anaesthetic agents following topical application is most rapid after intratracheal and bronchial administration. Lidocaine is also well-absorbed from the gastrointestinal tract, but little intact drug appears in the circulation because of biotransformation in the liver.

Normally about 65% of the lidocaine is bound to plasma proteins. Amide local anaesthetics are mainly bound to alpha-1-acid glycoprotein, although they are also bound to albumin.

Lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion.

The main elimination pathway of lidocaine is by liver metabolism. The primary route of lidocaine in human is N-dealkylation to monoethylglycine-xylidine (MEGX), followed by hydrolysis to 2,6-xylidine and hydroxylation to 4-hydroxy-2,6-xylidide. MEGX can also be further dealkylated to glycine xylidide (GX).

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. Approximately 90% of the lidocaine administered intravenously is excreted in the form of various metabolites, while less than 10% is excreted unchanged in the urine. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-xylidine, accounting for about 70-80% of the dose excreted in the urine.

The elimination half-life of lidocaine following an intravenous bolus injection is typically 1.5 to 2.0 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. 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.

Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 g free base per ml.

Less than 50% of hydrocortisone is absorbed following rectal application. When administered by topical application, particularly under an occlusive dressing or when the skin is broken, sufficient corticosteroid may be absorbed to give systemic effects. Corticosteroids in the circulation are extensively bound to plasma proteins, mainly to globulin and less to albumin. Only unbound hydrocortisone has pharmacological effects or is metabolised. Corticosteroids are metabolised mainly in the liver but also in the kidney, and are excreted in the urine.

**Preclinical safety data**

In animal studies the toxicity noted after high doses of lidocaine consisted of effects on the central nervous and cardiovascular systems. No drug-related adverse effects were seen in reproduction toxicity studies, neither did lidocaine show a mutagenic potential in either in vitro or in vivo mutagenicity tests. Cancer studies have not been performed with
lidocaine, due to the area and duration of therapeutic use for this drug.

**List of excipients**

Ointment:
Aluminium acetate basic powder, Zink oxide, Stearyl alcohol, Cetyl alcohol, Polyethylene glycol (400 and 3350), Purified water.

*Suppository:*
Zink oxide, Aluminium acetate basic powder, Hard fat (Witepsol W25).

**Shelf-life**
Please refer to expiry date on outer carton.

**Special precautions for storage**
- Xyloproct ointment: Store at 5°C (2–8°C). Two months at 25°C is allowed for use by the consumer.
- Xyloproct suppository: Store at 5°C (2–8°C). Do not freeze. During treatment the consumer can store Xyloproct suppositories at room temperature (25°C) for two months.

**Pack size**
Please refer to outer carton for pack size.

**Instructions for use/handling**
The protective membrane of the tube is perforated when applying the cap.

**Date of revision of text**
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