SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Xyloproct rectal ointment
Xyloproct suppositories

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g *rectal ointment* contains: lidocaine 50 mg, hydrocortisone acetate 2.5 mg.

1 *suppository* contains: lidocaine 60 mg, hydrocortisone acetate 5 mg.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Rectal ointment
Suppository

Rectal ointment: White to pale yellow homogenous ointment.

Suppositories: White or pale yellow suppositories.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Xyloproct rectal ointment and Xyloproct suppositories are intended for the treatment of adult patients.

The treatment of haemorrhoids, painful bowel movements and anal fissures as well as postoperatively following anorectal procedures or in connection with anorectal examinations.

For the self-care of haemorrhoids and superficial rectal irritation.

4.2 Posology and method of administration

Rectal ointment
A thin layer of the rectal ointment is applied in and around the rectal opening once or several times daily. Up to 6 g of rectal ointment can be applied per 24 hours. The treatment duration may vary between 10 days and 3 weeks. A treatment-free period is recommended for patients for whom an extended treatment period is planned.

Suppositories
One suppository is inserted into the rectal opening morning and evening as well as when required following each bowel movement. Up to 5 suppositories can be applied per 24 hours. In the case of painful bowel evacuations, insert the suppository several minutes prior to the bowel evacuation. It is important that the suppository remain in place until it has melted.

The treatment duration may vary between 10 days and 3 weeks. A treatment-free period is recommended for patients for whom an extended treatment period is planned.

The treatment period should not exceed 3 weeks; see section 4.4, Special warnings and precautions for use.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

An examination should be performed prior to prescribing, in order to eliminate the presence of a malignant process.

Avoid contact with the eyes. Wash hands thoroughly after use.

Long-term use of large amounts of hydrocortisone may result in systemic effects or local effects such as skin atrophy. Systemic effects of hydrocortisone are unlikely at the recommended doses and for treatment periods that do not excced 3 weeks.

Local glucocorticoids should not be used without concomitant causal therapy in the case of infections caused by virus, bacteria, pathogenic fungus or parasites.

In the case of irritation or rectal bleeding, treatment should be discontinued and the patient examined.
Local irritation is sometimes attributed to hypersensitivity to lidocaine or hydrocortisone; in such cases, treatment should be discontinued.

At the recommended doses and treatment intervals, systemic effects of lidocaine are judged to be unlikely. As the systemic availability is relatively large following rectal application, it is possible that overdose of Xyloproct or short intervals between doses may result in high plasma levels of lidocaine and serious adverse reactions such as effects on the central nervous system. Patients should be instructed to carefully follow recommended doses.

Patients treated with antiarrhythmic class III agents (e.g. amiodarone) should be monitored closely and ECG monitoring should be considered as the cardiac effects may be additive.

Xyloproct rectal ointment contains cetyl alcohol and stearyl alcohol, which can cause local skin reactions (e.g. contact dermatitis).

The active ingredient lidocaine is likely to be porphyrogenic and should only be prescribed for patients with acute porphyria if there is no safer alternative available. Precautions should be taken for all patients with porphyria.

4.5 Interaction with other medicinal products and other forms of interaction

The following combinations with Xyloproct may require dosage adjustment:
Xyloproct should be used with caution in combination with dental anaesthesia administered by injection, other local anaesthetics or substances structurally related to amide-type local anaesthetics, such as class IB antiarrhythmics, as the toxic effects are additive (see section 4.9, Overdose).

Patients treated with antiarrhythmic class III agents (e.g. amiodarone) should be monitored closely and ECG monitoring should be considered as the cardiac effects may be additive. Medicinal products that inhibit the metabolism of lidocaine (e.g. cimetidine and beta blockers) can cause potentially toxic plasma concentrations when lidocaine is given in repeated high doses over a long time period. Such interactions are not clinically relevant in short-term lidocaine therapy at recommended doses.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no adequate data on the treatment of pregnant women with Xyloproct.

Hydrocortisone
Although effects on the foetus and newborn have been seen following long-term use of oral corticosteroids, systemic exposure to a weak corticosteroid such as hydrocortisone is judged to be so low following topical application to a limited area that no corticosteroid-induced effects are expected.

Lidocaine
Animal studies are incomplete with regards to the effects on pregnancy, development of the embryo/foetus, childbirth and postnatal development (see section 5.3, Preclinical safety data). It is reasonable to assume that lidocaine has been used in a large number of pregnant women and women of childbearing age. No negative impacts on reproductive processes, such as increased malformations or direct or indirect effects on the foetus, have been reported. However, the risks for humans have not been investigated. The lowest possible dose and shortest possible treatment time should therefore be sought when using Xyloproct during pregnancy.

Breastfeeding
Lidocaine and hydrocortisone acetate are excreted into human milk but the risk of impact on the child is considered unlikely at therapeutic doses.

4.7 Effects on ability to drive and use machines

Depending on the size of the dose, local anaesthetics may have a mild, transient effect on mobility and coordination. These effects are unlikely at the recommended doses of Xyloproct.

4.8 Undesirable effects

Organ system	**Frequency**	**Adverse reaction**
Skin and subcutaneous tissue disorders	Uncommon (≥1/1,000, <1/100)	Contact dermatitis.
Immune system disorders	Rare (≥1/10,000, <1/1,000)	Allergic reactions; in the most severe cases: anaphylactic shock.

The risk of undesirable effects increases with a longer duration of treatment.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Healthcare professionals are asked to report any suspected adverse reactions via (see details below).

[To be completed nationally]

4.9 Overdose

Lidocaine can cause acute toxic effects following overdose. No toxic effects have been reported in connection with the use of recommended doses of Xyloproct.
If symptoms of systemic toxicity should arise, these are expected to be of the same type as those observed following the administration of local anaesthetics by other routes.

In the case of concomitant administration of other local anaesthetics, e.g. topically or by injection, the toxic effects are additive and may result in overdose with toxic systemic reactions.

Overdose of local anaesthetics causes symptoms impacting the central nervous system, and in severe cases even the heart and blood circulation.

Treatment:
If signs of acute systemic toxicity appear, administration of the local anaesthetic must be immediately suspended. Treatment must be given to maintain good ventilation, oxygen supply and circulation. Oxygen is always administered; if required, controlled ventilation is to be administered. If the convulsions have not ceased spontaneously within 15–20 seconds, administer thiopental sodium 1–3 mg/kg IV to permit adequate ventilation or diazepam 0.1 mg/kg IV (somewhat slower onset of effect). Convulsions of long duration are a risk to the patient's breathing and oxygenation. The injection of a muscle relaxant (e.g. suxamethonium 1 mg/kg) creates more favourable conditions for ventilation and oxygenation of the patient, but requires experience of tracheal intubation and controlled ventilation. In the case of a drop in blood pressure or bradycardia, administer a vasopressor (e.g. ephedrine 5–10 mg IV, which can be repeated after 2–3 minutes).
In the case of circulatory arrest, cardiopulmonary resuscitation should be commenced immediately. It is important to maintain a good oxygen supply, breathing and circulation, and to treat acidosis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihaemorrhoidal for topical use, ATC code: C05AA01

Lidocaine is an analgesic and acts via a reversible blockade of nerve impulses.
Hydrocortisone has anti-inflammatory properties.

5.2 Pharmacokinetic properties

The absorption rate and absorbed amount of lidocaine are dose-dependent but are also affected by the application site and exposure time. Lidocaine is well absorbed in the gastrointestinal tract, however due to first pass metabolism only a small portion reaches the circulation in unchanged form. Lidocaine is eliminated primarily through metabolism. Dealkalisation to monoethylglycinexylidide (MEGX) is mediated primarily by cytochrome

P450 3A4. MEGX is metabolised to 2,6-xylidine and glycine xylidide (GX). 2,6-xylidine is further transformed by CYP2A6 to 4-hydroxy-2,6-xylidine which comprises the primary metabolite in urine (80%) and is excreted as a conjugate. MEGX has convulsive activity equivalent to that of lidocaine; GX has no convulsive activity.
MEGX appears to occur in similar plasma concentrations as the parent substance. The elimination half lives of lidocaine and MEGX following an intravenous bolus dose are approx. 1.5–2 and 2.5 hours, respectively.
Plasma protein binding occurs primarily to the alpha-1-acid glycoprotein. Due to the rapid hepatic metabolism, the pharmacokinetics is sensitive to any liver conditions. The half life may be more than doubled in patients with impaired hepatic function. Renal impairment does not affect the pharmacokinetics but may increase accumulation of metabolites.
Lidocaine crosses the blood-brain barrier and crosses to the placenta. This most likely occurs by passive diffusion.

Less than 50% of the hydrocortisone is absorbed following rectal application. In the circulation, hydrocortisone is present bound to plasma proteins – primarily globulin, and to a lesser extent albumin. Hydrocortisone is primarily metabolised in the liver and excreted in the urine.

5.3 Preclinical safety data

Lidocaine
Genotoxicity and carcinogenicity
Genotoxicity studies of lidocaine were negative. However, genotoxic potential has been seen *in vitro* for 2,6-xylidine, which is a metabolite of lidocaine. In a carcinogenicity study in rats exposed to 2,6-xylidine both *in utero* and postnatally over the entire lifespan, tumours were seen in the nostrils, subcutaneous tissue and liver.
High doses of 2,6-xylidin were required to induce tumours in animal studies.
The clinical relevance of the observed tumour-inducing effect of 2,6-xylidine to intermittent use of lidocaine is unknown.
Frequent use of high doses of lidocaine is not recommended.

Reproduction toxicology
No teratogenic effects were seen in studies of embryonic and foetal development in rats and rabbits administered the medicinal product during organogenesis. Embryotoxicity and decreased postnatal survival were only seen following doses significantly higher than clinical doses. These effects are therefore judged to be of no clinical significance.
No comparison to exposure in humans can be made as there is no data on systemic exposure in rats and rabbits.

Hydrocortisone
Reproduction toxicology
In animal studies, corticosteroids have been shown to cause various congenital defects (cleft palate, skeletal malformations). Reduced placental and birth weights have also been noted following treatment of animals throughout the entire gestation.

There is no preclinical safety data of relevance additional to that which has already been taken into consideration in the summary of product characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Rectal ointment
Aluminium diacetate
Zinc oxide
Stearyl alcohol
Cetyl alcohol
Macrogol
Purified water

Suppositories
Aluminium diacetate
Zinc oxide
Hard fat

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Rectal ointment
2 years when stored in a refrigerator (2 ˚C–8 ˚C).
2 months when stored at a maximum temperature of 25 °C.

Suppositories
30 months when stored in a refrigerator (2 ˚C–8 ˚C). Do not freeze.
2 months when stored at a maximum temperature of 25 °C.

6.4 Special precautions for storage

Refer to section 6.3 for storage instructions.

6.5 Nature and contents of container

Rectal ointment
Aluminium tube, 20 g.

Suppositories
Carton containing 10 and 50 suppositories, respectively.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Aspen Pharma Trading Limited
3016 Lake Drive, Citywest Business Campus
Dublin 24, Ireland

8 MARKETING AUTHORISATION NUMBERS

Rectal ointment: 8340
Suppositories: 8341

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Rectal ointment: 24 January 1969/29 August 2008
Suppositories: 24 January 1969/29 August 2008

10 DATE OF REVISION OF THE TEXT

2024-06-03