IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0970/056/001
Case No: 2044051

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

AstraZeneca UK Limited

600 Capability Green, **Luton**, **LU1 3LU**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Xyloproct 5%/0.275% w/w Rectal Ointment

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **17/12/2008**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Xyloproct 5%/0.275% w/w Rectal Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition for 100 g:
Lidocaine 5 g.
Hydrocortisone Acetate 0.275 g.

Also contains: Stearyl alcohol 0.9% w/w and Cetyl alcohol 7.4% w/w

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Rectal Ointment
A white to slightly yellowish rectal ointment.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the relief of symptoms associated with such anal and perianal conditions as haemorrhoids, proctitis, fissure in ano, anal fissure, fistula or pruritus ani or perinei.

4.2 Posology and method of administration

To be applied one to four times daily after bowel evacuation or as directed by the physician. For intrarectal use, apply the ointment with the special applicator. Cleanse the applicator thoroughly after use.

A daily dose of 6 g 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, e.g. by a patch test.

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

4.3 Contraindications

Xyloproct Ointment should not be used in patients with untreated infections of bacterial, viral, tuberculous or fungal origin or in patients with known hypersensitivity to any of the ingredients. Use on atrophic skin. Xyloproct should not be used by patients being treated with a class III anti-arrhythmic drug outside of hospital (see section 4.4 and 4.5).

4.4 Special warnings and precautions for use

Continuous treatment for longer than 3 weeks should be avoided in patients under the age of three years because of the possibility of adrenocortical suppression.

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.

Appropriate antibacterial, antiviral or antifungal therapy should be given with Xyloproct if infection is present at the site of application.

The possibility of malignancy should be excluded before use.

If irritation or rectal bleeding develops, treatment should be discontinued.

Patients treated with antiarrhythmic drugs class III (e.g. amiodarone) should be kept under close surveillance and ECG monitoring considered, since cardiac effects may be additive.

When using the special applicator, care should be taken to avoid instillation of excessive amounts of Xyloproct Ointment into the rectum. This is of particular importance in infants and children.

Systemic absorption of lidocaine may occur from the rectum, and large doses may result in CNS side-effects. On rare occasions convulsions have occurred in children.

Prolonged and excessive use of hydrocortisone may produce systemic corticosteroid effects or local effects such as skin atrophy. With the recommended dosage systemic effects of hydrocortisone are unlikely.

Xyloproct ointment is possibly porphyrinogenic and should only be prescribed to patients with acute porphyria when no safer alternative is available. Appropriate precautions should be taken for vulnerable patients.

Xyloproct ointment contains cetyl alcohol and stearyl alcohol. These may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

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.

Lidocaine should be used with caution in patients receiving antiarrhythmic drugs, since the toxic effects are additive (see sections 4.3 and 4.4).

4.6 Pregnancy and lactation

Xyloproct Ointment should not be used in pregnancy unless considered essential by the physician.

Lidocaine and hydrocortisone acetate are excreted into breast milk but in such small quantities that adverse effects on the child are unlikely at therapeutic doses.

4.7 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.

4.8 Undesirable effects

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.

In extremely rare cases amide-type local anaesthetic preparations have been associated with allergic reactions (in the most severe instances anaphylactic shock).

4.9 Overdose

When using the special applicator care should be taken to avoid instillation of excessive amounts of Xyloproct Ointment into the rectum. This is of particular importance in infants and children.

Systemic absorption of lidocaine may occur from the rectum, and large doses may result in CNS side-effects. On rare occasions convulsions have occurred in children.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: C05A A01

Lidocaine exerts a local anaesthetic effect by stabilising the neural membrane and preventing the initiation and conduction of nerve impulses.

Hydrocortisone acetate belongs to the mild group of corticosteroids and is effective because of its anti-inflammatory and anti-pruritic action.

5.2 Pharmacokinetic properties

The onset of action of lidocaine is 3 - 5 minutes on mucous membranes. Lidocaine can be absorbed following application to mucous membranes with metabolism taking place in the liver. Normally about 65% of the lidocaine is bound to plasma proteins. Metabolites and unchanged drug are excreted in the urine.

Absorption of hydrocortisone may occur from normal intact skin and mucous membranes. Corticosteroids are metabolised mainly in the liver but also in the kidney, and are excreted in the urine.

5.3 Preclinical safety data

Genotoxicity tests with lidocaine showed no evidence of mutagenic potential. A metabolite of lidocaine, 2,6-xylidine, showed weak evidence of activity in some genotoxicity tests. The metabolite 2,6-xylidine has been shown to have carcinogenicity potential in preclinical toxicological studies evaluating chronic exposure. Risk assessments comparing the calculated maximum human exposure from intermittent use of lidocaine, with the exposure used in preclinical studies indicate a wide margin of safety for clinical use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Zinc Oxide
Aluminium Acetate basic powder
Stearyl Alcohol
Cetyl Alcohol
Water Purified
Macrogol (3350 and 400)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf-life of this product is 24 months when stored between 2°C and 8°C and two months when stored up to 25°C.

6.4 Special precautions for storage

Store at 2°C-8°C (in a refrigerator). The patient may store the product at temperatures up to 25°C for 2 months. Any remaining ointment should then be discarded.

6.5 Nature and contents of container

20 g aluminium tube with a polypropylene cap. The cap has a spike on the upper surface to allow perforation of the tube membrane. Each tube is supplied with an applicator. 1 tube per pack.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

AstraZeneca UK Ltd
600 Capability Green
Luton
LU1 3LU
UK

8 MARKETING AUTHORISATION NUMBER

PA 970/56/1 (transfer date 17th May 2002)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1978

Date of last renewal: 01 April 2008

10 DATE OF REVISION OF THE TEXT

December 2008