IRISH MEDICINES BOARD ACTS 1995 AND 2006

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

(S.I. No.540 of 2007)

PPA1151/123/002
Case No: 2066400

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

Imbat Limited

Unit L2, **North Ring Business Park**, **Santry**, **Dublin 9**

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

Scheriproct 1mg + 1mg suppositories

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 **30/10/2009**.

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

Scheriproct 1mg + 1mg suppositories

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains prednisolone caproate equivalent to 1mg of prednisolone and 1mg of cinchocaine hydrochloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suppository

Product imported from the UK:
White to yellowish bullet shaped suppositories.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the management of symptoms of internal or external haemorrhoids, anal fissures and proctitis.

4.2 Posology and method of administration

The anal region should be cleaned thoroughly before using Scheriproct, which is best applied after defaecation.

One suppository daily as directed. If symptoms are severe one suppository two or three times on the first day.

Only on the first day may more than 1 suppository be used if the symptoms are severe.

Duration of treatment should not usually exceed 1 week.

Specific treatment of the condition giving rise to the haemorrhoids may be required.

4.3 Contraindications

Use in the presence of untreated infections of bacterial, viral, tuberculous or fungal origin

4.4 Special warnings and precautions for use

Additional specific therapy is required in bacterial and/or fungal infections.
There have been a few reports in the literature of the development of cataracts in patients who have been using corticosteroids for prolonged periods of time. Although it is not possible to rule out systemic corticosteroids as a known factor, prescribers should be aware of the possible role of corticosteroids in cataract development.

4.5 Interaction with other medicinal products and other forms of interaction

None so far known.

4.6 Pregnancy and lactation

Animal experimental studies with glucocorticosteroids have shown reproductive toxicity (cf. section ‘5.3 Preclinical safety data’).

A number of epidemiological studies suggest that there could possibly be an increased risk of oral clefts among newborns of women who were treated with systemic glucocorticosteroids during the first trimester of pregnancy. Oral clefts are a rare disorder and if systemic glucocorticosteroids are teratogenic, these may account for an increase of only one or two cases per 1000 women treated while pregnant. Data concerning topical glucocorticosteroid use during pregnancy are insufficient; however, a lower risk might be expected since systemic availability of topically applied glucocorticosteroids is very low.

As a general rule, topical preparations containing corticoids should not be applied during the first trimester of pregnancy. The clinical indication for treatment with Scheriproct must be carefully reviewed and the benefits weighed against the risks in pregnant and lactating women. In particular, prolonged use must be avoided.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

If Scheriproct is applied for long periods of time local concomitant symptoms such as atrophy of the skin cannot be excluded.
Allergic skin reactions may occur in rare cases.

4.9 Overdose

On the basis of results from toxicity studies with prednisolone and cinchocaine hydrochloride, no risk of acute intoxication is to be expected following single rectal or perianal administration of Scheriproct, even in the case of inadvertent overdose. In the case of accidental oral intake of the preparation (e. g. by swallowing a few grams of the ointment or several suppositories) mainly systemic effects of the local anaesthetic cinchocaine hydrochloride are to be expected, which, according to the dose, may manifest themselves as severe cardiovascular (depression to cessation of cardiac function) and CNS symptoms (convulsions; inhibition to arrest of respiratory function).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Prednisolone exerts an antiinflammatory, antiallergic and antipruritic effect. Capillary dilatation, intercellular oedema and tissue infiltration regress; capillary proliferation is suppressed.
As a local anaesthetic, cinchocaine eases the pain.

5.2 Pharmacokinetic properties

The Scheriproct haemorrhoidals are topical preparations which display their anti-inflammatory and analgesic effects at the site of application. The active ingredients diffuse out of the preparations into the inflamed tissue, are partly absorbed, distributed by the circulatory system, metabolised and finally excreted. In order to obtain a local therapeutic effect, pharmacologically effective plasma levels are not required.

Prednisolone-caproate

In order to assess the risk of systemic adverse corticosteroid effects, it is necessary to know the systemic corticosteroid bioavailability after rectal application. Studies with a series of corticosteroids in an animal model (baboon) and in volunteers showed that absorption of corticosteroids after rectal application is rarely complete.
Even under the assumption of a complete absorption of prednisolone-caproate after application of Scheriproct haemorrhoidals according to the instructions, the amount of corticosteroid delivered to the body is not high enough to lead to systemic corticosteroid effects.
As with other corticosteroid-21-esters, it can be assumed that prednisolone caproate is rapidly hydrolysed already during or immediately after absorption into prednisolone and hexanoic acid. Prednisolone is eliminated from the plasma after intravenous administration with a half-life of ca. 3 hours. The total plasma clearance (ca. 1 – 3 ml/min/kg) increases with the dose due to the saturable binding of prednisolone to CBG. Prednisolone is converted in the liver into a series of metabolites, which are mainly excreted with the urine. Unchanged prednisolone is likewise found in the urine in portion between 10 and 25%.

Cinchocaine

Like the corticosteroid, cinchocaine exerts its analgesic effect locally.
Analgesic effective cinchocaine plasma levels are not a necessary prerequisite.
Since no absorption studies are available, risk assessment was performed under assumption of a complete absorption. Under this worst case assumption, the absorbed dose of cinchocaine is too low to elicit adverse effects, when Scheriproct is applied according to the instructions.
Following absorption, cinchocaine is biotransformed into a number of metabolites. Of importance are the oxidative de-ethylation of the di-ethylamino function, hydroxylation and oxidative degradation of the butyloxy-chain and the additional formation of unidentified polar metabolites.

5.3 Preclinical safety data

In systemic tolerance studies following repeated administration of prednisolone no findings occurred which would be prohibitive of the prescribed use of Scheriproct.

The intolerance symptoms documented for highly effective local anaesthetics are not to be expected due to the low amounts of cinchocaine hydrochloride bioavailable following repeated topical administration of the required therapeutic dose.

Embryotoxicity studies with Scheriproct led to results typical for glucocorticoids, i.e. embryolethal and/or teratogenic effects are induced in the appropriate test system. In view of these findings, particular care should be taken when prescribing Scheriproct during pregnancy. The results of epidemiological studies are summarized under section ‘4.6 Pregnancy and lactation’.

Neither animal-experimental nor epidemiological data are available for assessment of the embryotoxic potential of cinchocaine hydrochloride. In comparison with local anaesthetics of the acidic amide type which are similar in structure and effect, no embryotoxic effects are to be expected in humans following administration of the topical dose required for therapy. Cinchocaine hydrochloride is considered to be non-genotoxic on the basis of results obtained in bacterial and mammalian mutagenicity tests *in vitro* and *in vivo*.

Investigations of prednisolone in a bacterial test system for detection of gene mutations gave indications of weak genotoxic potential. On the other hand, only negative results are reported in the literature from gene mutation tests with mammalian cells. As no relevant indications of a genotoxic effect are available for any of the glucocorticoid substance class, such effects are not to be expected of prednisolone either. The investigations of cinchocaine hydrochloride in various test systems whether on mammalian cells or on bacteria gave no relevant indication of point-mutation effects.

In a tumorigenicity study on rats, prednisolone caused an increase in the occurrence of hepatic tumours. Other investigators either found no influence or an even lower tumour rate following administration of prednisolone or prednisone in tumorigenicity studies on rodents.

Epidemiological studies have as yet not given any indication of a causative relationship between glucocorticoid therapy and increased tumour incidence in humans. No specific tumorigenicity studies have been carried out with cinchocaine hydrochloride. Knowledge of the structure, the pharmacological mechanism and the results from animal-experimental tolerance studies following repeated administration gave no indication of a tumorigenic potential.

Investigation to detect a possible sensitizing effect of Scheriproct or of the active ingredients contained therein has not been carried out. According to relevant data gained from spontaneous reports as well as contained in the literature, it is possible that not only individual ingredients of the formulation base but also the active ingredients themselves are responsible for the allergenic skin reactions which were observed only sporadically after the use of Scheriproct. There is, however, no risk of a sensitizing effect occurring other than in sporadic cases.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hard fat.

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

The shelf life expiry date of this product shall be the date shown on the blister strips and outer carton of the product as marketed in the country of origin.

6.4 Special precautions for storage

Store below 25C.

6.5 Nature and contents of container

Laminated aluminium foil packs placed in an over-labelled cardboard carton.
Pack size: 12 suppositories.

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.

7 Parallel Product Authorisation Holder

Imbat Limited
Unit L2
North Ring Business Park
Santry
Dublin 9

8 Parallel Product Authorisation Number

PPA 1151/123/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30th October 2009

10 DATE OF REVISION OF THE TEXT