SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Scheriproct 1.5 mg/g + 5mg/g rectal ointment.

2. Qualitative and Quantitative Composition

1g of ointment contains prednisolone caproate equivalent to 1.5 mg of prednisolone and 5 mg of cinchocaine hydrochloride.

For a full list of excipients, see section 6.1.

3. Pharmaceutical Form

Rectal ointment
Colourless to faintly yellow homogeneous translucent ointment

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.
Usual application twice daily. On the first day, for faster symptomatic relief, up to four times. Protruding lumps should be smeared and carefully pressed back with the finger.

Duration of treatment should not usually exceed 1 week. Specific treatment of the condition giving rise to the haemorrhoids may be required.

Before applying within the rectum, the enclosed applicator should be screwed onto the tube (for use and cleaning of the applicator see section 6.6).

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.

The excipients (castor oil refined, castor oil hydrogenated, macrogol-400-monoricinoleate and perfume oil chypre) in Scheriproct rectal ointment may reduce the effectiveness of latex products such as condoms.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.
Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

4.6 Fertility, 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, large-area or 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.

<u>Reporting of suspected adverse reactions</u>
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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail:medsafety@hpra.ie.

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 the 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 portions 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 Fertility, 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

Octyldodecanol
Castor oil, refined
Castor oil, hydrogenated
Macrogol–400–monoricinoleate
Perfume oil, Chypre

6.2 Incompatibilities

Not applicable

6.3 Shelf life

As packaged for sale:2 years
After first opening: 3 months

6.4 Special precautions for storage

Do not store above 25°C. Replace the cap tightly after use.

6.5 Nature and contents of container

Aluminium tubes with 10 g or 30 g. The rectal cannula is made of natural polypropylene and the protective cap is made of low density polyethylene.

Not all pack sizes may be marketed.

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

Use of the applicator
Do not use the applicator if damaged. Screw the applicator completely on the tube. After each use, clean the applicator with a paper towel, then remove the remaining product in the applicator with a cotton swab and clean it again with a paper towel. Rinse the applicator under warm water for about 1 minute and dry the applicator with a paper towel.

7. Marketing Authorisation Holder

Bayer Limited
The Atrium
Blackthorn Road
Dublin 18
Ireland

8. Marketing Authorisation Number(s)

PA 1410/71/1

9. Date of First Authorisation / Renewal of the Authorisation

Date of first authorization: 1 April 1978
Date of last renewal: 1 April 2008

10. Date of Revision of the Text

October 2018