Approved professional information for SCHERIPROCT SUPPOSITORIES

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

SCHERIPROCT SUPPOSITORIES

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 suppository contains prednisolone hexanoate 1,3 mg and cinchocaine hydrochloride 1 mg.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Yellowish-white suppositories without cosmetic defects

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short term (5 – 7 days) symptomatic relief of perianal discomfort, inflammation and itching caused by thrombosed haemorrhoids, anal fissure and pruritus ani.

4.2 Posology and method of administration

Posology

The anal region should be cleaned thoroughly before using **SCHERIPROCT SUPPOSITORIES**, which is best inserted after defaecation.

Unless otherwise prescribed by the doctor, generally insert one suppository daily high into the rectum. If symptoms are severe, insert one suppository two to three times on the first day.

There is usually a rapid improvement, but this should not mislead one into stopping treatment too soon.

4.3 Contraindications

- Hypersensitivity to prednisolone hexanoate, cinchocaine hydrochloride or to any of the other excipients of **SCHERIPROCT SUPPOSITORIES**.
- Viral infections, primary bacterial or fungal infections in the treatment area.
- Virus diseases (e.g. vaccinia, chickenpox).
- Secondary infections of the skin in the absence of appropriate anti-infective therapy.
- Known sensitivity to local anaesthetics.
- Corticosteroids have been shown to be teratogenic in animals

  Corticosteroids have been shown to be teratogenic in animals following dermal application. As these agents are absorbed percutaneously, teratogenicity following topical application cannot be excluded. Therefore, **SCHERIPROCT SUPPOSITORIES** should not be used during pregnancy.
- Tuberculous or syphilitic processes in the area to be treated

4.4 Special warnings and precautions for use

This product should not be used continuously for more than 7 days. If symptoms do not disappear quickly, discontinue treatment and consult your doctor. Certain anal disorders require specific treatment and a proctological examination. In case of bleeding, consult a doctor promptly.

In infants, long-term continuous therapy with topical corticosteroids should be avoided. Occlusion is not appropriate on the perineum. Adrenal suppression can occur, even without occlusion. There is a risk of developing skin atrophy following extensive therapy. The application of unusually large quantities of topical corticoids may result in the absorption of systemically active amounts of corticoid. Infections or secondarily infected dermatoses definitely require additional therapy with antibiotics or chemotherapeutic agents. This treatment can often be topical, but for heavy infections systemic antibacterial therapy may be necessary. If fungal infections are present, a topically active antimycotic should be applied.

The excipients in **SCHERIPROCT SUPPOSITORIES** may reduce the effectiveness of latex products such as condoms.

Inadvertent contact of the preparation with the eyes should be avoided. Careful hand-washing after use is recommended.

Visual disturbance:

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes, which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 Interactions with other medicines 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, including adrenal suppression.

The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side effects, in which case the patients should be monitored for systemic corticosteroid side-effects.

4.6 Fertility, pregnancy and lactation

Pregnancy

Corticosteroids have been shown to be teratogenic in animals following dermal application. As these agents are absorbed percutaneously, teratogenicity following topical application cannot be excluded.

Therefore. **SCHERIPROCT SUPPOSITORIES** is contraindicated for use during pregnancy.

There is insufficient data on the use of **SCHERIPROCT SUPPOSITORIES** in pregnant women. Studies in animals (mice and rats) have shown reproductive toxicity for prednisolone hexanoate. In general, the use of topical preparations containing glucocorticoids should be avoided during the first trimester of pregnancy.

Epidemiological studies suggest that there could possibly be an increased risk of oral clefts among newborns of women who were treated with glucocorticoids during the first trimester of pregnancy.

Lactation

There is insufficient information on the excretion of prednisolone hexanoate and cinchocaine hydrochloride in human milk.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

There is a risk of developing skin atrophy following extensive therapy (more than 4 weeks).

Allergic skin reactions may occur.

Eye disorders

Not known (frequency cannot be estimated from the available data):

Vision, blurred (see also section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8}

4.9 Overdose

In the case of accidental oral intake of the preparation (e.g. by swallowing 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

A. 11.8 Anal suppositories and ointments.

Topical agents for the treatment of hemorrhoids and anal fissures – C05AA04.

Prednisolone hexanoate exerts an anti-inflammatory and antipruritic effect. Capillary dilatation, intercellular oedema and tissue infiltration regress; capillary proliferation is suppressed.

Cinchocaine hydrochloride has a local anaesthetic effect on mucous membranes and, in combination with prednisolone hexanoate, provides quick relief of painful and pruritic symptoms.

5.2 Pharmacokinetic properties

SCHERIPROCT SUPPOSITORIES is a rectal preparation which displays its anti-inflammatory and analgesic effects at the site of application.

The active substance diffuses out of the preparation 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 hexanoate

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 hexanoate after insertion of **SCHERIPROCT SUPPOSITORIES** 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 hexanoate is rapidly hydrolysed 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

Alike 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 the assumption of a complete absorption. Under this worst-case assumption, the absorbed dose of cinchocaine is too low to elicit adverse effects when **SCHERIPROCT SUPPOSITORIES** is inserted according to the instructions.

Following absorption, cinchocaine is biotransformed into a number of metabolites. Of special importance here 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 SUPPOSITORIES**.

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 SUPPOSITORIES** led to results typical for glucocorticoids, i.e. embryolethal and/or teratogenic effects are induced in the appropriate test system (see section 4.6).

Neither animal-experimental nor epidemiological data are available for assessment of the embryotoxic potential of cinchocaine hydrochloride. In comparison with local anesthetics 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.

Investigation 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.

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*.

In tumorigenicity study on rats prednisolone caused an increase in the occurrence of hepatic tumors. Other investigators either found no influence or an even lower tumor 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 tumor 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.

Investigations to detect a possible sensitizing effect of **SCHERIPROCT SUPPOSITORIES** or of the active ingredients contained therein have 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 substances themselves are responsible for the allergenic skin reactions which were observed only sporadically after the use of **SCHERIPROCT SUPPOSITORIES**. There is, however, no risk of a sensitising effect occurring other than in sporadic cases.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hard fat

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a refrigerator between 2 to 8 °C.

Do not freeze.

Store in the original packaging.

Keep the packaging in the outer carton.

For shelf life, please refer to the imprint on the pack.

6.5 Nature and contents of container

Cardboard boxes containing 12 suppositories packed in strips made of aluminium, soft tempered with thickness of 50 µm and laminated with low-density polyethylene as inner layer.

Not all packs and pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The consistency of suppositories that have become softened by warmth should be restored by immersion in cold water before the covering is removed.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand

1685

South Africa

0860 ADCOCK (232625)

8. REGISTRATION NUMBER(S)

E/11.8/0668

Namibia 06/11.8/0341 NS2

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

3 August 2000

10. DATE OF REVISION OF THE TEXT

19 April 2022