

NEW ZEALAND DATA SHEET

1 ULTRAPROCT®

ULTRAPROCT® fluocortolone pivalate 0.918 mg/g, fluocortolone hexanoate 0.945 mg/g and 5 mg/g cinchocaine hydrochloride ointment

ULTRAPROCT® 0.612 mg fluocortolone pivalate, 0.63 mg fluocortolone hexanoate and 1 mg cinchocaine hydrochloride suppositories

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ointment: 1 g colourless to faintly yellowish ointment contains 0.92 mg fluocortolone pivalate, 0.95 mg fluocortolone hexanoate and 5 mg cinchocaine hydrochloride.

Suppositories: 1 yellowish white suppository contains 0.61 mg fluocortolone pivalate, 0.63 mg fluocortolone hexanoate and 1 mg cinchocaine hydrochloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Topical ointment

Suppositories

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Haemorrhoids, superficial anal fissures, proctitis.

4.2 Dose and method of administration

The anal region should be cleaned thoroughly before using ULTRAPROCT®, which is best applied after defaecation. There is usually a rapid improvement, but this should not mislead one into stopping treatment too soon. To avoid relapses, ULTRAPROCT® should be continued for at least one week, though less frequently (ointment once a day or one suppository every other day), even when the symptoms have completely disappeared. However, duration of treatment should, as far as possible, not exceed 4 weeks.

Ointment

Generally, ULTRAPROCT® ointment is applied twice daily. On the first day for faster symptomatic relief, it can be applied up to four times a day. A little ointment (about the size of a pea) is smeared around the anus and in the anal ring with a finger, using the fingertip to overcome the resistance of the sphincter. Before applying within the rectum, the enclosed nozzle should be screwed on to the tube. However, for very inflamed and hence painful lesions, it is advisable initially to apply the ointment internally with the finger. Protruding lumps should be smeared thickly and pressed carefully back with the finger.

Suppositories

In general, one suppository daily is inserted high into the rectum. If symptoms are severe, one suppository can be inserted two to three times on the first day. The consistency of suppositories that

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have become soft due to heat can be restored by placing them in cold water before the covering is removed.

4.3 Contraindications

Tuberculous or syphilitic processes in the area to be treated; virus diseases (e. g. vaccinia, chickenpox); hypersensitivity to individual components (see Further Information: List of Excipients).

4.4 Special warnings and precautions for use

Additional specific therapy is required in fungal infections.

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

Prolonged use (more than 4 weeks) may lead to local concomitant symptoms, such as atrophy of the skin (see Adverse Effects).

4.5 Interaction with other medicines and other forms of interaction

None so far known.

4.6 Fertility, pregnancy and lactation

Use in Pregnancy

Animal experimental studies with glucocorticosteroids have shown reproductive toxicity (refer to the preclinical data in the Warnings and Precautions section of this leaflet).

A number of epidemiological studies suggest that there could be increased risk of oral cleft among new-borns 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 ULTRAPROCT® must be carefully reviewed and the benefits weighed against the risks in pregnant and lactating women. In particular, prolonged use must be avoided.

Use in Lactation

The excretion of effective amounts of glucocorticoid with the breast milk is improbable.

4.7 Effects on ability to drive and use machines

Not known.

4.8 Undesirable effects

If ULTRAPROCT® is applied for long periods of time (more than 4 weeks), local concomitant symptoms, such as atrophy of the skin cannot be excluded.

Allergic skin reactions may occur in rare cases.

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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 <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

In accordance with the results from acute toxicity studies with the fluocortolone esters and cinchocaine hydrochloride no acute risk of intoxication is to be expected following single rectal or perianal administration of ULTRAPROCT[®], even after inadvertent overdose. Following inadvertent oral intake of the preparation (e. g. after ingestion of some grams of the ointment or of several suppositories) mainly systemic effects of cinchocaine hydrochloride are to be expected which, according to the dose, could also manifest themselves as severe cardiovascular (depression to cessation of cardiac function) and CNS symptoms (convulsions; inhibition to arrest of respiratory function).

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

As ULTRAPROCT[®] contains two fluocortolone esters, which start to exert their main effect at different times, a rapidly established and long-lasting effect results (biphasic action). As a local anaesthetic, cinchocaine eases the pain.

5.2 Pharmacokinetic properties

Because of their different lipophilicity and molecular weights, fluocortolone pivalate and fluocortolone hexanoate diffuse at different rates at the site of inflammation, resulting in a rapid onset of action and in a protracted duration of action. It can be assumed that, after topical application, the two esters are hydrolysed to free fluocortolone and the corresponding acids at the level of the perianal skin or rectal mucosa -but at the latest after the first liver pass - by esterases occurring ubiquitously in the body.

No studies into the degree of systemic availability after rectal use are available for the ULTRAPROCT[®] formulations themselves. Studies with preparations with a similar composition have shown that less than 15 % of the dose of fluocortolone pivalate applied is absorbed rectally. Absorbed fluocortolone is broken down in the liver into metabolites, the overwhelming majority of which are excreted in the urine.

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 ULTRAPROCT[®] is applied according to the instructions. Following absorption, cinchocaine is biotransformed into a number of metabolites. The principal metabolic routes 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.

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Even under the assumption of complete absorption, systemic effects can be ruled out when the two formulations are used according to instructions because of the low dosage.

5.3 Preclinical safety data

In systemic tolerance studies following repeated administration of the fluocortolone esters and the cinchocaine hydrochloride contained in ULTRAPROCT® no findings occurred which might be prohibitive of the prescriptive use of the preparation.

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 fluocortolone and fluocortolone hexanoate led to results typical of glucocorticoids, i. e. following sufficiently high exposure embryoethal and/or teratogenic effects could be induced given the appropriate test systems. Since epidemiological studies have as yet given no indications of embryotoxic effects due to systemic glucocorticoid therapy, no embryotoxic effects are to be expected from the glucocorticoids contained in ULTRAPROCT® under therapeutic conditions. However, taking animal-experimental results into consideration, particular care should be taken when prescribing ULTRAPROCT® during pregnancy (see Pregnancy and Lactation section, below).

There are neither data from animal experiments nor epidemiological data on cinchocaine hydrochloride, which enable the evaluation of the teratogenic potential. However, in analogy with structure- and effect-related local anaesthetics of the amide class, no embryotoxic effects are to be expected in humans following topical use of the therapeutic dose. 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.

The investigation of fluocortolone in a bacterial test system aimed at detection of point mutagenic effects gave no indications of a genotoxic potential. Since no relevant indications of a mutagenic potential exist for any member of the substance category glucocorticoids, such effects are not to be expected for the fluocortolone esters either. The investigations of cinchocaine hydrochloride for point mutagenic effects in bacteria or in mammalian cells gave no relevant indications of a genotoxic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ointment: 2-Octyldodecanol, castor oil, hydrogenated castor oil, macrogol 400-monoricinoleate, citrus-rose perfume oil.

Suppositories: Hard fat (Witepsol W 35).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Ultraproct® ointment

Shelf life: 24 months

Ultraproct® suppositories

Shelf life: 36 months

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6.4 Special precautions for storage

Ultraproct® ointment

Special precautions for storage: Store below 25°C

Ultraproct® suppositories

Special precautions for storage: Store at 2 to 8°C. Refrigerate, do not freeze.

Store all drugs properly and keep them out of reach of children

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Ointment: Tubes of pure aluminium, interior wall coated with epoxy resin, and with a polyester-based external coating, fold seal ring is made of polyamide based heat sealable material. The screw cap is made of high density polyethylene. Tubes containing 30 g of ointment.

Suppositories: Aluminium-foil laminated with polypropylene/ polyethylene or PVC-foil laminated with polyethylene. Packs containing 12 suppositories.

6.6 Special precautions for disposal <and other handling>

None

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

AFT Pharmaceuticals Ltd

P O Box 33203

Takapuna

AUCKLAND 0740

9 DATE OF FIRST APPROVAL

31/12/1969

10 DATE OF REVISION OF THE TEXT

31/08/2020

SUMMARY TABLE OF CHANGES

| Section affected | Summary of new information |
|------------------|--|
| 8 Sponsor | Change to the sponsor name and address |