Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ultraproct 0.92mg/g + 0.95mg/g + 5mg/g Rectal Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1g of ointment contains 0.92 mg of Fluocortolone Pivalate, 0.95 mg of Fluocortolone Caproate and 5 mg of Cinchocaine Hydrochloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Rectal Ointment.

A colourless to faintly yellow 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 Ultraproct, 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.

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

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 *(see 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 Ultraproct 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 Ultraproct 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.

Reporting of suspected adverse reactions
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 the fluocortolone esters and cinchocaine hydrochloride, no risk of acute intoxication is to be expected following single rectal or perianal administration of Ultraproct, 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

Fluocortolone exerts an anti-inflammatory, antiallergic 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 caproate diffuse at different rates at the site of inflammation, resulting on the one hand in a rapid onset of action and, on the other, in a protracted duration of action.

It can be assumed that, after topical application, the two esters are hydrolyzed 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 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 with the urine.

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 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. 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.

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 Ultraproct 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 Ultraproct during pregnancy. The results of epidemiological studies are summarized under section ‘4.6 Pregnancy and lactation’.

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 hydro-chloride 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.

Specific tumorigenicity tests have not been carried out with the active substances contained in Ultraproct. On the basis of knowledge concerning the structures, the pharmacological effect mechanism and the results of systemic toxicity studies following repeated administration, there are no indications of a tumorigenic potential.

No local intolerance reactions were observed in the dog following repeated rectal administration of the active substance combination in the form of suppositories. Many years of therapeutic use of Ultraproct in humans have not revealed any undesired local effects worth mentioning. The sporadic side-effects which have been reported are mainly concerned with suspicion of contact allergy.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

2-Octyldodecanol
Castor oil refined
Castor oil, hydrogenated
Polyethylene glycol-400-monoricinoleate
Citrus-rose perfume oil

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

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

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Tubes of 10, 15, 30, 40, or 60 g, made of pure aluminium, interior wall coated with epoxy resins 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.

Not all pack sizes may be marketed.

The applicator consists of a rectal cannula; which is made from polypropylene, natural and a cap; which is made from low-density polyethylene PE-LD, natural.

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 MARKETING AUTHORISATION HOLDER

Bayer Limited
The Atrium
Blackthorn Road
Dublin 18
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1410/074/001

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

March 2017