**APPLICATION FOR RECLASSIFICATION**

# ULTRAPROCT OINTMENT
# ULTRAPROCT SUPPOSITORIES

***Part A***
**Classification Change Sought**

**1. International Non-Proprietary name of Medicine**

fluocortolone pivalate, fluocortolone caproate and cinchocaine hydrochloride.

**2. Proprietary Name**

Ultraproct ointment

Ultraproct suppositories

**3. Name of Company**

Schering (NZ) Ltd

P O Box 10-1691

NSMC

AUCKLAND

**4. Dose form and strength for which reclassification is sought**

Ultraproct ointment contains 0.92 mg fluocortolone pivalate, 0.95 mg fluocortolone caproate and 5 mg cinchocaine hydrochloride per 1g of ointment. Tubes of 30gms are available.

Ultraproct suppositories contain 0.61 mg fluocortolone pivalate, 0.63 mg fluocortolone caproate and 1 mg cinchocaine hydrochloride. Packs of 12 suppositories are available.

**5. Pack size**

Ultraproct ointment comes in tubes of 30 gms. There is no other presentation on the market.

Ultraproct suppositories come in packs of 12 suppositories. There are no other presentations on the market.

**6. Indications**

The exemption is sought for the registered indication of Ultraproct. These are:

Haemorrhoids, superficial anal fissures, proctitis.

## 7. Present Classification

Ultraproct is currently a Prescription Medicine.

## 8. Classification Sought

We propose that an exemption is granted for Ultraproct to be dispensed as Restricted Medicine in pack sizes not exceeding 35 gm (for the ointment) and packs of 12 for the suppositories.

## 9. Classification status in other countries (especially Australia, UK, USA, Canada)

In general Ultraproct is sold as a Prescription Medicine. Unless, requested by the Committee we would not intend to change the labeled classification.

## 10. Extent of usage in NZ and elsewhere (e.g. sales volumes) and dates of original consent to distribute

Ultraproct has been available in New Zealand since 1970. Our unit sales for 2000 were:-

| Ultraproct Sales 2000 units | |
|---|---|
| Ointment 30g | 26,045 |
| Supp | 19,744 |

## 11. Labelling or draft labelling for the proposed new presentations

With the pack size restriction applying to the pharmacist only prescription, we would not intend to change our existing labeling unless requested to do so by the Classifications Committee. An example of the outer label for Ultraproct ointment and suppositories is included.

## 12. Proposed warning statements if applicable

Non applicable.

## 13. Other products containing the same active ingredient(s) and which would be affected by the proposed change

Because Ultraproct is a combination product, there are no other products that contain the same ingredients on the New Zealand market, which would be affected by the classification process.

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***Part B***
**Reasons for requesting classification change**

**1. A statement of the benefits to both the consumer and to the public expected from the proposed change**

In view of the intended delisting of Ultraproct from the Pharmaceutical Schedule, from the 1 December 2001,the consumer and public would be expected to gain continued access to the product subsequent to it being re-classified as a restricted medicine. Currently, four antihemorrhoidal preparations are available for prescription and from 1 December 2001, only Proctosedyl will be funded. Pharmac announced in their correspondence of 30 May 2001, that they considered that it was likely that Ultraproct, Xyloproct or Kenoid would continue to be available for purchase over-the-counter from pharmacies from that date.

**2. Ease of self-diagnosis or diagnosis by a pharmacist for the condition indicated**

A number of the antihemorrhoidal preparations have already been classified for pharmacist prescription and some are available OTC. Customers and pharmacist are familiar with providing these types of medicines for these indications.

**3. Relevant comparative data for like compounds**

Please see our re-classification summary.

**4. Local data or special considerations relating to NZ**

We consider the recent move by Pharmac constitutes special conditions relating to the New Zealand market. Customers who are familiar with this preparation are likely to want it to continue to be available.

**5. Interactions with other medicines**

There are no relevant interactions known to interfere with this medicine or any other medicine which the patient might be taking.

**6. Contraindications**

The only contraindication to this medicine (viral disease in the affected area) is listed in our Data Sheet.

## 7. Possible resistance

There is no concern about antibacterial resistance.

## 8. Adverse Events

Ultraproct has a very high safety profile as seen in our re-classification summary and international safety summary.

## 9. Potential for abuse or misuse

There is virtually no potential for abuse with antihemorrhoidal products.

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## Summary

Ultraproct fulfils the criteria for re-classification as a pharmacist only (restricted) medicine because it clearly fulfils the criteria of the 1990 Commission of the European Communities for OTC sale:

> *Medicinal products which may be available without prescription shall show a substantial safety in use in the treatment of minor ailments or symptoms, usually capable of rapid and spontaneous relief, which are easily identifiable by users and do not justify a medical consultation.*

Ultraproct is available in ointment and suppository form and is indicated for haemorrhoids, superficial anal fissures and proctitis.

Ultraproct has been available in New Zealand since its registration on 31.12.1969.

We have reviewed all the aspects the classification committee would want to consider and we can see no objection to Ultraproct being reclassified. Each item the committee is likely to consider is discussed below.

- **Has been marketed for three years or more**

  Ultraproct has been on the market since 31.12.1969

- **Has had a wide use for three years or more**

  Ultraproct has consistently held around 30% of the prescription market for anti-haemorrhoidals and 19,744 packs of 12 suppositories and 26,045 packs of 30g ointment were sold during the year 2000.

- **Has a low adverse reaction profile with serious reactions occurring only rarely**

  We have supplied the International Safety summary from Corporate Drug Safety for Ultraproct covering the years from January 1, 1990 to March 31, 1997. During this time it has been estimated that over 26 million patients received Ultraproct (ointment or suppositories).

  A total of 7 spontaneous ADR reports were received during the reporting period. All these reports were non-serious allergic type reactions like contact eczema, redness, oozing dermatitis, itching and erythematous maculae. In four of these cases an allergy test was

positive for cinchocaine hydrochloride, one of the active ingredients of Ultraproct.

The safety summary data was in accordance to the known safety profile of Ultraproct. There was no evidence of any substance-related events, which were not expected, and compared to the high number of exposed patients the number of reports on ADRs was extremely low. Thus the very favourable risk-benefit ratio for Ultraproct was confirmed.

- **Consumer convenience**

  A number of the anti-haemorrhoidal preparations are all ready available for OTC use. Therefore the symptomatic relief of this condition is already viewed as being suitable for self-treatment (with the guidance of a pharmacist in the restricted medicine category).

- **Potency**

  Ultraproct ointment contains two mild fluocortolone esters that start to exert their main effects at different times. The rapidly established and long-lasting effect results in a biphasic action. A local anesthetic, cinchocaine eases the pain. These fluocortolone esters have been in the market since the 1970's. They do not show the same potency as the more recently developed formulations. In addition, the limitation of pack size considered for the restricted medicine category remains a further barrier to long term use or misuse. In addition, classed in the category containing 0.2% of fluocortolone esters this formulation is considered just slightly stronger than 0.25 –2% hydrocortisone.

- **Current availability**

  This application is intended to ensure continued availability of a product as the recommendation to doctors made by Pharmac is that the preparation is likely to be available over the counter from pharmacies.

- **Therapeutic index**

  The very wide safety index is demonstrated by our Safety report covering 26 million packs of Ultraproct sold.

- **Abuse potential**

  In our view there is little or no risk of abuse potential in the application of either ULTRAPROCT ointment or ULTRAPROCT suppositories.

- **Inappropriate use**

  With the appropriate Pharmacist counseling and prescription there is little or no concern for inappropriate use. It is likely that the Pharmacist will ensure that any long-term condition is monitored by the patients'

general practitioner. The fact that similar preparations have a restricted classification means that the disease category is considered appropriate for self-monitoring and medication.

- **Precautions**

  The precautions for Ultraproct are outlined in our Data Sheet. The only listed contraindication is: -

  *Tuberculous or syphilitic processes in the area to be treated; virus diseases (e. g. vaccinia, chickenpox).*

  And the precautions listed as

  *Additional specific therapy is required in fungal infections. Inadvertent contact of the preparation with the eyes should be avoided. Careful hand washing after use is recommended.*

- **Communal harm**

  There is absolutely no possibility of communal harm that would influence a decision not to reclassify ULTRAPROCT.

In conclusion, Ultraproct ointment and suppositories contain weak cortico-steroid formulations, fluocortolone pivalate, and fluocortolone caproate and cinchocaine hydrochloride.

We are aware of the discussions concerning the comparison of mild corticosteroids with 1% hydrocortisone. We conducted a comprehensive literature search spanning MEDLINE, EMBAE, SCISEARCH, BIOSIS, and the DERWENT DRUG FILE we were only able to locate 6 references that linked in any way the two ingredients.

A study conducted by Portnoy in 1969 showed a borderline significance in improved efficacy between 1% hydrocortisone and 0.2% fluocortolone. For the skin condition of psoriasis, which normally requires a stronger formulation, there was no significant difference between the two treatments.

Although the committee have recently expressed some measure of concern about the availability of corticosteroids into the OTC market, we consider that with the restricted medicine classification, coupled with a pack restriction of <35g for the ointment and not more than 12 suppositories, there could be no health concerns regarding this reclassification proposal.

Schering (NZ) Ltd
PO Box 101-691 North Shore Mail Centre
Auckland.

***References:***

Ultraproct DATA Sheet; www.medsafe.govt.nz

Ultraproct Ointment and suppository Packaging; Outer box and inserts

Pharmac fax of 30 May 2001, Page 7 of 12

Martindale the Extra Pharmacopoeia, 30th Edition, page 732 Corticosteroids

Avery's Drug Treatment 4th Edition: Table II; Relative activities of topical corticosteroid preparations, Skin Disease, p 635.

Literature search, Ultraproct in comparison with Hydrocortisone.

Portnoy, Drug Trial: A comparison between the Topical Efficacy of 1% hydrocortisone and 0.2% fluocortolone. Aust J Derm (1969), 10:183,184

Schering AG, Corporate Regulatory Affairs Safety summary Ultraproct, January 1st 1990 – March 31st 1997, Dated 28,05.1997

*NOTE: A copy of the references can be made available on request to Schering (NZ) Ltd, PO Box 101-691 North Shore Mail Centre Auckland.*