PROCTOSEDYL®

(HYDROCORTISONE, CINCHOCAINE HYDROCHLORIDE)

RECLASSIFICATION APPLICATION

SANOFI-AVENTIS GROUP

27 SIRIUS ROAD

LANE COVE

NSW 2066

AUSTRALIA

JULY 2005

Group sanofi aventis

Because health matters

TABLE OF CONTENTS

TABLE OF TABLES

ABBREVIATIONS

ADR	Adverse Drug Reaction
CARM	Centre for Adverse Reactions Monitoring
CMI	Consumer Medicine Information
GSL	General Sales List
HMO	Health Maintenance Organisation
IMS	ims health (company providing pharmaceutical market intelligence)
NDPSC	National Drugs and Poisons Scheduling Committee
OTC	Over The Counter
P	Pharmacy
POM	Prescription Only Medicine
PSUR	Periodic Safety Update Report
TGA	Therapeutic Goods Administration
UK	United Kingdom
USA	United States of America

EXECUTIVE SUMMARY

1. Purpose of the Application

Hydrocortisone and cinchocaine hydrochloride (Tradename Proctosedyl®) ointment and suppositories are currently approved for:

- symptomatic relief of external and internal haemorrhoids, anal pruritus, anal fissure, perianal eczema.
- Pre and post-operative treatment of haemorrhoidectomy patients.
- Post-partum haemorrhoidal conditions.
- Non-infective proctitis.

This application seeks to reclassify Restricted hydrocortisone and Pharmacy Only cinchocaine hydrochloride ointment and suppositories to Pharmacy Only, via the reclassification of hydrocortisone in rectal medicines, for the treatment of haemorrhoids and other anorectal conditions for a maximum of 7 days.

2. Background

It is already accepted that the treatment of haemorrhoids and other anorectal conditions does not always require the supervision of a healthcare professional. This is demonstrated by the availability of a range of over the counter (OTC) products for the treatment of haemorrhoids and other anorectal conditions.

The following products, with their approved indications, are currently available as Pharmacy Only products:

- Anusol suppositories (zinc oxide, Peru balsam); uncomplicated haemorrhoids, simple anorectal inflammation.
- Anusol ointment (zinc oxide, Peru balsam); uncomplicated haemorrhoids, simple anorectal inflammation.

The following product, with its approved indication, is currently available as General Sale:

- Pharma witch hazel (Hamamelis extract); symptomatic relief of haemorrhoids

Although the current classification for Proctosedyl allows for consumer access without a prescription, the requirement for pharmacist supervision prevents it from being made available concurrently with other Pharmacy Only therapies for haemorrhoids and other

anorectal conditions. This is particularly significant for haemorrhoids and other anorectal conditions, in which following initial diagnosis by a healthcare professional, therapeutic agents continue to be self-selected by consumers. Proctosedyl suppositories must be stored between 2°C and 8°C in a refrigerator, which in a pharmacy would normally be located behind the pharmacy counter. The reclassification of hydrocortisone in rectal medicines will still allow access to these products without a pharmacist's intervention, even though the suppositories may not necessarily be available for the consumer to view. Proctosedyl ointment will be clearly visible to the consumers for self-selection.

The efficacy and safety of hydrocortisone and cinchocaine hydrochloride ointment and suppositories are at least equivalent to the other therapies that are available for the treatment of haemorrhoids and other anorectal conditions.

3. Major Points

- Haemorrhoids and other anorectal conditions are currently regarded as conditions that are appropriate for self-diagnosis, as is evident from the other therapies already available without pharmacist supervision. Often patients prefer to access them without consulting a pharmacist due to the perceived embarrassing nature of the condition. In the event of inadequate relief of their symptoms, patients will be encouraged to seek advice from their doctor.

- Proctosedyl ointment and suppositories are at least as safe and effective as other Pharmacy Only treatments for haemorrhoids and other anorectal conditions such as Anusol. Furthermore, prescribing is restricted to seven days unless a doctor has told the consumer otherwise, therefore limiting any potential for harm to occur.

- Significant international post-marketing data are available. Hydrocortisone and cinchocaine hydrochloride has been marketed internationally since March 1966 and in New Zealand since approximately January 1970. Safety data gathered post-marketing have not revealed any new findings or increased reporting frequency for hydrocortisone and cinchocaine hydrochloride.

- Hydrocortisone for dermal use in medicines containing 0.5% or less by weight of hydrocortisone base with no other active ingredient except an antifungal and in a

quantity of 30 grams or less or 30 millilitres or less per container, is already available as Pharmacy Only.

- To assist the pharmacy assistants with handling enquires about Proctosedyl following the reclassification of hydrocortisone in rectal medicines, the following educational strategies will be employed:
    - A team of sanofi-aventis pharmacy only sales representatives will be available nationwide to present a Proctosedyl training module for pharmacy assistants and answer questions from the pharmacy assistants on Proctosedyl.
    - The key points on Proctosedyl will be communicated to all pharmacies as a mailer as soon as possible after the reclassification announcement.
    - Advertising in pharmacy magazines will take place to notify pharmacy assistants of the reclassification, along with instructions for the appropriate use of Proctosedyl.

4. Conclusion

Proctosedyl is a highly effective short-term treatment for haemorrhoids and other anorectal conditions. The reclassification of Proctosedyl, via the reclassification of hydrocortisone in rectal medicines, as a Pharmacy Only medicine, would allow consumers easier access to a treatment for haemorrhoids and other anorectal conditions which is at least as safe and effective as those other products which are currently classified Pharmacy Only medicines. Hydrocortisone and cinchocaine hydrochloride have an excellent safety profile and the rectal route of administration results in a low potential for systemic toxicity.

PART A

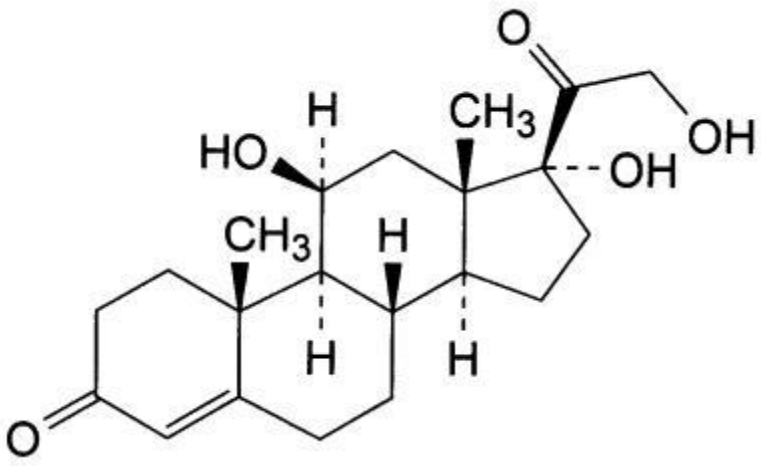
1. International Non-Proprietary Name

Name:	Hydrocortisone	Cinchocaine hydrochloride
Chemical name:	11 beta, 17, 21-trihydroxypregn-4-ene-3,20-dione	2-butoxy-N-[2-(diethylamino)ethyl]-4-quinolinecarboxamide monohydrochloride
Molecular formula:	$C_{21}H_{30}O5$	$C_{20}H_{29}N_3O_2$, HCl
CAS Registry Number:	50-23-7	61-12-1

1.1 Physico-Chemical Properties

1.1.1 Hydrocortisone

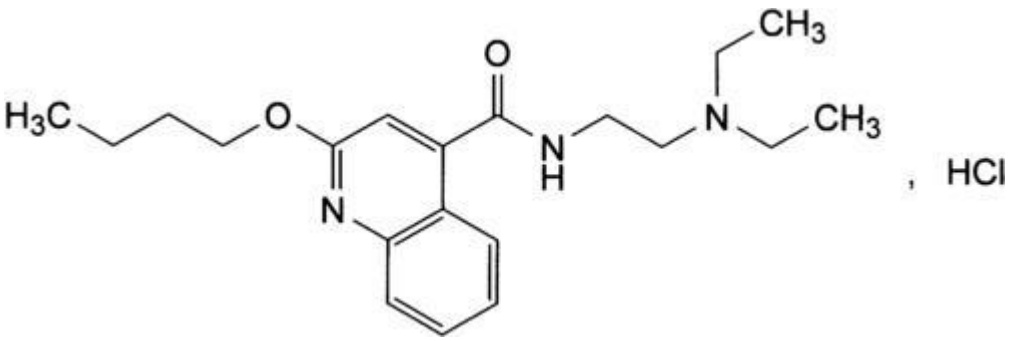
Structural Formula:



Hydrocortisone is a naturally occurring glucocorticoid. It is practically insoluble in water, sparingly soluble in acetone and in alcohol and slightly soluble in methylene chloride.

1.1.2 Cinchocaine hydrochloride

Structural Formula:



Cinchocaine hydrochloride is a local anaesthetic. It is hygroscopic, very soluble in water, freely soluble in acetone, in alcohol and in methylene chloride and it agglomerates very easily.

2. Proprietary Name

Proctosedyl

3. Name of Company Requesting Reclassification

Aventis Pharma Pty Limited
27 Sirius Road
Lane Cove, NSW 2066
Australia

Tel: +61 2 9422 6455
Fax: +61 2 9422 6659
e-mail: katrina.willis2@sanofi-aventis.com

Contact Person: Katrina Willis, Regulatory Affairs Contractor

4. Dose Forms and Strengths for Which a Change is Sought

Ointment 5mg/g
Suppository 5mg

4.1 Formulation

4.1.1 Ointment

Active Ingredient	mg per g	(%w/w)
Hydrocortisone	5.0	0.5
Cinchocaine hydrochloride	5.0	0.5
Excipients		
Lanolin	100.0	10
White soft paraffin	740.0	74
Liquid paraffin	150.0	15

4.1.2 Suppository

Active Ingredient	mg per suppository
Hydrocortisone	5.0
Cinchocaine hydrochloride	5.0
Excipients	
Hard fat	q.s. ad 1800

5. Pack Size and Other Qualifications

5.1 Ointment

15g with cannula

30g with cannula

5.2 Suppository

Strip pack of 12 suppositories

6. Indications for Which Change is Sought

Hydrocortisone and cinchocaine hydrochloride (Tradename Proctosedyl) ointment and suppositories are currently approved for:

- symptomatic relief of external and internal haemorrhoids, anal pruritus, anal fissure, perianal eczema.
- Pre and post-operative treatment of haemorrhoidectomy patients.
- Post-partum haemorrhoidal conditions.
- Non-infective proctitis.

7. Present Classification of Medicine

Hydrocortisone and hydrocortisone acetate but no other esters of hydrocortisone, are classified as Pharmacy Only, with the following conditions:
for dermal use in medicines containing 0.5% or less by weight of hydrocortisone base with no other active ingredient except an antifungal and in a quantity of 30 grams or less or 30 millilitres or less per container.

Hydrocortisone and hydrocortisone acetate but no other esters of hydrocortisone, are classified as Restricted, with the following conditions:
for dermal use in medicines containing 1% or less but more than 0.5% by weight of hydrocortisone base with no other active ingredient except an antifungal and in a quantity of 30 grams or less or 30 millilitres or less per container; in rectal medicines containing 1% or less by weight of hydrocortisone base and in combination with a local anaesthetic and in a quantity of not more than 35 grams per container or 12 suppositories per pack.

Hydrocortisone is classified as Prescription except when specified elsewhere in the Schedule.

Cinchocaine hydrochloride is classified as Pharmacy Only.

The current classification of Proctosedyl is therefore Restricted.

8. Classification Sought

Pharmacy Only, via the reclassification of hydrocortisone in rectal medicines to Pharmacy Only. The suggested reclassification could be as follows:

Hydrocortisone and hydrocortisone acetate but no other esters of hydrocortisone, are classified as Pharmacy Only, with the following conditions:
for dermal use in medicines containing 0.5% or less by weight of hydrocortisone base with no other active ingredient except an antifungal and in a quantity of 30 grams or less or 30 millilitres or less per container; in rectal medicines containing 1% or less by weight of hydrocortisone base and in combination with a local anaesthetic and in a quantity of not more than 35 grams per container or 12 suppositories per pack.

Hydrocortisone and hydrocortisone acetate but no other esters of hydrocortisone, are classified as Restricted, with the following conditions:

for dermal use in medicines containing 1% or less but more than 0.5% by weight of hydrocortisone base with no other active ingredient except an antifungal and in a quantity of 30 grams or less or 30 millilitres or less per container.

Hydrocortisone is classified as Prescription except when specified elsewhere in the Schedule.

9. Classification Status in Other Countries

Hydrocortisone and cinchocaine hydrochloride is classified as a Prescription Only Medicine (POM) in the United Kingdom (UK). However, hydrocortisone and lidocaine hydrochloride underwent a switch in 2004 from Pharmacy (P) to General Sales List (GSL); supplied for the symptomatic relief of anal and perianal itch, irritation and pain associated with external haemorrhoids[i]. Other hydrocortisone and hydrocortisone acetate containing products for the treatment of haemorrhoids and other anorectal conditions are available as P and GSL products.

In Australia, hydrocortisone and hydrocortisone acetate, but excluding other salts and derivatives, in preparations containing 1% or less of hydrocortisone, for rectal use, when combined with a local anaesthetic but no other therapeutically active substance except unscheduled astringents; in undivided preparations, in packs of 35g or less, or in packs containing 12 or less suppositories, is currently classified as Schedule 3 (Pharmacist Only). However an application to reschedule the product, via the rescheduling of hydrocortisone, was submitted in June 2005 to the National Drugs and Poisons Scheduling Committee (NDPSC). Cinchocaine in preparations for topical use other than eye drops, containing 0.5% or less of total local anaesthetic substances is already a Schedule 2 (Pharmacy Only) product.

In the United States of America (USA), Anusol HC, a product containing hydrocortisone for the treatment of haemorrhoids and other anorectal conditions, is classified as a prescription product.

10. Extent of Usage in New Zealand and Elsewhere

Hydrocortisone and cinchocaine hydrochloride is registered in 55 countries throughout the world. The approval dates of hydrocortisone and cinchocaine hydrochloride in New Zealand and other recognised countries are listed in Table 1.

Table 1: Approval dates for hydrocortisone and cinchocaine hydrochloride

Country	Date of Approval
Australia	26 June 1992
Finland	17 July 1995
France	22 November 1993
Japan	11 March 1966
New Zealand	31 December 1969
UK	30 September 1988

Since 1997, 540,767 tubes of ointment (151,927 15g and 388,840 30g) and 382,683 packs of suppositories have been sold in New Zealand. In 2004, 91,756 (7,250 15g and 84,506 30g) tubes of ointment and 63,441 packs of suppositories were sold in New Zealand.

As per the Five Year Summary Bridging Report (see Appendix 8), it is not possible to calculate the exact patient exposure with hydrocortisone, since therapy is usually administered at different dosage levels i.e. tapering doses. A total of 961,313,483 counting units were sold worldwide from July 1999 to December 2003. This estimate represents 34 countries reporting IMS data, including data from hospitals and miscellaneous sources in the US (clinics, federal hospitals, US food stores, US Health Maintenance Organisation [HMO], Homecare, long term care, US mail order, non federal hospitals, etc).

Estimates on patient exposure should be interpreted with caution, since sales to hospital are inconsistently reported in the IMS figures. It must also be recognised that this figure represents an estimate of the number of patients, and that wholesale stocks have not been taken into account in the calculation. Further more, the number of estimated doses may not reflect actual patient exposure.

11. Labelling or Draft Labelling for the Proposed New Presentations

The labelling will be as currently registered, except ‘Pharmacist Only Medicine’ will be replaced with ‘Pharmacy Only Medicine’.

11. Proposed Warning Statements

The same warning statements on the labelling and in the package insert as currently applied for other OTC products for the treatment of haemorrhoids and other anorectal conditions will be applied to Proctosedyl.

In addition to the current warning statements:

- CAUTION – Do not use for children under 2 years old unless a doctor has told you to
- Do not use for more than 7 days unless a doctor has told you to
- For rectal use only

The following additional warning statements will be added to the labelling:

- If irritation occurs, stop use immediately and seek medical advice
- If symptoms persist, seek medical advice

13. Other Products Containing the Same Active Ingredients and Which Would be Affected by the Proposed Change

Hydrocortisone is a corticosteroid that has been registered for many years as a cream and ointment for the treatment of dermatitis, eczema, psoriasis, pruritus and anorectal conditions.

Cinchocaine is an anaesthetic which has been registered for many years as a local anaesthetic used in the treatment of a haemorrhoids and itchy anti-fungal infections.

A tabulated summary of the products marketed in New Zealand containing hydrocortisone or cinchocaine hydrochloride as an active ingredient for use in the proposed disease state, is provided in Table 2. These products may be affected by the reclassification of Proctosedyl.

Table 2: Products marketed in New Zealand containing hydrocortisone or cinchocaine hydrochloride

Product	Active Ingredient(s)	Indication	Sponsor	Current Classification
Colifoam rectal foam	Hydrocortisone acetate	Inflammation of rectal mucosa e.g. ulcerative colitis, proctosigmoiditis, granular proctitis	Anspec NZ	Prescription only
Proctosedyl ointment	Cinchocaine hydrochloride, hydrocortisone	Treatment of haemorrhoids, anal pruritus, anal fissures, proctitis	Aventis Pharma Limited	Restricted
Proctosedyl suppositories	Cinchocaine hydrochloride, hydrocortisone	Treatment of haemorrhoids, anal pruritus, anal fissures, proctitis	Aventis Pharma Limited	Restricted
Ultraproct ointment	Cinchocaine hydrochloride, fluocortolone hexonate, fluocortolone pivalate	Treatment of haemorrhoids, superficial anal fissures, proctitis	Schering NZ	Prescription only
Ultraproct suppository	Cinchocaine hydrochloride, fluocortolone hexonate, fluocortolone pivalate	Treatment of haemorrhoids, superficial anal fissures, proctitis	Schering NZ	Prescription only
Xyloproct ointment	Lignocaine, hydrocortisone acetate, aluminium acetate, zinc oxide	Treatment of haemorrhoids, milder forms anal fissures, proctitis	AstraZeneca Limited	Restricted
Xyloproct suppositories	Lignocaine, hydrocortisone acetate, aluminium acetate, zinc oxide	Treatment of haemorrhoids, milder forms anal fissures, proctitis	AstraZeneca Limited	Restricted

PART B

1. Benefits to the Consumer and the Public Expected from the Proposed Change

Haemorrhoids are an extremely common problem, with surveys suggesting that as many as 50% of people 40 years of age and over may suffer some form of mild to severe discomfort from them[ii].

Creams, ointments and suppositories are frequently used for the treatment of haemorrhoids and other anorectal conditions. Anusol (zinc oxide, peru balsm – Pfizer Consumer Healthcare) and Pharma witch hazel (hemamelis extract – HMG), are already available in New Zealand as Pharmacy Only or General Sale medicines. Patients often prefer to access treatments for haemorrhoids and other anorectal conditions without consulting a pharmacist due to the perceived embarrassing nature of the condition.

Patients who do not receive relief from the existing OTC treatments of haemorrhoids and other anorectal conditions will benefit as they will have access to more OTC treatments. The quality of life of these patients would be enhanced by increasing access to these products. Consumers have a greater desire to play an increasing role in making decisions about their health and the availability of similar products over the counter.

The unique presentation of Proctosedyl as suppositories or tubes with cannulas, ensures that they are used only for the intended indication. These features enhance the safety of these products. Furthermore, they offer a convenient application method that facilitates patient compliance. The reclassification of Proctosedyl would further enhance patient compliance, as consumers would have easier access to a safe and effective treatment for haemorrhoids and other anorectal conditions. This is particularly significant for an indication such haemorrhoids and other anorectal conditions, in which therapeutic agents are often self-selected by consumers.

A study published in 1970[iii] concluded ‘the use of Proctosedyl ointment is a valuable method of treating acute fissure-in-ano and in particular may spare the patient an anaesthetic, especially important in children and the elderly’.

The rationale of the combination used in Proctosedyl is to combine the local anaesthetic, analgesic and spasmolytic effect of cinchocaine with the antipruritic and anti-inflammatory action of hydrocortisone. These ingredients are presented in emollient vehicles.

Topical corticosteroids have anti-inflammatory, anti-pruritic and vasoconstrictive actions. Hydrocortisone is a low potency glucocorticoid that is safe and effective as a topical anti-inflammatory drug in the concentration employed in Proctosedyl. Cinchocaine hydrochloride is a local anaesthetic agent. It is recognised as being one of the longest acting of those agents commonly employed. It is included in Proctosedyl for the relief of pain and spasm.

Corticosteroids, in general, decrease inflammation by a multitude of mechanisms, including the stabilisation of leukocyte lysosomal membranes, the prevention of the release of leukocytic acid hydrolyses, the inhibition of macrophage accumulation in inflamed areas and the reduction of capillary wall permeation.

Theoretically, there may be concern about the systemic absorption of hydrocortisone from the rectum. However, suppression of secretion of endogenous cortisone and atrophy of the adrenal gland occur only when doses of corticosteroid exceed physiological amounts, i.e. greater than 7.5mg orally of prednisolone daily (equivalent to 30mg of hydrocortisone daily) and when the duration of therapy is prolonged[iv].

A maximum of 50% of hydrocortisone administered rectally is absorbed by patients with proctitis[v]. Thus, the maximum amount of hydrocortisone that could be absorbed from Proctosedyl is 7.5mg per day (assuming maximum recommended dosage). If this amount of hydrocortisone were absorbed, this would have no clinical significance. Even if twice the maximum recommended dosage was used, i.e. 2g of ointment three times daily, the maximum systemic absorption of hydrocortisone would be 15mg per day; still well under the safe level of 30mg per day.

Finally, to assist the pharmacy assistants with handling enquires about Proctosedyl following the reclassification of hydrocortisone in rectal medicines, the following educational strategies will be employed:

- A team of sanofi-aventis pharmacy only sales representatives will be available nationwide to present a Proctosedyl training module for pharmacy assistants and answer questions from the pharmacy assistants on Proctosedyl.
- The key points on Proctosedyl will be communicated to all pharmacies as a mailer as soon as possible after the reclassification announcement.

- Advertising in pharmacy magazines will take place to notify pharmacy assistants of the reclassification, along with instructions for appropriate use of Proctosedyl.

2. Ease of Self Diagnosis for the Condition Indicated

Haemorrhoids and other anorectal conditions are self-limiting conditions and are currently regarded as conditions that are appropriate for self-diagnosis, as is evident from the other therapies already available without pharmacist supervision. Initial diagnosis will have often been confirmed by a Doctor, with subsequent episodes being self-treated by the patient who is familiar with their disease state. However, inadequate relief of their symptoms will encourage patients to seek advice from their doctor and use is restricted to seven days unless advice from a doctor is received otherwise.

The symptoms of haemorrhoids and other anorectal conditions are often readily identifiable by the patient. Haemorrhoids and other anorectal conditions are already regarded as a condition that is appropriate for self-diagnosis as is evident from the other therapies already available without any pharmacist supervision. In most instances patients learn to identify the symptoms. Misdiagnosis would appear unlikely as patients will have usually presented to a medical practitioner for an initial diagnosis.

The availability of a Consumer Medicine Information (CMI) as a package insert would provide sufficient information for the consumer use of Proctosedyl without the intervention of a Pharmacist. The current Australia/New Zealand CMI is included in Appendix 1 and instructs the patient on how to use the product, when the product should not be used, when to stop taking the product, what else should be done i.e. in relation to fluid intake, diet, etc., when to see the doctor and how to store the product. If the committee deems it necessary, the CMI could be further enhanced with additional information.

3. Relative Comparative Data for Like Compounds

The following products, with their approved indications, are currently available as Pharmacy Only products:

- Anusol suppositories (zinc oxide, Peru balsam); uncomplicated haemorrhoids, simple anorectal inflammation.
- Anusol ointment (zinc oxide, Peru balsam); uncomplicated haemorrhoids, simple anorectal inflammation.

The following product, with its approved indication, is currently available as General Sale:

- Pharma witch hazel (Hamamelis extract); symptomatic relief of haemorrhoids

4. Local Data or Special Considerations Relating to New Zealand

Available in other relevant sections.

5. Interactions with Other Medicines

There are no documented interactions with other medicines. There is some concern that hydrocortisone can increase the absorption of other therapies. Even if it were likely, Proctosedyl is for short-term topical rectal use, so any impact would be minimal.

6. Contraindications

The currently registered contraindications on the Proctosedyl Data Sheet (dated 12 May 2003) are as follows:

- Hypersensitivity to hydrocortisone or cinchocaine.
- All steroid preparations are contraindicated in uncontrolled infections, viral infections (eg. herpes simplex, herpes zoster and vaccinia), and when infective pathologies of sexually transmissible diseases occur in the area to be treated.
- When fungal infection is present additional therapy with a topical antimycotic should be instituted.
- In tuberculosis the use of steroids may exacerbate the disease process.

7. Possible Resistance

There are no documented reasons to expect possible resistance.

8. Adverse Effects

8.1 Clinical Trials

A clinical study published in 1988 investigated the safety and efficacy of Proctosedyl ointment and suppositories in 39 patients[vi]. The authors concluded that 'the present study had confirmed the efficacy and lack of side effects [of Proctosedyl]… used for the relief of symptoms associated with second degree haemorrhoids.' The formulation of Proctosedyl used in this study is identical to the New Zealand formulation except it also included the aminoglycoside antibiotic framycetin sulfate and esculin. Although

framycetin sulfate and esculin were originally included in Proctosedyl suppositories and ointment supplied in New Zealand, they were removed in 1992.

8.2 Post-Marketing Experience

The following Periodic Safety Update Reports (PSUR) are provided in Appendix 2-8:

- PSUR # 2 – 14 May 1995 – 25 November 1998
- PSUR # 3 – 26 November 1998 – 25 November 1999
- PSUR # 4 – 26 November 1999 – 24 November 2000
- PSUR # 5 – 25 November 2000 – 10 November 2001
- PSUR # 6 – 11 November 2001 – 10 November 2002
- PSUR # 7 - 11 November 2002 to 11 November 2003
- Five year summary bridging report – 26 November 1999 to 25 May 2004

These contain information on all adverse effects from all sources reported to Aventis Pharma in association with hydrocortisone. Extensive safety data gathered from this exposure have not revealed any new findings, trends or increased reporting frequency for hydrocortisone.

The adverse systemic effects of hydrocortisone are a concern. This concern is usually raised as: 'When applied to particularly large areas, when the skin is broken, or under occlusive dressings, corticosteroids may be absorbed in sufficient amounts to cause systemic effects.[vii]' As haemorrhoids do not occur over large areas the risk of systemic effects due to Proctosedyl is significantly reduced. Additionally, due to the sensitive site of application, it is unlikely that patients will over apply the preparation.

It should be also noted that hypersensitivity reactions to local anaesthetic are generally rare and occur more frequently with agents of the ester type than with amide-type agents[viii]. There appears to be no cross-sensitivity between ester- and amide-type local anaesthetics.

In general practice, products containing hydrocortisone 5mg/g and cinchocaine hydrochloride 5mg/g have excellent safety profiles. Being a topical product, serious side effects would not be expected for Proctosedyl.

8.2.1 Proctosedyl in New Zealand

We requested a Medicine Summary for Proctosedyl from the Centre for Adverse Reactions Monitoring (CARM) to determine the adverse effect profile from local experience in New Zealand. Unfortunately CARM were unable to supply the requested information by the deadline for submission.

8.2.2 Proctosedyl in Australia

Only 16 adverse reactions have been reported by all sources to the Adverse Drug Reaction (ADR) Section of the Therapeutic Goods Administration (TGA) (See Table 3).

Table 3: TGA Medicine summary for Proctosedyl

		Total	Sole Suspected
		16	10
Cardiac disorders	Arrhythmia	1	1
	Myocarditis	1	0
Gastrointestinal disorders	Pruritus ani	2	2
General disorders and administration site conditions	Pyrexia	1	0
Immune system disorders	Hypersensitivity	2	2
Injury, poisoning and procedural complaints	Application site reaction	1	1
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract infection	1	0
Skin and subcutaneous tissue disorders	Urticaria	1	1
	Pruritus	3	2
	Rash	3	1

These included: arrhythmia (6.25%), myocarditis (6.25%), pruritus ani (12.5%), pyrexia (6.25%), hypersensitivity (12.5%), application site reaction (6.25%), upper respiratory tract infection (6.25%), urticaria (6.25%), pruritus (18.75%) and rash (18.75%).

Considering that rash and pruritus are minor, self-limiting conditions, Proctosedyl in practice is an extremely safe medicine.

9. Potential for Abuse or Misuse

There is minimal potential for abuse or misuse, both due to the active ingredients and the nature of the way the product is presented i.e. as a suppository or a tube with an applicator.

A detailed description of the symptoms of haemorrhoids and clear warnings and precautions for the use of this product are provided in the labelling and the CMI to help in correct diagnosis and also to enure safe use without the advice of a pharmacist.

In the event of an incorrect diagnosis, it is unlikely that treatment with the product would aggravate the condition.

Treatment with Proctosedyl is limited to three weeks by the Data Sheet[ix] and only seven days unless a doctor has told the consumer otherwise. This maximum duration of therapy is also reflected on the product label and the CMI.

10. Conclusions

The reclassification of Proctosedyl as a Pharmacy Only medicine, via the reclassification of hydrocortisone in rectal medicines, would allow consumers easier access to a treatment for haemorrhoids and other anorectal conditions that is at least as safe and effective as those products that are currently available as Pharmacy Only or General Sale. The safety and efficacy profile of hydrocortisone and cinchocaine hydrochloride is equivalent to other treatments for haemorrhoids and other anorectal conditions such as Anusol and Pharma witch hazel, which have already been approved for sale as Pharmacy Only or General Sale medicines.

The treatment of haemorrhoids and other anorectal conditions is already regarded as a condition that is appropriate for self-diagnosis. This is evident from the other therapies already available without pharmacist supervision.

Although the current classification for hydrocortisone and cinchocaine hydrochloride allows for consumer access without a prescription, the requirement for pharmacist

supervision prevents it being made available concurrently with other Pharmacy Only treatments for haemorrhoids and other anorectal conditions therapies. This is particularly significant for these indications, in which therapeutic agents are often self-selected by consumers.

Most of the adverse effects experienced with hydrocortisone and cinchocaine hydrochloride are readily recognisable and low to moderate in severity. Substantial international post-marketing experience has been provided, and data gathered from this exposure have not revealed any new findings, trends or increased reporting frequency for hydrocortisone and cinchocaine hydrochloride.

An application to reschedule Proctosedyl, via the rescheduling of hydrocortisone, was submitted in June 2005 to the National Drugs and Poisons Scheduling Committee (NDPSC) in Australia.

In conclusion, we submit that hydrocortisone and cinchocaine hydrochloride does not warrant supervision by a pharmacist when used for the treatment of haemorrhoids and other anorectal conditions and request that hydrocortisone in rectal medicines be reclassified from Restricted to Pharmacy Only.

APPENDICIES

Appendix 1 Current CMI

Appendix 2 PSUR # 2 – 14 May 1995 – 25 November 1998 (attachments not included however are available upon request)

Appendix 3 PSUR # 3 – 26 November 1998 – 25 November 1999 (attachments not included however are available upon request)

Appendix 4 PSUR # 4 – 26 November 1999 – 24 November 2000 (attachments not included however are available upon request)

Appendix 5 PSUR # 5 – 25 November 2000 – 10 November 2001 (attachments not included however are available upon request)

Appendix 6 PSUR # 6 – 11 November 2001 – 10 November 2002 (attachments not included however are available upon request)

Appendix 7 PSUR # 7 - 11 November 2002 - 11 November 2003 (attachments not included however are available upon request)

Appendix 8 Five year summary bridging report – 26 November 1999 to 25 May 2004 (attachments not included however are available upon request)

REFERENCES

[i] MHRA website. Licensing of medicines: Legal status and reclassification of medicines. Last updated 28 April 2005

[ii] Dimmer C, Martin B, Reeves N and Sullivan F. Squatting for the prevention of haemorrhoids? Townsend Letter for Doctors & Patients 1996; 159: 66-70

[iii] A General Practioner group. A general practitioner study to evaluate the efficacy of 'Proctosedyl' ointment in the treatment of acute fissure-in-ano. Br J Clin Prac 1970; 24 (7): 289-91

[iv] Sweetman SC, editor. Martindale: the complete drug reference. 33rd edition. London: The Pharmaceutical Press, 2002: 1039-1061

[v] Coliform Rectal Foam MIMS full prescribing information. eMIMS 01 Apr 2005 – 31 Jul 2005

[vi] Smith RB and Moodie J. Comparative efficacy and tolerability of two ointment and suppository preparations ('Unirod' and 'Proctosedyl') in the treatment of second degree haemorrhoids in general practice. Curr Med Res Opin 1988; 11(1): 34-40

[vii] Sweetman SC, editor. Martindale: the complete drug reference. 33rd edition. London: The Pharmaceutical Press, 2002: 1039-1061

[viii] Dukes MNG. Local Anaesthetics. In: Dukes MNG, editor. Meyler's Side Effects of Drugs, 13th Edition. Elsevier science publishers 1996: 285-297

[ix] Proctosedyl Data Sheet 12 May 2003