Eumovate cream
(Clobetasone butyrate 0.05% w/w)

Proposal
Reclassify Eumovate (clobetasone butyrate) eczema & dermatitis cream from prescription medicine to restricted medicine.

Background to current classification position
Prescription only medicine since registration in NZ in 1976.

Recommendation
Decline

Investigation

1. **The proposed strength, quantity, dosage form, dose and route of administration of the medicine including indication**
   Clobetasone butyrate 0.05 % w/w
   15g tube
   Apply sparingly to affected area twice a day up to 14 days

2. **Approved indication(s)**
   Adults and children aged 10 years and over (use in children under 10 years – only on the advice of a doctor), for short-term treatment and control of patches of eczema and dermatitis including atopic and seborrhoeic eczema and primary irritant and allergic dermatitis.

   [Current indication: Eumovate is suitable for treating atopic eczema, photodermatitis, otitis externa, primary irritant and allergic dermatitis, prurigo nodularis, seborrhoeic dermatitis, and other steroid responsive skin conditions which do not require the use of a more active topical corticosteroid in children and adults. In the more resistant dermatoses, Eumovate may be used as maintenance therapy between courses of one of the more active topical steroids.]

3. **How long has the particular product been marketed?**
   First registered in NZ in April 1976.
   Available on prescription in NZ under the trade name Eumovate cream since 1978.

4. **Overseas regulatory status**
   Prescription only.
   Submitted for reclassification to over-the-counter in Denmark, Finland, Iceland, Ireland, Sweden, Switzerland, UK, (and as a delayed submission, requires complete part II, to Belgium, Germany, Netherlands).

5. **Demonstrated efficacy (i.e. its ability to produce a wanted pharmacological effect at the proposed dosage)**
   Most studies of Eumovate were undertaken in the 70s and 80s, hence are not directly comparable to today's standards. Assessments of potency have

used the vasoconstriction test, which places Eumovate in the moderately potent group.

The largest uncontrolled study was in 1983 in 529 paediatric patients with eczema, treated for up to 28 days. Clinical healing/significant improvement was noted in 62% at 7 days and 84% at 14 days. Side effects were reported in 2.4%, none serious, mostly local redness and burning.

Clobetasone butyrate has been compared with hydrocortisone 1% (the 0.05% strength of clobetasone was statistically more effective), and with alclometasone dipropionate 0.05% (clobetasone was found to be of similar benefit). Clobetasone has also been compared to the more potent steroids with conflicting results, mostly because of small numbers.

6. **Is the product intended for treatment of a minor ailment or symptom readily identifiable by the user, which is capable of rapid spontaneous resolution and for which a medical consultation is not necessary?**
   The product is intended for the treatment of skin ailments such as dermatitis. These are often chronic relapsing conditions, which after initial diagnosis (or response to corticosteroids in the past) should be easily recognisable. Flare-ups often start with itch and redness. However more severe forms can be difficult to manage and prone to superinfection of lesions.

7. **Likelihood of mis-diagnosing, masking or compromising the appropriate medical management of a disease**
   Once eczema or dermatitis has been diagnosed and the condition is relatively mild it is likely that the patient would be able to recognise flare-ups appropriately. Early treatment with topical corticosteroids is likely to limit progression and superinfection.

   The major concern would be mis-diagnosing the presence of infection, in particular fungal infections whereby administration of topical corticosteroid could significantly worsen an infected lesion. There are many other causes of rash and inappropriate use of topical corticosteroid may delay diagnosis.

   Steroid creams are contraindicated in most viral infections of the skin, such as vaccinia, varicella and herpes simplex, also tuberculosis and acne rosacea, perioral dermatitis, fungal skin infections (moniliasis) and ulcerative conditions. The company have identified most of these conditions in their labelling.

8. **Requirement for professional advice from a medical practitioner, dentist or pharmacist**
   A medical practitioner ideally should be involved for the initial diagnosis, because the first presentation of a skin condition may be difficult to diagnose, and may be mistaken for other conditions. Patients may need advice on avoidance of irritants and adequate cutaneous hydration. If the condition is severe oral steroids and antibiotics may be required alongside monitoring of the condition by the doctor. If allergic contact dermatitis is

suspected then the causative allergen needs to be identified and removed, this is done by careful questioning regarding occupational exposures, use of topical and oral medications.

If the dermatitis is extensive or requiring potent steroids to treat, this should be done under medical supervision, as the risk of adverse effects is higher and gaining control of the condition likely to be more difficult.

9. **Requirement for supervision of sale by a pharmacist**

If this product becomes a restricted medicine the pharmacist and patient will need to assess together the requirement for a mild or moderately potent topical steroid. The pharmacist will need to emphasise that Eumovate is more potent than hydrocortisone 1%, that it should be used for flare-ups only and not on a chronic basis, and that for less severe attacks the patient should consider a less potent steroid.

The pharmacist should warn about possible adverse effects (hypersensitivity, skin thinning) and emphasise that if the lesion does not improve within a few weeks or if it worsens then medical help should be sort. A pharmacist may also be able to help identify a skin condition that would be better treated by a doctor.

10. **Proposed labelling and warning statements**

Labelling:

Don't use Eumovate eczema & dermatitis cream:

- If you have ever had a reaction to Eumovate eczema & dermatitis cream or any of its ingredients
- If you are pregnant, may be pregnant or breastfeeding
- If you are using any other topical corticosteroids
- On children under 10
- On broken or infected skin e.g. cold sores, athletes foot, impetigo or thrush
- To treat psoriasis
- To treat acne

In these cases, ask a pharmacist or doctor for advice

The cream should not be used on the following areas:

- On your face
- On private parts
- Between the toes

If your skin does not improve or gets worse within a week, stop using Eumovate eczema &dermatitis cream and see your doctor.

Always read the enclosed leaflet.

11. **Hazard potential, including likelihood for any adverse effects**

The company has submitted a summary of safety data concerning the following areas:

(a) Skin thinning/atrophy potential Much of the data provided is in small studies over 15 years ago. On balance clobetasone butyrate seems to have less thinning potential than the more potent steroids, and may be

equal or slightly greater than 1% hydrocortisone. Many of the studies used treatment durations of at least 4 weeks. This thinning is likely to be reversible on stopping, especially if use of the cream is restricted to 7 days.

(b) Potential for absorption and systemic effects Again the data is not recent. A study in 1976 claimed that the hypothalamic-pituitary-axis (HPA) suppression rebounds to normal within 3 days of stopping steroid application. Ointments are said to cause more HPA suppression than creams. 2 recent studies used the synacthen test: 1995, 14 paediatric subjects, 3-10 days treatment, no suppression; 2000, 35 subjects, less suppression than the potent steroid group. A 1998 study comparing fluticasone propionate 0.05% and clobetasone 0.05%, in the clobetasone group of 9 subjects aged under 8, use for under 4 weeks, showed no change in urinary cortisol. A 1997 study did not find any growth suppressive effects.

(c) Allergy to steroid creams Studies have not shown an increased propensity compared to other steroid creams.

12. **Any relevant data on post-marketing experience**

Between 1997 and 1999, 404000 units of 30g dose pack and 24400 units of 100g dose pack of Eumovate cream and 20000 units of 30g and 14500 units of 100g dose pack of Eumovate ointment were sold in NZ on a prescription medicine basis.

Eumovate has been used extensively - from May 1990 until the end of Feb 2000 approximately 24 million tubes of Eumovate cream and 40 million tubes of Eumovate ointment have been sold worldwide.

The company holds 96 spontaneous reports of adverse events up to 29/2/2000. 48 from the cream and 27 from the ointment, 21 unknown. There are other preparations scalp, eye drops, combination with antibacterial, which were not included. 9 were classed as serious. 80% were skin reactions. 3 reports of Cushing's/ adrenal suppression. (One was in a 52 year old woman who had also taken steroids for Crohn's disease; the other was a male who had used many different types of topical steroids for over 20 years). 1 case of Stevens Johnson, 1 anaphylactoid reaction in an infant, 2 facial oedemas, 1 angioneurotic oedema (negative rechallenge).

CARM holds no adverse event reports up to the end of March 2000.

13. **Potential for inappropriate use of the medicine**

Low if used according to pack instructions. However patients may be tempted to use this steroid chronically believing it to be mild as it is available over the counter. It is not clear from the label nor consumer information that Eumovate is a more potent topical steroid than 1%hydrocortisone.

14. **Potential for abuse of the medicine (e.g. non-therapeutic use of the medicine for self-gratification)**

Nil.

15. **Current availability of other products with similar benefits**

Hydrocortisone 0.5% (pharmacy only) and 1% (restricted medicine) are available over-the-counter in pharmacies.

The MCC is considering an application for alclomethasone 0.05% to be reclassified from prescription medicine to restricted medicine. This is a mild-moderate potency steroid.

All other corticosteroids for dermal application are prescription medicines.

16. **Any public health advantage associated with the availability of these medicines**

Patients with minor conditions will be able to self-manage in the community without needing to see a doctor in the first instance.

17. **Patient convenience including geographical factors**

Increase in patient convenience for those that require more effective steroid than 1% hydrocortisone.

Conclusion

Eumovate is a moderately potent steroid with less potential for adverse effects such as systemic absorption and skin thinning than the potent steroids, but a slightly higher potential than hydrocortisone 1%. Efficacy data dates back to the 70s and 80s. There has been extensive use and relatively few spontaneous adverse reports, so the evidence points to relative safety.

However for a restricted medicine classification the patient and the pharmacist must be able to identify which strength of steroid is required to treat the skin condition. Ideally 1% hydrocortisone should be tried first. If alclometasone becomes available as restricted medicine then this will help those who need a higher strength than hydrocortisone1%. If there is concern that stronger steroids may be required the patient should be referred to a medical practitioner as this no longer constitutes a mild form of the disease.