Ophthalmology Subcommittee of PTAC meeting held 14 May 2010

(minutes for web publishing)

Ophthalmology Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2008*.

Note that this document is not necessarily a complete record of the Ophthalmology Subcommittee meeting; only the relevant portions of the minutes relating to Ophthalmology Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are published.

The Ophthalmology Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;
(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or
(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes were reviewed by PTAC at its meeting on 5 & 6 August 2010, the record of which is available on the PHARMAC website.

Contents

1 Ciprofloxacin 2
2 Carbonic anhydrase inhibitors 2
3 Prostaglandin analogue group 2
4 Alphagan P 3
5 Timolol maleate 3
6 Topical Bevacizumab for Corneal Neovascularisation 3
7 Cyclosporin for Keratoconjunctivitis and Dry Eyes 4
8 Combination glaucoma eye products 6

1 Ciprofloxacin

1.1 The subcommittee commented that the usage of ciprofloxacin eye drops is increasing and this is a concern as overuse would result in increased microbial resistance. Members **recommended** that some form of restriction like a requirement for an endorsement be introduced instead of the current note which reads," For treatment of bacterial keratitis or severe bacterial conjunctivitis resistant to chloramphenicol" which cannot be enforced or audited.

2 Carbonic anhydrase inhibitors

2.1 Members noted that currently there are Prescribing Guidelines in the Pharmaceutical Schedule for the carbonic anhydrase inhibitors:

> Prescribing Guidelines
> *Trusopt, Cosopt and Azopt are subsidised for use as either monotherapy or as an adjunctive agent for the treatment of glaucoma.*
> *Trusopt, Cosopt and Azopt should not be prescribed for a person in whom less expensive first line agents for the treatment of glaucoma are not contraindicated unless:*
>
> *1) that person has previously trialled all other such subsidised agents (Except brimonidine tartrate); and*
> *2) those trials have indicated that that person does not respond adequately to treatment with those other agents.*

2.2 The Subcommittee **recommended** removing the guidelines as they do not reflect current prescribing and removal would be unlikely to result in increased patient numbers if they were removed.

3 Prostaglandin analogue group

3.1 The Subcommittee **recommended** removing the prescribing guidelines (as highlighted below) for the prostaglandin analogue group as they did not reflect current clinical practice:

> Bimatoprost, latanoprost and travoprost are subsidised for use in the treatment of glaucoma as either monotherapy or as an adjunctive agent for patients in whom prostaglandin analogue monotherapy has been ineffective in controlling intraocular pressure.

Bimatoprost, latanoprost and travoprost should not be prescribed for a person in whom less expensive first line agents for the treatment of glaucoma are not contraindicated unless:

1) *That person has previously trialled all other such subsidised agents (beta-blockers, pilocarpine, carbonic anhydrase inhibitors): and*
2) *Those trials have indicated that the person does not respond adequately to treatment with those other agents.*

3.2 Members considered it unlikely that the removal of these guidelines would have any effect on prescribing of prostaglandin analogues in New Zealand.

4 Alphagan P

4.1 The Subcommittee considered that, Alphagan P (brimonidine tartrate 0.15%) and the currently subsidised AFT brand (brimonidine tartrate 0.2%) have similar efficacy but Alphagan P does not contain the preservative benzalkonium chloride which could cause ocular irritation in some patients. Members **recommended** listing both products and Alphagan P could be listed with a Special Authority to target its use to patients who could not tolerate benzalkonium chloride.

5 Timolol maleate

5.1 The Subcommittee considered that a preservative-free or a formulation of timolol maleate without benzalkonium chloride be listed on the Pharmaceutical Schedule. In view of the potentially high cost of such a product, the members **recommended** listing it with a Special Authority restriction.

6 Topical bevacizumab for corneal neovascularisation

6.1 The Subcommittee noted that PHARMAC has received applications for topical bevacizumab for the treatment of corneal neovascularisation through HEC. The members reviewed clinical data presented by PHARMAC staff on this indication. It was noted that all of the trials involved small patient numbers and were not randomised.

6.2 The Subcommittee noted the following tabled trials which suggest that the bevacizumab produces some clinical benefit in this indication. The Koenig trial (Koenig et al (2009) 'Graefes Arch Clin Exp Ophthalmol.' 247(10): 1375-82) showed that topical bevacizumab produced a mean reduction in vascularised area of 61% ($p=0.0182$) and a mean reduction in vessel diameter of 24% ($p<0.005$). The Subcommittee noted the quality of the trials available (Dastjerdi et al (2009) 'Arch Ophthalmol.' 127(4): 381-9 and Kim et al (2008) 'Ophthalmology'. Jun; 115(6):e33-8) is not good enough to make a decision at this point in time. The members noted that standardised large-scale trials would be difficult to carry out due to the diverse and unique nature of the disease. Members considered that not all cases of corneal neovascularisation are the same as they have different underlying causes.

6.3 Members considered that there could be potential long-term usage in some cases as it is for symptom management rather than treating the cause. In some cases like corneal neovascularisation due to trauma, it might be short term usage. The Subcommittee **recommended** seeking the opinion of an anterior eye specialist for further input.

7 Cyclosporin for keratoconjunctivitis and dry eyes

7.1 The Subcommittee noted that there have been 68 CEC/HEC applications for cyclosporin eye ointment/drops for the treatment of atopic and vernal keratoconjunctivitis as well as dry eyes received over the last five years. Members noted that Auckland DHB requested the eye ointment rather than the eye drops be made available on the Discretionary Community Supply (DCS) list. The Subcommittee noted the November 2006 HPAC (Hospital Pharmaceuticals Advisory Committee) meeting minutes and the Subcommittee considered it would be more appropriate to consider listing cyclosporin eye treatment in Section B rather than on the DCS list.

7.2 Members noted that there is currently no registered ophthalmic preparation of cyclosporin in New Zealand. Members noted that Allergan was in the process of registering Restasis (cyclosporin 0.05% ophthalmic emulsion) in Australia which has been registered in the US for the treatment of keratoconjunctivitis sicca.

7.3 The Subcommittee reviewed clinical evidence identified by PHARMAC staff, examining the efficacy of cyclosporin eye preparations for the three indications mentioned above.

Keratoconjuntivitis

7.4 Members concluded that there was evidence that cyclosporin was effective for the treatment of both atopic and vernal keratoconjunctivitis but the evidence for the latter was better. Members considered that clinical evidence was of good quality and included randomised, double-blind controlled trials (Daniell et al (2006) 'Br J Ophthalmol'. Apr; 90(4):461-4, Kilic et al (2006) 'Can J Ophthalmol.' Dec; 41(6):693-8, Spadavecchia et al (2006) 'Pediatr Allergy Immunol.' Nov; 17(7):527-32, Pucci et al (2002) 'Ann Allergy Asthma Immunol. Sept; 89(3): 298-303, Akpek et al (2004) 'Ophthalmology' 111:476-482 and Ebihara et al (2009) 'J Ocul Pharmacol Ther.' Aug; 25(4): 365-72).

7.5 The subcommittee considered that cyclosporin had a similar therapeutic effect to steroids and would be used as a steroid-sparing agent or in conjunction with steroids at a lower steroid dose. Members noted that steroidal eye preparations are currently listed without restriction on the pharmaceutical schedule.

7.6 Members considered that cyclosporin provided additional health benefit and the risks (i.e. eye irritation and infectious corneal complications) were acceptable when compared to steroids. Members noted that no systemic effects were observed.

7.7 The Subcommittee considered that there was no difference in therapeutic effect between cyclosporin ointment and eye drops. Members considered that the ointment would adhere better after application but could be more uncomfortable. Members noted

that there had been no head to head trials of the two preparations and considered that the type of preparation would be more dependent on prescriber and patient choice.

7.8 Members considered that the population which would benefit most from cyclosporin for this indication would be young adults and children. Members noted that the treatment would also be more cost-effective in this group given their age. Members noted that atopic keratoconjunctivitis was more common in Maori/Pacific people.

7.9 The Subcommittee **recommended** that if cyclosporin is listed for these indications, it should be restricted to patients with more severe forms of the disease.

7.10 Members considered that cyclosporin, if listed, would reduce the cost to DHBs by decreasing the incidence of steroid side-effects and the costs associated with managing them. Members noted that ophthalmic steroid use would also decrease.

7.11 The Subcommittee **recommended** that topical cyclosporin should be listed on the Pharmaceutical Schedule with high priority for the treatment of severe forms of atopic and vernal keratoconjunctivitis.

Dry eyes

7.12 The Subcommittee reviewed clinical evidence on the use of cyclosporin eye drops for the treatment of dry eye syndrome. The Subcommittee noted that the trials including Sall et al (2000) 'Ophthalmology' 107 (4): 631-9 and Stonecipher et al (2005) 'Curr Med Res Opin' 21(7): 1057-63 were clinical trials involving a large number of patients. The Sall et al (2000) trial did not reveal a dose-response effect for the 0.05% and 0.1% ophthalmic emulsions. Members noted that the changes from baseline in corneal staining for the cyclosporin emulsions did not reach statistical significance when compared with the vehicle control at most time points during the trial. The improvement with treatment may not be clinically significant given the small effect. The Stonecipher et al (2005) trial showed that cyclosporin 0.05% topical emulsion was effective in reducing symptom severity after 30 and 60 days compared to baseline ($p<0.001$).

7.13 Members noted that the evidence supporting the use of cyclosporin for this indication was fair but the severity of dry eyes in the patients was not clearly stratified in most of the trials. Members considered that trials targeting patients with severe disease would be helpful.

7.14 Members considered that topical cyclosporin would be used in conjunction with topical steroids and artificial tears which are currently fully funded on the pharmaceutical schedule. The use of artificial tears is ongoing for these patients.

7.15 The Subcommittee considered that there were no additional risks associated with topical cyclosporin when compared with topical steroids. Members noted that there was a marginal clinical benefit when using topical cyclosporin.

7.16 The Subcommittee considered that the patient population which would benefit most from topical cyclosporin would be the elderly and individuals with connective tissue disease and rheumatoid arthritis. Members noted however that some of these patients (e.g. lupus erythematosus) would also be on an oral immunosuppressant like cyclosporin.

7.17 The subcommittee **recommended** that topical cyclosporin should be listed with medium priority on the Pharmaceutical Schedule and should be restricted to patients with severe dry eyes and patients with connective tissue disease. The members also **recommended** that PHARMAC seek the opinion of an anterior eye specialist on this issue.

8 Combination glaucoma eye products

8.1 The Subcommittee noted that PHARMAC had previously received applications for listing of combination glaucoma products i.e. Xalacom (latanoprost and timolol maleate), Duotrav (travoprost and timolol maleate) and Ganfort (bimatoprost and timolol maleate). Members noted that PTAC had considered that the combination products were slightly less efficacious than the individual products used concomitantly based on clinical evidence. However, PTAC considered that there was no clinical reason not to list the combination product and **recommended** that the combination products be listed only if cost-neutral to the individual components and taking into account the cost of the generic individual components.

8.2 Members considered that the efficacy of the individual products used concomitantly was slightly better than the combination products. Members noted that compliance is an important issue in glaucoma and the combination products do improve patient compliance with treatment.

8.3 The Subcommittee considered that beta-blockers were more efficacious when used in the morning and it is now common for beta-blockers to be used once-a-day rather than twice daily.

8.4 Members considered that approximately 10% of patients would switch to the combination products if they are listed.

8.5 The Subcommittee **recommended** that combination products be listed only if cost neutral to the individual components and taking into account the cost of the generic individual components.