CSL Biotherapies

Submission for Reclassification

Fucithalmic®

(Fusidic Acid 1% Eye Drops)

From Prescription Medicine to

Restricted Medicine (Pharmacist Only Medicine)

CSL Biotherapies (NZ) Limited
666 Great South Road
Penrose
Auckland 6.

Contents

Part A

1. International Non-proprietary Name

Fusidic Acid

2. Proprietary name

Fucithalmic®

3. Name of company

CSL Biotherapies (NZ) Limited
666 Great South Road
Penrose
Auckland 6.

4. Dose form(s) and strength(s) for which a change is sought

Dose form: Eye Drop

Strength: 10 mg /g

5. Pack size and other qualifications

5 g tubes packaged in a tamper evident carton with accompanying patient information leaflet.

6. Indications for which change is sought

Treatment of bacterial eye infections.

7. Present classification of medicine

Prescription Medicine

8. Classification sought

Restricted Medicine (Pharmacist Only Medicine)

9. Classification status in other countries

OTC: Belgium (2005).

Prescription Medicine: Rest of the world.

Sulfacetamide also an antibiotic is classified as a restricted medicine in New Zealand for ocular use. In the UK, the antibiotic chloramphenicol, was reclassified from Prescription Medicine to Pharmacy Medicine for conjunctivitis in 2005.

10. Extent of usage in NZ and elsewhere

Fucithalmic eye drops have been available in New Zealand since March 1990 and internationally since November 1985.

Since March 1990, New Zealand doctors have written just over one million prescriptions for Fucithalmic.

11. Proposed Labelling and CMI

Refer to Attachment 1 for proposed draft labelling and CMI

12. Proposed warning statements if applicable

- For external use only.
- If symptoms have not improved within a few days or become worse consult your doctor.
- Do not wear contact lenses during treatment and for 24 hours after the end of your treatment.
- Discard after one month from opening.

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

There are no other products containing fusidic acid for ocular use, although other products containing fusidic acid are available.

Part B

INTRODUCTION

Bacterial eye infections are a common minor disorder which tends to be more prevalent in children and the elderly. Antiseptic treatments can be sourced directly from a pharmacy, however the most widely used topical antibiotic treatments are prescription medicines and require a visit to a GP delaying the start of treatment.

Eye disorders such as acute conjunctivitis are usually self-limiting, however with antibiotic treatment the symptoms can be resolved quicker, hence reducing severity, potential spread of infection and infectious complications.

This application seeks approval to change the classification of Fucithalmic Eye Drops, a topical antibiotic used to treat eye infections from prescription medicine to Pharmacist Only Medicine.

BENEFIT TO CONSUMER AND PUBLIC

Speed of Access to Treatment
Fucithalmic as a Pharmacist Only Medicine would improve the speed at which a consumer can begin treatment. Presenting to a GP to obtain a prescription is a timely process. Removing the GP step improves the speed of access to treatment which in turn reduces severity, potential spread of infection and improves the time to remission. Pharmacists already have experience and tools to diagnose eye infections. In addition, moving patients with a so called minor condition to community pharmacy frees up GPs for more serious aliments.

Speed of Remission
Most cases of eye infections, specifically bacterial conjunctivitis, resolve spontaneously[1]. However treatment with antibiotics can significantly improve rates of early clinical remission and microbial remission[2].

Convenience
Compared to other treatments which can require up to 6-8 applications, Fucithalmic only needs to be administered twice daily. The convenience of only two applications per day facilitates improved compliance rates.

EASE OF DIAGNOSIS BY PHARMACIST

The diagnosis of acute conjunctivitis by a pharmacist is already an established practice as guidelines for diagnosis are available by the Pharmacy Guild of New Zealand for treatment with sulphacetamide[3]. The Guild has also published referral guidelines for pharmacists regarding patients presenting with eye infections[4]. Furthermore the Pharmacy Council of New Zealand Guidelines and Protocols support the capability of pharmacists to diagnose and treat minor acute conditions such as bacterial conjunctivitis with Pharmacist Only Medicines[5].

Medicines indicated for treatment of eye infections such as sulfacetamide and propamidine isethionate (including dibromopropamidine isethionate) are currently available OTC indicating the established practice of pharmacist diagnosis. In the last year a combined total of over 110 000 units of these medicines were sold[6] supporting the experience of diagnosis at a Pharmacist level.

In 2005 the antibiotic chloramphenicol, also used for eye infections, was reclassified to Pharmacy Medicine in the UK. Comprehensive practice guidelines for pharmacists have been developed[7] and CSL are more than happy to work with the Pharmacy Guild to develop similar guidelines for diagnosis and treatment with Fucithalmic eye drops.

The risk of misdiagnosis of viral conjunctivitis is just as likely to occur whether a patient presents to a GP or pharmacist for initial diagnosis. Rietveld et al[11] noted that GPs do not feel able to differentiate between a bacterial and non bacterial cause of conjunctivitis. Furthermore it was noted in the New Zealand Family Physician Journal that despite contrary reports in ophthalmologic texts, there is no research supporting the usefulness of any signs or symptoms which differentiate viral from bacterial conjunctivitis[8].

When the UK reclassified chloramphenicol from Prescription to Pharmacy Medicine the issue of misdiagnosis was raised. An article in The Pharmaceutical Journal dismissed this issue due to the experience which pharmacists already have dealing with conjunctivitis, and the fact that diagnosis is straight forward[9].

Guidelines and algorithms are already in place from the Pharmacy Guild of New Zealand to minimise the potential for a pharmacist to misdiagnose other, sometimes more serious, conditions (Refer References 3 and 4).

COMPARATIVE DATA FOR LIKE COMPOUNDS

Current treatments available in New Zealand.

The treatments currently available in New Zealand for eye infections are listed in table below.

Table 1

Product	Classification	Type	Dosage regimen
Fucithalmic	***Prescription***	***Antibiotic***	***1 drop twice daily.***
Chloramphenicol	Prescription	Antibiotic	1-2 drops every 2-6 hours.
Chlormyxin	Prescription	Antibiotic	1 drop every 2 hours awake for the first 2 days, 1 drop every 4 hours awake for the next 5 days
Ciprofloxacin	Prescription	Antibiotic	1 drop every 2 hours awake for the first 2 days, 1 drop every 4 hours awake for the next 5 days
Gentamicin	Prescription	Antibiotic	1-2 drops, 4 hourly
Tobramycin	Prescription	Antibiotic	1-2 drops, 4 hourly
Sulfacetamide	Restricted Medicine	Antibiotic	1-2 drops 2-3 hourly
Framycetin	Prescription	Antibiotic	Initially 2 drops 2 hourly reducing to 2-3 drops 3 times daily.
Propamidine and dibromopropamidine isethionate	Pharmacy Medicine	Antiseptic	1-2 drops 4 times daily

As indicated in Table 1 the dosage regimen of Fucithalmic is much simpler than comparative antibiotic and antiseptic treatments.

Sulfacetamide is the only antibiotic which is currently available without a prescription in New Zealand.

Comparative Data

Chloramphenicol is currently the most widely used antibiotic treatment for eye infections in New Zealand[6] with approximately 300,000 units (drops and ointment) sold in the last 12 months compared to 52,000 units of Fucithalmic. Normann et al[10] evaluated the clinical and bacteriological effects of Fucithalmic (fusidic acid 1%) and chloramphenicol 5% in 456 neonates with acute bacterial conjunctivitis. No difference in effectiveness was noted, however treating neonates with Fucithalmic was easier than chloramphenicol due to reduced applications.

In the Netherlands chloramphenicol is listed in practice guidelines as the first choice ocular antibiotic, however in practice, fusidic acid is the most frequently prescribed antibiotic for acute infectious conjunctivitis[11]. The reasons noted for this practice are the reduced applications required for fusidic acid as well as the lack of potential serious adverse events.

Jackson et al[12] compared the efficacy, safety and acceptability of Fucithalmic (1% fusidic acid) and 0.3% tobramycin drops in 484 patients. Results showed there was no significant difference in efficacy between the treatment groups. Compliance was similar in older patient between the treatment groups, however for those aged 2-9 years compliance was significantly better in the Fucithalmic group. Fucithalmic treatment was rated as being convenient or very convenient by significantly more patients ($p<0.001$) compared to the tobramycin group. The authors concluded that the clinical effect of Fucithalmic as well as the convenient twice daily dosage regimen establishes this antibiotic as first-line treatment for suspected acute bacterial conjunctivitis.

Results of a randomised controlled study (n=181) assessing fusidic acid vs. placebo highlight the self limiting nature of acute bacterial conjunctivitis[11]. At 7 days the cure rates with fusidic acid and placebo were similar however statistical limitations could not exclude clinically relevant treatment differences. Bacterial eradication rates however, showed larger differences with 76% after 7 days in the treatment group compared to 41% in the placebo group. No clinically serious adverse events were noted in either treatment arms.

JUSTIFICATION OF PATIENT POPULATION AND TREATMENT DURATION

Patient Population
Based on the Pharmacy Guild counselling guide and algorithm (References 3 and 4) the patient population proposed will exclude infants less than 2 months old due to the potential of other more serious conditions in this sub-group. Hence as per current guidelines pharmacists will be advised to refer infants less than 2 months to their GP. In addition, the CMI (package insert) will reflect that this medicine is not to be given to infants less than 2 months unless directed by your doctor.

Treatment Duration
Fucithalmic is required to be administered 48 hours after the eye returns to normal as indicated in the datasheet. To ensure that patients only treat for a maximum of 7 days, as treatment post 7 days has limited benefit, the labelling will advise the patient to see their doctor if symptoms have not resolved within 5 days.

SAFETY PROFILE

Fucithalmic Eye Drops has a very favourable safety profile. The only contraindication noted in the datasheet[13] is hypersensitivity, and the only adverse event in addition to hypersensitivity is transient stinging after application. In addition, no interactions are noted. In the most recent PSUR[14] covering December 2005 to November 2006, it was estimated that over 8.8 million treatment doses had been prescribed during this period. During this time only 24 case reports representing 36 adverse drug reactions were reported which resulted in no new safety concerns and no change to the prescribing information. It should also be noted that this period covered the OTC distribution of Fucithalmic in Belgium.

RESISTANCE

The occurrence of resistance with fusidic acid has been reported and documented. In a study conducted by Rietveld et al[11], it was noted that 66% of the cultured species were resistant to fusidic acid. However despite the higher resistance rates compared to other ocular antibiotics, fusidic acid was just as effective.

In 2006, Diagnostic Medlab reported fusidic acid resistance in New Zealand as 23%[15]. It is not anticipated that the proposed change in classification will affect the general trend of increasing resistance with antibiotics. Patients presenting with eye infections will still be required to be assessed by a health professional for diagnosis prior to being prescribed treatment. Due to the difficulties in differentiating between viral and bacterial conjunctivitis noted above, pharmacist diagnosis is highly unlikely to contribute to an increase in inappropriate antibiotic use compared to GP diagnosis. Hence the potential for increased resistance still remains whether fusidic acid is a prescription or restricted medicine.

CONCLUSION

Fucithalmic eye drops are a convenient, safe and effective medicine for use in eye infections.

Fucithalmic has an excellent safety profile making it an appropriate for sale under the supervision of a Pharmacist.

The risks of inappropriate use are very small, as the proposed indication is currently diagnosed and treated by a Pharmacist. The risk of misuse is no different if prescribed by a GP or sold under the advice from a Pharmacist.

As a Pharmacist Only Medicine, Fucithalmic will provide consumers with the benefit of a quick trip to the pharmacy instead of a pre-scheduled GP appointment together with the convenience of twice daily administration.

Appendices

Appendix 1 – Proposed draft labelling including CMI.

References

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[2] Sheikh, Aziz and Hurwitz, Brian. Topical antibiotics for acute bacterial conjunctivitis: Cochrane systematic review and meta-analysis update. British Journal of General Practice, December 2005 p. 962-964.

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[5] Guidelines and Protocols. Protocol for the Sale and Supply of Pharmacist Only Medicines for Chronic Conditions. Pharmacy Council of New Zealand. Available from: www.pharmacycouncil.org.nz [accessed 20 July 2007].

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[7] Practice Guidance: OTC Chloramphenicol Eye Drops. Royal Pharmaceutical Society of Great Britian. www.rpsgb.org [accessed 23 July 2007]

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[10] Normann et al. Treatment of acute neonatal bacterial conjunctivitis: a comparison of fucidic acid to chloramphenicol eye drops. Acta Opthalmol Scand. 2002 Apr; 80(2):183-7.

[11] Reitveld et al The treatment of acute infectious conjunctivitis with fusidic acid: a randomised controlled trial. British Journal of General Practice, December 2005 p. 924-930.

[12] Jackson et al. Treatment of acute bacterial conjunctivitis: 1% fusidic acid viscous drops vs. 0.3% tobramycin drops. Can J. Opthalmol. 2002 Jun; 37(4) p. 228-237.

[13] Fucithalmic Datasheet dated September 2002.

[14] Fucithalmic PSUR - 1 December 2005 to 30 November 2006.

[15] Clinicians – Antibiotic Susceptibility. Summary of Susceptibility Testing for 2006. Diagnostic Medlab. www.dml.co.nz [accessed 22 July 2007].