OPTREX INFECTED EYES EYE OINTMENT

PL 00062/0052

UKPAR

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Optrex Limited a Marketing Authorisation (licence) for the medicinal product Optrex Infected Eyes Eye Ointment (PL 00062/0052) on 30th July 2007. The application was submitted as a simple abridged application in association with a reclassification application, and claims to be a generic medicinal product of, and equivalent to, the approved product, Chloramphenicol Eye Ointment (PL 12762/0038), a prescription only medicine (POM) licence held by Goldshield Pharmaceuticals and granted in February 2002.

Optrex Infected Eyes Eye Ointment is a pharmacy only (P) medicine used to treat bacterial infections that affect the front surfaces of the eye. It contains the active ingredient Chloramphenicol, which belongs to a group of medicines called antibiotics, and is used in the treatment of bacterial infections that affect the front surfaces of the eye. The most common type of infection in this area is called acute bacterial conjunctivitis. The symptoms are the white part of one or both eyes will be red and / or the eyelids will be red or swollen. A sticky discharge may make the eye difficult to open in the morning and the eye may feel gritty or irritated.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of using Optrex Infected Eyes Eye Ointment as a pharmacy only medicine outweigh the risks, hence a Marketing Authorisation has been granted.

OPTREX INFECTED EYES EYE OINTMENT

PL 00062/0052

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product Optrex Infected Eyes Eye Ointment (PL 00062/0052) to Optrex Limited on 30th July 2007. This application was submitted as a reclassification simple abridged application according to article 10(c) of Directive 2001/83/EC, as amended, and claims to be a generic medicinal product and equivalent to the approved product, Chloramphenicol Eye Ointment (PL 12762/0038), a POM licence held by Goldshield Pharmaceuticals and granted in February 2002.

The Marketing Authorisation Application was assessed separately and in parallel with the reclassification application. The proposed Marketing Authorisation (MA) is identical to the reference MA, apart from some differences which relate directly to the reclassification. The reclassification of the product, from POM to P status has been assessed and deemed satisfactory, following review by the Commission on Human Medicines.

No new data was submitted nor was it necessary for this simple application, as the data is identical to that of the previously granted cross-reference product.

Optrex Infected Eyes Eye Ointment contains the active ingredient choramphenicol, a broad spectrum antibiotic, and is used in the treatment of bacterial infections that affect the front surfaces of the eye. The most common type of infection in this area is called acute bacterial conjunctivitis. The symptoms are the white part of one or both eyes will be red and / or the eyelids will be red or swollen. A sticky discharge may make the eye difficult to open in the morning and the eye may feel gritty or irritated. Chloramphenicol is a potent inhibitor of bacterial protein synthesis, and exerts its effects by interfering with the transfer of activated amino acids from soluble RNA to ribosomes.

PHARMACEUTICAL ASSESSMENT

LICENCE NO:	PL 00062/0052
PROPRIETARY NAME:	Optrex Infected Eyes Eye Ointment
ACTIVE(S):	Chloramphenicol 1%
COMPANY NAME:	Optrex Limited
E.C. ARTICLE:	10(c) of Directive 2001/83/EC, as amended
LEGAL STATUS:	P

1. INTRODUCTION

Crookes Healthcare have submitted a reclassification application for Chloramphenicol 1% Eye Ointment to be available as a Pharmacy medicine for the treatment of acute bacterial conjunctivitis in adults and children aged two years and over, with a pack size of 4G. The proposed name is Optrex Infected Eyes Eye Ointment and the proposed dosage is:

'Apply a small amount (~ 1cm) to the affected eye *either* at night (if drops used during the day) or 3 – 4 times daily (if eye ointment used alone), for 5 days.'

The reclassification application is linked to a simple abridged application, also submitted by Crookes Healthcare. The product is claimed to be a generic medicinal product of a POM licence, Chloramphenicol Eye Ointment (PL 12762/0038) held by Goldshield Pharmaceuticals and granted in February 2002.

The present POM product is indicated for the treatment of bacterial conjunctivitis caused by chloramphenicol susceptible organisms.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed product name is Optrex Infected Eyes Eye Ointment. This is consistent with the name of the eye drop product, Optrex Infected Eyes Eye Drops which is already available as a Pharmacy product. The proposed name is acceptable.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Optrex Infected Eyes Eye Ointment contains the active ingredient chloramphenicol. Topical chloramphenicol is the treatment of choice for minor ocular infections. The approved pack size for the POM product is 4G and the applicant is proposing no change. The applicant considers that, as the dosage for the eye ointment is unchanged from the POM product, a change in pack size is not considered necessary. This is acceptable.

The ointment is supplied in a screw cap tube containing 4g. The proposed shelf-life (4 years unopened, 28 days opened) and storage conditions (Do not store above 25°C) are consistent with the details registered for the cross-reference product.

2.3 Legal status

On approval, the product will be available as a pharmacy only medicine.

2.4 Marketing authorisation holder/Contact Persons/Company

The proposed Marketing Authorisation holder is:

Optrex Limited,
1 Thane Road West,
Nottingham, NG2 3AA

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers

The proposed manufacturing site is consistent with that registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification

The proposed finished product specification is in line with the details registered for the cross-reference product.

2.9 Drug substance specification

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance

No materials of animal or human origin are included in the product. This is consistent with the cross reference product.

3. EXPERT REPORTS

The applicant has provided non-clinical and clinical expert reports written by suitably qualified experts.

4. PRODUCT NAME & APPEARANCE

See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product, a smooth uniform translucent greasy ointment.

5. SUMMARY OF PRODUCT CHARACTERISTICS

The proposed SmPC is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON

PIL

The patient information leaflet has been prepared in-line with the details registered for the cross-reference product. The current version of the Patient information leaflet has not yet been user tested. The applicant has justified this on the basis that it is consistent with the leaflet for Optrex Eye Drops, approved previously. A user test is in progress for both products and the updated versions will be submitted for approval, as appropriate.

Carton and blister

The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS

The data submitted with the application is acceptable. The proposed MA is identical to the reference MA, apart from differences which relate directly to the associated reclassification application.

The applicant, in the Pharmaceutical Expert Report, has confirmed that the chemical and pharmaceutical data are identical to the cross-reference product. The FPS and the MAA form have been updated. There are no changes to the product itself and no pharmaceutical issues to address. A Marketing Authorisation should be granted.

RECLASSIFICATION APPLICATION

An expert report in support of the pharmacy indication for chloramphenicol 1.0% eye ointment has been provided. A safety and efficacy summary has also been provided.

The applicant proposes the POM to P reclassification of chloramphenicol eye ointment for the treatment of acute bacterial conjunctivitis for adults, children aged 2 years and over and the elderly. The proposed posology is a small amount of ointment to be applied to the affected eye *either* at night (if drops used during the day) or 3 – 4 times daily (if eye ointment used alone). The course of treatment is 5 days. The proposed posology is in line with the BNF.

Chloramphenicol eye drops are already available as a P medicine for the treatment of bacterial conjunctivitis. The applicant considers that making chloramphenicol eye ointment available as a P product would provide a choice for patients to use the pharmaceutical form, which suits their individual needs. The ointment has longer residence time in the eye, making it particularly suitable for night-time use. The drops cause less blurring of vision and for a shorter time than the ointment, which makes them more suitable for day-time use. Individuals may find either the drops or the ointment easier to administer. Some people find the taste of the drops unpleasant. The ointment has the benefit of reducing the tendency for the eyelids to stick together overnight. The ointment does not need to be stored in the fridge whereas the drops do.

1 EFFICACY

The applicant states that the clinical data to support the current clinical practice for treating acute bacterial conjunctivitis with topical antibiotics is taken from two major reviews (Cochrane and Clinical Evidence). All the studies considered in these reviews are randomised controlled trials and include topical antibiotics but not chloramphenicol.

The Cochrane review (2000) assessed whether antibiotics had a significant benefit in the treatment of acute bacterial conjunctivitis. Three randomised controlled trials were analysed in the review, which involved selected specialist care patients and used different broad-spectrum topical antibiotics, but not chloramphenicol. One of the studies involved children, whilst the two others involved adults. The review concluded that bacterial conjunctivitis is usually a self-limiting condition as clinical remission (cure or significant improvement) occurred by days two to five in 64% of those treated with placebo (99% CI: 57-71%). Treatment with antibiotics was associated with significantly better rates of early clinical remission (RR at day 2-5: 1.31; 99% CI: 1.11-1.55) with only a suggestion that this was maintained for late clinical remission (RR day 6-10: 1.27; 99% CI: 0.92-1.74). Improved rates of microbiological remission were seen in those treated with antibiotics (RR at day 2-5: 1.71; 99% CI: 1.32-2.21; RR at day 6-10: 1.71; 99% CI: 1.26-2.34).

Clinical Evidence has reviewed the clinical data on the treatment of bacterial conjunctivitis with topical antibiotics. It was concluded that empirical treatment with topical antibiotics in people with suspected bacterial conjunctivitis were considered likely to be beneficial.

Since the completion of these reviews a new randomised clinical trial has been published by Rose et al. This study compared the efficacy of chloramphenicol 0.5% eye drops with placebo in children with a clinical diagnosis of conjunctivitis, and did not find any

difference in clinical cure in children treated with either chloramphenicol or placebo. The applicant states that the results of this study confirm that acute bacterial conjunctivitis is self-limiting; therefore, this condition is appropriate for self-medication. The study found a statistically non-significant higher rate of clinical cure from day 2 to 7 and a significantly greater bacterial eradication rate with chloramphenicol (40%) compared with placebo (23%). The applicant concludes that taking into account the existing body of evidence the results of the Rose study do not change our understanding of the clinical progression of acute infective conjunctivitis nor do they alter the reasons for treatment with chloramphenicol. Immediate treatment with topical antibiotic is therefore justified to reduce the risk of transmission, to facilitate an earlier return to work, school or childcare, to prevent secondary bacterial infections with viral conjunctivitis, to reduce the small risk of complications.

Another study by Rietveld et al was carried out in a primary care setting involving adult patients and investigated the efficacy of fusidic acid compared to placebo. At day 7, cure rates in the treatment and the placebo group were similar. In culture positive patients the treatment effect tended to be stronger.

Sheikh et al updated the original Cochrane review by including the studies by Rietveld and Rose . This updated meta-analysis shows that topical antibiotics seem to be of slight benefit in improving early (day 2-5) clinical (RR: 1.24, 95% CI: 1.05-1.45) and microbiological (RR: 1.77, 95% CI: 1.23-2.54) remission, with these benefits being reduced, but still persisting for late (day 7-10) clinical (RR: 1.11, 95% CI: 1.01-1.21) and microbiological (RR: 1.56, 95% CI: 1.17-2.09) remission.

The applicant claims that immediate treatment with topical antibiotic is justified to reduce the risk of transmission and to prevent secondary bacterial infections. Although this is a reasonable argument, no clinical data have been provided to show the efficacy of chloramphenicol eye ointment in preventing the spread of conjunctivitis. Furthermore, the proposed indication is the treatment of acute bacterial conjunctivitis.

2 SAFETY AND CONSIDERATION OF POM CRITERIA

The EC Directive on the *Classification for Supply of Medicinal Products for Human Use* (2001/83/EC) classifies medicines into those subject to medical prescription and those not subject to prescription control. Prescription control is required for medicines which meet the following criteria:

- a direct or indirect danger exists to human health, even when used correctly, if utilised without medical supervision
- there is frequent incorrect use which could lead to a direct or indirect danger to human health
- contain a substance the activity and/or the side effects of which require further investigation
- are normally prescribed by a doctor to be administered parenterally.

This assessment is directed at the first three criteria; the last is not relevant since the product is not to be administered parenterally.

2.1 First POM criterion:

- A direct or indirect danger exists to human health, even when used correctly, if utilised without medical supervision

The applicant states that the most frequent adverse effects of chloramphenicol ointment are likely to be hypersensitivity reactions including rashes, fever and angioedema. Chloramphenicol may cause serious and sometimes fatal adverse effects. The most serious adverse effect is bone marrow depression.

2.1.1 Chloramphenicol-induced aplastic anaemia

Chloramphenicol-induced bone marrow depression can take two forms. One of them is reversible, dose-related depression, the second one is non-dose related, irreversible aplastic anaemia. Case reports suggested association between topical chloramphenicol use and aplastic anaemia. However, epidemiological data do not show an increased risk with use of topical chloramphenicol above that observed in the general population.

Assessor's Comment:
The issue of bone marrow toxicity has been discussed by CSM when POM to P reclassification of chloramphenicol eye drops was considered. It has been accepted that the risk of aplastic anaemia and blood dyscrasias in association with topical chloramphenicol use is low. Since family or personal history of blood dyscrasias seems to be a predictor of the condition, these patients should be excluded from the pharmacy supply.

2.1.2 Resistance

Clinical data show very low levels of resistance to chloramphenicol in the main pathogens causing acute bacterial conjunctivitis (*Staphylococcus aureus, Streptococcus pneumoniae and Haemophilus influenzae*).

The applicant claims that there is a low potential for the development of resistance to ocular chloramphenicol, since the target pathogens are sensitive despite extensive prescription use for many years and pharmacy provision is not expected to increase use. The very high local concentrations should prevent emergence of resistant clones and there is a very limited systemic use of chloramphenicol

Assessor's Comment:
The issue of resistance to chloramphenicol has previously been considered by CSM. It was accepted that the local concentrations of chloramphenicol in the eye in topical use far exceed the minimal inhibitory concentration of the three above-mentioned pathogens (8μg/ml) and the resistant mutants. In these circumstances the development of chloramphenicol resistance even in patients with poorer compliance is unlikely. However, any potential risk of developing resistance should be weighed against the marginal benefit of topical antibiotic treatment of acute conjunctivitis.

Additionally, an increase in the usage after the reclassification may lead to an increase in resistance. The applicant should monitor ophthalmic chloramphenicol usage in the pharmacy setting.

2.1.3 Safety related to misdiagnosis

The applicant states that conjunctivitis is accepted as a suitable indication for self-diagnosis under the supervision of the pharmacist. Other common causes of conjunctivitis are allergic, viral and chlamydial, but these may be differentiated from bacterial conjunctivitis by the presenting symptoms. Other causes of 'red eye' are accompanied by pain and/or disturbance of vision. Patients with these symptoms will be referred to a doctor.

Assessor's Comment:
The issue of misdiagnosis has previously been discussed by CSM. It was accepted that a combination of symptoms and signs (presence of glued eye and lack of history of conjunctivitis and itching) provides optimal discrimination between bacterial, viral and allergic conjunctivitis. Incorporating these signs in the pharmacy protocol will minimise the risk of mis-diagnosis.

Contact lens wearers should be referred to their doctor or a contact lens practitioner. In contact lens users other than the most common pathogens can cause bacterial conjunctivitis, which can lead to serious consequences if the treatment is inappropriate.

2.2 Second POM criterion:

- There is frequent incorrect use, which could lead to a direct or indirect danger to human health

2.2.1 Safety related to overdose, misuse or abuse

The applicant states that chloramphenicol ointment does not have any effects that might lead to widespread misuse. It is not addictive and due to the presentation, dosage and limited pack size it is unlikely that it would be misused.

2.3 Third POM criterion:

- It is a substance the activity and/or side effects of which require further investigation

The applicant states that the safety of chloramphenicol ointment does not require further investigation.

3. PHARMACY PROTOCOL AND TRAINING

The applicant has not yet submitted a training manual. A manual for the eye drops is available and it will be important to update this, highlighting the differences between the eye drops and ointment so the pharmacist can give suitable advice to patients to help choose the most appropriate product for their circumstances. A suitable manual should be provided.

4. PRODUCT INFORMATION

The proposed SPC, patient information leaflet and label are supplied.

Changes to the product information have been made to reflect the non-prescription use of the product.

4.1 SPC

The SPC has been updated to reflect the non-prescription use of the product.

4.2 Patient Information Leaflet

The PIL has been updated in line with the approved SPC.

Following their meeting to discuss the reclassification application, the Commission of Human Medicines advised that the leaflet should be standardised to be consistent with other chloramphenicol 1% eye ointment products available as pharmacy medicines.

4.3 Labelling

The PIL has been updated in line with the approved SPC. In addition:

- Posology has been included.
- Warnings related to seek medical advice if symptoms do not improve after 2 days and seek immediate medical advice at any time if symptoms worsen should be included.

5. DISCUSSION

This application proposes that chloramphenicol eye ointment be reclassified from POM to P for the treatment of acute bacterial conjunctivitis for adults (including the elderly) and children 2 years and over.

In 2004 the CSM considered the POM to P reclassification of chloramphenicol 0.5% eye drops and advised that the product could safely be supplied without prescription for the treatment of acute bacterial conjunctivitis. Chloramphenicol eye ointment is considered a useful addition to the eye drops to improve patients' choice.

Since the reclassification of chloramphenicol eye drops the results of a clinical study by Rose et al have been published, which found that children presenting with infective conjunctivitis in primary care did not need treatment with an antibiotic. The results of this study have been included in a meta-analysis with four other studies. It was concluded that overall topical antibiotic treatment of acute bacterial conjunctivitis is of benefit in improving early clinical and microbiological remission rates. Another study included in the meta-analysis involved children and found that topical antibiotic treatment was effective in this treatment population.

Although acute infective conjunctivitis is a self-limiting condition, it is currently treated by topical antibiotics in primary care. It is considered that there is an advantage of antibiotic treatment of infective conjunctivitis to increase the rate of resolution of bacterial infection, which reduces the risk of transmission. However, no clinical data are available to support this latter claim.

There are very low levels of resistance to chloramphenicol in the main causative pathogens. Since the local concentrations of chloramphenicol in the eye in topical use far exceed the minimal inhibitory concentration of these pathogens, the development of chloramphenicol resistance is unlikely. However, any potential risk of developing resistance should be weighed against the marginal benefit of topical antibiotic treatment.

Topical chloramphenicol has an established safety profile. Pharmacists have already been involved with the management of conjunctivitis and chloramphenicol eye drops may be supplied as a pharmacy medicine to suitable patients, identified using an agreed protocol. They are trained to differentiate between the various causes of "red eye". In case of serious conditions where there is pain and disturbed vision the pharmacist would refer the patient to the doctor.

6. ADVICE SOUGHT

The Commission's advice was sought as to whether chloramphenicol 1.0% eye ointment for the treatment of acute bacterial conjunctivitis may safely be supplied without prescription under the following conditions:

- Used for the treatment of acute bacterial conjunctivitis in adults and children aged 2 years and over
- Eye ointment
- Maximum strength 1%
- Maximum pack 4G.

The Commission was also asked to endorse the proposal to:

- ask the applicant to put forward proposals to monitor chloramphenicol usage in the pharmacy setting.

7. CHM CONSIDERATION

On 20th July 2006 the Commission considered applications for pharmacy availability of chloramphenicol eye ointment. A number of general issues associated with the applications were considered and the following points were agreed:

- The risk-benefit balance of chloramphenicol eye ointment for the treatment of acute bacterial conjunctivitis for adults and children aged 2 years and over continues to be favourable.
- There were no new issues of concern in relation to the development of antimicrobial resistance.
- Making chloramphenicol eye ointment available without prescription, in addition to the eye drops, is of benefit to the patient.
- The posology should be in line with the BNF, i.e. the ointment should be applied either at night if the eye drops are used during the day or 3-4 times daily if the eye ointment is used alone.
- Suitable training material should be developed to support pharmacy provision of both the eye drops and ointment, as appropriate; it should also be tailored for pharmacy assistant staff as well as pharmacists.

In order to help avoid the possibility of antimicrobial resistance emerging, the Commission also advised the applicant should put forward proposals to monitor chloramphenicol usage in the pharmacy setting. The applicant should report any overall increase in total usage (both prescription and OTC) to the Agency, together with risk minimisation plans regarding potential changes to resistance patterns.

The commission concluded that the product could be made available for non-prescription supply, under the conditions stated in Section 6.

8. CONSULTATION

A consultation exercise was implemented, whereby a document proposing pharmacy availability of chloramphenicol eye ointment was issued to various advisory bodies and organisations. The document was circulated on 28 November 2006, with a deadline for comments of 4 January 2007.

There were 21 responses, of which two made no comment. Of the responses with comments, 18 were generally in favour and 1 was not.

9. DISCUSSION FOLLOWING CONSULTATION

Overall, the responses to consultation have been favourable. In the light of comments received, the following proposals were implemented

i. The SPC and patient information leaflet should be amended to include an option for contact lens wearers to seek advice from either their doctor or optometrist prior to use of chloramphenicol eye ointment. The applicant should also be asked to incorporate this advice into the information for the eye drop products as soon as possible.
ii. The pharmacist protocol for referral should be updated from “severe pain” to “any significant pain in the eye”.
iii. Suitable mechanisms to monitor the impact of overall volumes of chloramphenicol used, both OTC sales and prescribed.

10. CONCLUSION

The proposed reclassification for pharmacy availability of chloramphenicol eye ointment in packs of 4g is acceptable, subject to implementation of the points i. – iii outlined above.

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PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied with this Marketing Authorisation application and none are required for an application of this type.

OVERALL CONCLUSIONS AND RISK BENEFIT ASSESSMENT

QUALITY

The data for this application is consistent with that previously assessed for the cross-reference product and as such has been judged to be satisfactory.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY

Chloramphenicol is a well known drug and has been widely used as a broad spectrum antibiotic for many years. The applicant has demonstrated Optrex Infected Eyes Eye Ointment to be a generic medicinal product of the cross-reference product, Chloramphenicol Eye Ointment (PL 12762/0038).

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with chloramphenicol is considered to have demonstrated its therapeutic value. The risk benefit is therefore considered to be positive.

OPTREX INFECTED EYES EYE OINTMENT

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation application on 03/11/2005
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 14/11/2005
3	Advice was sought in June 2006 from the Commission on Human Medicines with regards to the Reclassification application. The Commission met on 20th July 2006 and issued their advice
4	A consultation exercise was implemented and the consultation document was issued on 28th November 2006, with a deadline for responses of 4th January 2007
5	Following assessment of the application the MHRA requested further information on 21/03/2007. The applicant responded to the MHRA's requests, providing further information on 27/03/2007
6	Following assessment of the response the MHRA requested further information on 29/03/2007. The applicant responded to the MHRA's requests, providing further information on 02/04/2007 and 04/04/2007
7	Following assessment of the response the MHRA requested further information on 04/04/2007. The applicant responded to the MHRA's requests, providing further information on 05/04/2007, 13/04/2007 and 02/05/2007
8	The application was determined on 30/07/2007

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STEPS TAKEN AFTER AUTHORISATION

Date submitted	Application type	Scope	Outcome
16/08/2007	Label and leaflet self-certification	Correction of a typographical error on the leaflet relating to the statement of active content.	Application granted 05/09/2007

OPTREX INFECTED EYES EYE OINTMENT

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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Optrex Infected Eyes Eye Ointment
When sold by Boots The Chemist, the name will be Boots Pharmacy Antibiotic Eye Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Chloramphenicol 1.0% w/v.
Each 1 gram of ointment contains 10mg chloramphenicol
For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Eye ointment.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Treatment of acute bacterial conjunctivitis.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Topical administration to the eye only.

Adults, children aged 2 years and over and elderly

The recommended dose is a small amount of ointment (~ 1cm) to be applied to the affected eye(s). The ointment should be applied either at night if eye drops are used during the day, or 3 to 4 times a day if eye ointment is used alone

The pharmacist will advise on the most suitable treatment. Treatment should continue for 5 days even if symptoms improve.

4.3 CONTRAINDICATIONS

Chloramphenicol eye ointment must not be administered to:
Patients who have a history of hypersensitivity to chloramphenicol or to any other ingredient of the ointment.
Patients who have experienced myelosuppression during previous exposure to chloramphenicol.
Patients with a family history of blood dyscrasias.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Chloramphenicol is absorbed systemically from the eye and systemic toxicity has been reported (see section 4.8).

In severe bacterial conjunctivitis and in cases where infection is not confined to the conjunctivae, the topical use of chloramphenicol should be supplemented by appropriate systemic treatment. Therefore, the patient should be referred to seek medical advice.

The use of topical chloramphenicol may occasionally result in overgrowth of non-susceptible organisms including fungi. If any new infection appears during treatment, the patient should be referred to the doctor.

Prolonged or frequent intermittent topical application of chloramphenicol should be avoided since it may increase the likelihood of sensitisation and emergence of resistant organisms.

Do not use for more than 5 days without consulting your doctor.

The label will state:
If symptoms do not improve within 48 hours talk to your doctor
Seek further immediate medical advice at any time if symptoms worsen
Do not use if you are allergic to chloramphenicol or any of the ingredients
Discard any remaining eye ointment after the five day course of treatment

For external use only.

Keep all medicines out of the sight and reach of children.

Patients should be referred to a doctor if any of the following apply:
Disturbed vision
Any significant pain within the eye
Photophobia
Eye inflammation associated with a rash on the scalp or face
The eye looks cloudy
The pupil looks unusual
Suspected foreign body in the eye

Patients should also be referred to their doctor if any of the following in his/her medical history apply:
Previous conjunctivitis in the recent past
Glaucoma
Dry eye syndrome
Eye surgery or laser treatment in the last 6 months
Eye injury
Current use of other eye drops or eye ointment

If you wear contact lenses, seek advice either from your optometrist, contact lens practitioner or doctor before you use this product. You should not wear your contact lenses during the course of treatment. If you wear soft contact lenses do not start wearing them for at least 24 hours after you have finished using the eye ointment.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Bone marrow depressant drugs

4.6 PREGNANCY AND LACTATION

The safety of chloramphenicol eye drops during pregnancy and lactation has not been established. As this product is for sale without prescription it is not recommended for use during pregnancy.

In view of the fact that chloramphenicol may appear in breast milk, use of the product during lactation should be avoided.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Blurring of vision can occur with the ointment and patients should be warned not to drive or operate machinery unless their vision is clear.

4.8 UNDESIRABLE EFFECTS

Transient burning or stinging sensations may occur with the use of chloramphenicol eye ointment. Serious side effects include hypersensitivity reactions that may manifest as angioneurotic oedema, anaphylaxis, urticaria, fever, and vesicular and maculopapular dermatitis. Treatment must be discontinued immediately in such cases.

Bone marrow depression, including the idiosyncratic type of irreversible and fatal aplastic anaemia that is recognised to occur with systemic therapy, has been reported in association with topical administration of chloramphenicol.

4.9 OVERDOSE

In view of the relatively small amount of chloramphenicol in chloramphenicol eye ointment, overdosage with this product is unlikely to constitute a hazard.
If irritation, pain, swelling, lacrimation or photophobia occur after undesired eye contact, the exposed eye(s) should be irrigated for at least 15 minutes. If symptoms persist after this, an opthalmological examination should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Chloramphenicol is a potent inhibitor of bacterial protein synthesis, and exerts its effects by interfering with the transfer of activated amino acids from soluble RNA to ribosomes.

Escherichia coli, Haemophilus influenzae, Staphyloccus aureus, Streptococcus haemolyticus, Morax anenfeld, Klebsiella/Enterobacter species and others.
Entrobacteriaceae are variably resistant while Pseudomonas and Mycobacteria are usually resistant.

5.2 PHARMACOKINETIC PROPERTIES

Chloramphenicol enters the aqueous humour following topical application.

Chloramphenicol is widely distributed in body tissues and fluids: it enters the CSF, giving concentrations of about 50% of those existing in the blood even in the absence of inflamed meninges; it diffuses across the placenta into the fetal circulation, into breast milk, and into the aqueous and vitreous humour of the eye. Up to about 60% in the circulation is bound to plasma protein. The half-life of chloramphenicol has been reported to range from 1.5 to 4 hours; the half-life is prolonged in patients with severe hepatic impairment and is also much longer in neonates. Renal impairment has relatively little effect on the half-life of the active drug, due to its extensive metabolism, but may lead to accumulation of the inactive metabolites. Chloramphenicol is excreted mainly in urine.

The absorption, metabolism, and excretion of chloramphenicol are subject to considerable interindividual variation, especially in infants and children, making monitoring of plasma concentrations necessary to determine pharmacokinetic in a given patient.

5.3 PRECLINICAL SAFETY DATA

Preclinical safety data does not add anything of further significance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Liquid Paraffin
Polyethylene in Mineral Oil (Plastibase 30W)

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

4 years

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25°C.

Although the shelf life once opened is 28 days, patients will be advised to discard the medicine after a 5 day course of treatment.

6.5 NATURE AND CONTENTS OF CONTAINER

4 gm laminated tube fitted with an ophthalmic nozzle and screw cap

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

None

7 MARKETING AUTHORISATION HOLDER

Optrex Limited
1 Thane Road West
Nottingham
NG2 3AA

8 MARKETING AUTHORISATION NUMBER(S)

PL 00062/0052

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
30/07/2007

10 DATE OF REVISION OF THE TEXT
30/07/2007

OPTREX INFECTED EYES EYE OINTMENT
PL 00062/0052

PRODUCT INFORMATION LEAFLET

Optrex

CRE 90352

INFECTED EYES

Eye Ointment

Chloramphenicol

Please read all of this leaflet carefully before you start using your eye ointment. Keep this leaflet. You may need to read it again.

What is in the pack?
The name of your medicine is Optrex Infected Eyes Eye Ointment.
The ointment contains 1% w/w chloramphenicol, which is equivalent to 10mg of chloramphenicol per 1 gram of ointment.
Also contains liquid paraffin and polyethylene in mineral oil.
Each pack contains 4g of the ointment.
Optrex Infected Eyes Eye Ointment belongs to a group of medicines called antibiotics.
Licence holder: Optrex Limited, 1 Thane Road West, Nottingham NG2 3AA, UK.
Manufactured by Patheon UK Limited, Kingfisher Drive, Covingham, Swindon SN3 5BZ, UK.
PL00062/0052

What is your medicine for?
Optrex Infected Eyes Eye Ointment is a topical ointment for administration to the eye only, it contains an antibiotic called chloramphenicol. When chloramphenicol is given in eye ointment, it is used to treat bacterial infections that affect the front surfaces of the eye. The most common type of infection in this area is called acute bacterial conjunctivitis. When you have acute bacterial conjunctivitis the white part of one or both of your eyes will be red and /or your eyelids will be red or swollen. There will be a sticky discharge, which can make the eye difficult to open in the morning and the eye may feel 'gritty' or 'irritated'. Chloramphenicol eye ointment is not suitable for treating eye infections that have spread to the deeper layers of the eye coverings or into the fluid within the eyeball. Antibiotic tablets or injections are needed to treat these deeper and more serious infections.

Before using your medicine
Optrex Infected Eyes Eye Ointment is recommended for use in adults, children aged 2 years and over and the elderly. It is recommended that a child below the age of 2 years with an eye infection should be seen by a doctor.
If you or any members of your family have ever had problems with your bone marrow making blood cells, you should not use the eye ointment.

Do not use this product if:
- You are allergic to chloramphenicol or any of the ingredients shown under 'What is in the pack?'
- You have ever had problems with your blood (in particular very low numbers of blood cells) during a previous course of treatment with chloramphenicol
- You or your family have a history of blood problems.

If any of the following statements apply to you, do not use this product and seek the advice of your doctor:
- Your eyesight is affected (loss of sight, reduced vision, blurred vision or halos around lights)
- You are experiencing pain within the eye
- Your eye has suffered a blow or other injury
- Your eye is inflamed and you have a rash on the scalp or face
- The pupil of your eye looks unusual or your eye looks cloudy
- If your eyes are sensitive to light
- You have (or think you have) a foreign body in your eye which has not been removed
- You have recently had an eye infection
- You suffer from or have ever suffered from glaucoma or dry eye syndrome
- You are currently using any other eye ointment or eye drops
- You have had eye surgery or laser treatment in the last 6 months.

If you wear contact lenses, seek advice either from your optometrist, contact lens practitioner or doctor before you use this product. You should not wear your contact lenses during the course of treatment. If you wear soft contact lenses do not start wearing them for at least 24 hours after you have finished using the eye ointment.

You must tell your pharmacist before using the product if the answer to any of the following questions is YES.
Are you pregnant, or planning to become pregnant?
Are you breastfeeding?
Are you taking any other medicines?
Do you suffer from any other eye problems?

After using this ointment you may temporarily get blurred vision. Do not drive or operate machinery until your vision is clear.
If in doubt, talk to your pharmacist or doctor.

How to use your medicine
To be used in the eye(s) only.
Check the tube seal is not broken before first using the eye ointment.
1. Wash and dry your hands.
2. Remove the cap. Take special care that the nozzle of the tube does not touch your eye, the skin around your eye or your fingers.
3. Use a mirror, this will help you see what you are doing.
4. Place the nozzle of the tube close to your eye. Gently pull the lower eyelid downwards and look up.
5. Squeeze the tube gently and apply about 1cm of ointment to the space between the lower eyelid and the eye.
6. Close your eye for a moment.
7. When both eyes are to be treated, repeat steps 3-6.
8. Replace the cap securely after use.

The dose is a small amount of ointment (approx 1 cm) to be applied to the affected eye(s).
- If you are using drops during the day and the ointment at night - apply the ointment at night, before going to bed. The course of treatment is 5 days.
- If you are using just the ointment - apply 3 to 4 times a day. The course of treatment is 5 days.

Your pharmacist will advise which is the most suitable treatment for you.
You should consult your doctor if symptoms do not improve within 48 hours.
You should seek further immediate medical advice at any time if symptoms worsen.
Do not use Optrex Infected Eyes Eye Ointment for more than 5 days without consulting your doctor.
- Do not breathe on or touch the nozzle of the tube.
- Do not touch the eyes or eyelids with the nozzle of the tube.
- Do not share your eye ointment with anyone else.
- Keep using this eye ointment for 5 days. Do not stop just because you feel better - this could make your condition worse.
- Discard any remaining eye ointment after the 5 day course of treatment.

Optrex Infected Eyes Eye Ointment is for external use only.

If you forget to use your ointment:
Have you only just missed a dose and is it a long time before the next dose is due?
If YES, put in the missed dose of ointment straight away.
Did you miss the dose sometime ago and is it nearly time for your NEXT dose?
If YES, just put in the next dose of ointment at the right time.
Never double up on the next dose to make up for the one you have missed.

After using your eye ointment
Some people may get one or more of these side effects. Some effects happen straight away but do not last long - others may only happen after several days of use.
- blurred vision, or mild burning or stinging when you put the ointment in (these should fade quickly)
- allergic effects such as itching, or rashes (get medical help straight away if you get a severe reaction with swelling or breathing problems)
- changes in the blood (anaemia) leading to severe tiredness or easy bruising.

If you do not feel well, or are worried about your health, talk to a pharmacist or doctor.

Storing your medicine
Replace the cap securely after use.
Do not store above 25°C.
Keep this and all medicines out of the sight and reach of children.
If your doctor tells you to stop treatment, return any left over ointment to your pharmacist.
Do not use after the 'use by' date shown on the carton and end of the tube.

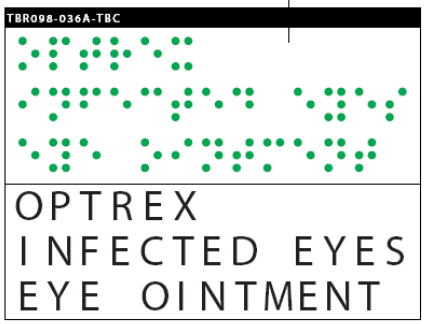
Remember - this medicine is for YOU. Never give it to other people - it may harm them, even if their symptoms appear to be the same.
If you have any questions or are not sure about anything, ask your pharmacist or doctor. They can obtain additional information about this medicine if necessary.

Leaflet prepared August 2007

CRE 90352

OPTREX INFECTED EYES EYE OINTMENT
PL 00062/0052

LABELLING



BHI ARTWORK PANEL

Trident Ref/Action:	TR19509 / F
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Brand Platform:	Eye Health & Beauty
Sub Platform:	Pharmacy Strength Care
Sub Brand:	Infected Eyes
Format:	Ointment
Delivery:	Ointment
Pack Size:	4g
Country:	UK
Cad Cam Ref (Cutter):	O-Crt-Path-036A-24x19x91.5mm
Component Code:	LJBZ4
Date Created:	23/01/2006
Date Modified:	03/04/2007
Printer:	Tubilux
Print Process(es)	Litho N/A
Material/Substrate:	Carton Board - Silver
Bulk Code (if applicable):	N/A
Updated:	N/A
Retail Barcode Type:	EAN 8
Number:	50065660
Edgemark Position:	TBC
Pharma No:	N/A N/E: N/A
Artist Name:	Jennifer Smith
BHI Contact:	Kieran Gamble

Cutter
Braille

Inks:
PANTONE 485 C
PANTONE 286 C
PANTONE 2925 C
PANTONE Process Cyan C
PANTONE 1495 C
Printed White

TRIDENT

Please note that any low resolution paper Canon colour copies associated with this job should be referred to for content, layout and colour separation only.

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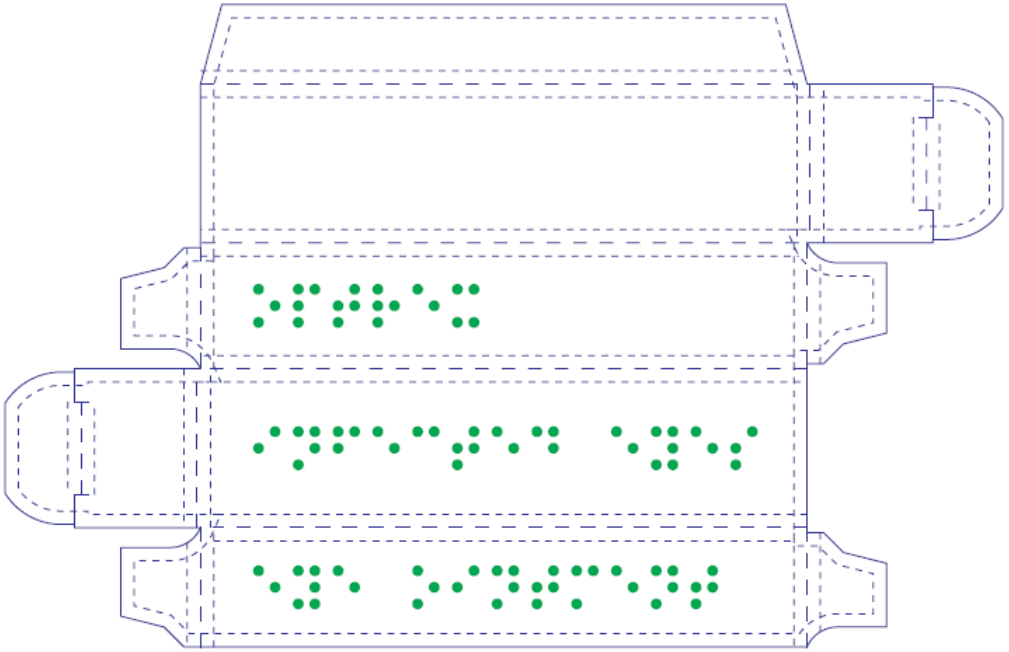

TBR098-036A-TBC

OPTREX
INFECTED EYES
EYE OINTMENT

BHI ARTWORK PANEL

Trident Ref/Action:	TR19509 / F
Brand:	Optrex
Brand Platform:	Eye Health & Beauty
Sub Platform:	Pharmacy Strength Care
Sub Brand:	Infected Eyes
Format:	Ointment
Delivery:	Ointment
Pack Size:	4g
Country:	UK
Cad Cam Ref (Cutter):	O-Crt-Path-036A-24x19x91.5mm
Component Code:	LJBZ4
Date Created:	23/01/2006
Date Modified:	03/04/2007
Printer:	Tubilux
Print Process(es)	Litho N/A
Material/Substrate:	Carton Board - Silver
Bulk Code (if applicable):	N/A
Updated:	N/A
Retail Barcode Type:	EAN 8
Number:	50065660
Edgemark Position:	TBC
Pharma No:	N/A N/E: N/A
Artist Name:	Jennifer Smith
BHI Contact:	Kieran Gamble

Cutter
Braille

Inks:
PANTONE 485 C
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PANTONE Process Cyan C
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TRIDENT

Please note that any low resolution paper Canon colour copies associated with this job should be referred to for content, layout and colour separation only.

BARCODE INFO (Non-Automated)

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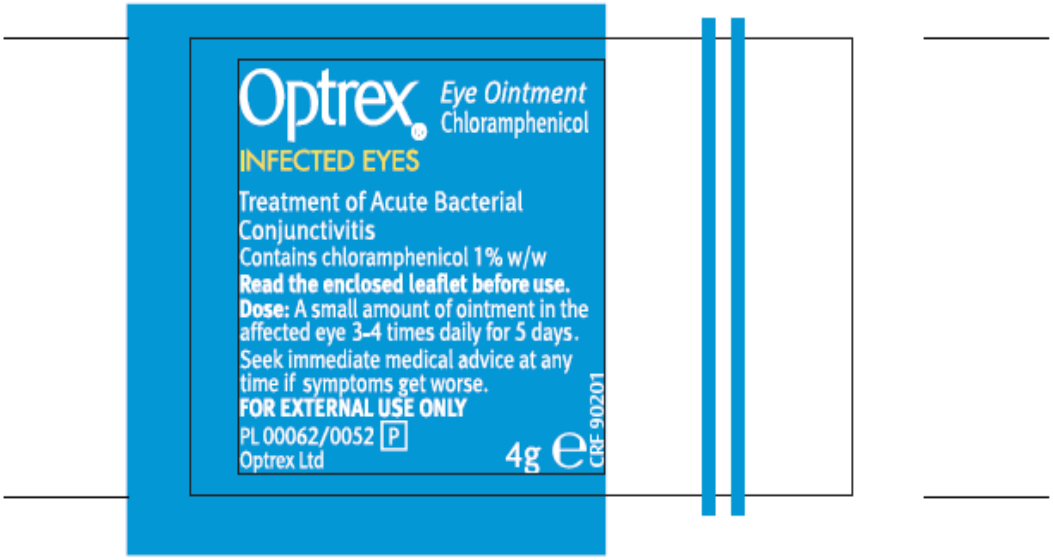
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