Sandwell and West Birmingham Hospitals NHS
NHS Trust

GUIDELINES FOR THE MANAGEMENT OF FUNGAL KERATITIS

Policy authors	Mr A.Aralikatti, Consultant Ophthalmic Surgeon Mr A Sharma, Consultant Ophthalmic Surgeon Dr N Wickramasinghe, Consultant Microbiologist Dr C Jamieson, Pharmacy Team Leader - Antimicrobial Therapy Mrs L.Titcomb, Lead Ophthalmic Pharmacist With input from: Mr M Quinlan, Consultant Ophthalmic Surgeon
Accountable Executive Lead	Clinical Director Ophthalmology Surgery B
Approving body	Governance Group – Surgery B Drugs and Therapeutic Committee
Policy reference	SWBH/BMEC/Ophth/039

Overall purpose of the guideline
To ensure safe guidance is in place for the management of suspected fungal keratitis

Principle target audience
Ophthalmology clinical staff

Application
The guideline applies to all patients

Scope
The guideline applies to all patients

National Guidance incorporated
n/a

DOCUMENT CONTROL AND HISTORY				
Version No	**Date Approved**	**Date of Implementation**	**Next Review Date**	**Reason for Change e.g. full rewrite, amendment to reflect new legislation, updated flowchart, etc.**
1	23-05-2011	23-05-2011	23-05-2014	Non-availability of econazole 1% eye drops
2	17-07-2013	17-07-2013	17-07-2016	
3	25-10-2016	November 2016	November 2019	Non-availability of clotrimazole 1% eye drops

1.0 Background

Fungal infection of the cornea is rare and is usually seen in the context of trauma (frequently organic in nature), tissue devitalization, or immunosuppression, including topical corticosteroid use. Other predisposing factors include a hot humid climate, agricultural work, dry eye or a neurotrophic cornea. Fungal infective agents can be divided into moulds (filamentary fungi) and yeasts. Of the former, *Fusarium* and *Aspergillus* commonly infect the cornea, and of the latter, *Candida* is a common infective organism.

2.0 Clinical Signs

In the case of yeast infections, the corneal involvement is often localized, with a 'button' appearance, an expanding stromal infiltrate and relatively small epithelial ulceration. Filamentary fungal infections initially produce a feathery, branching pattern. A severe anterior uveitis and hypopyon may develop. As the condition progresses, the characteristic patterns may disappear, and the appearance closely resembles an advanced bacterial keratitis.

3.0 Management

All patients suspected of microbial keratitis should have a proper corneal scrape for full microbiological analysis, including urgent Gram stain. This should include bacterial, fungal and viral isolation (*Herpes simplex*) and special media for *Acanthamoeba* if clinically indicated. See protocol for corneal scrapes.

A careful history should be taken to exclude systemic disease, e.g. autoimmune disease, immunosuppression (spontaneous or iatrogenic) or evidence of other opportunistic infection. Consider systemic work-up: full blood count, urea and electrolytes, liver function tests, vasculitic screen, blood cultures if pyrexical, chest X-ray and electrocardiogram.

Most patients with severe microbial keratitis need admission to hospital for intensive antimicrobial treatment.

As soon as relevant specimens have been taken, intensive topical therapy should be prescribed on the in-patient prescription chart:

3.1 Topical therapy

- Due to manufacturing problems, the availability of topical antifungal eye drops is limited. The following options are suggested, but prescribers are advised to consult the Eye Pharmacy at BMEC to check on availability of these eye drops prior to prescribing. Should the likelihood of any delay in obtaining supplies be advised by pharmacy, prescribers should consult the duty microbiologist for advice on alternative agents or routes of administration.

- Patients should be treated initially empirically with voriconazole 1% eye drops (unlicensed, non-formulary, held in stock and available from Eye pharmacy), given hourly day and night for the first 24–48 hours. Authorisation for the use of a non-formulary drug is obtained by contacting an officer of the Drug & Therapeutics committee.

- If a preservative free preparation is required, amphotericin 0.15% eye drops preservative-free (unlicensed, non-formulary) may be used following approval by DTC.

  NB. amphotericin 0.15% eye drops preservative-free are available from Liverpool Pharmacy Manufacturing Unit on request but are not held in stock and have a short shelf life. Implementation of therapy will be delayed until pharmacy obtains stocks.

- Cycloplegic drops should be given: atropine 1% eye drops twice daily or cyclopentolate 1% eye drops twice daily.

- Topical antifungal therapy can be gradually tapered based on clinical response. Treatment is usually required for many weeks.

3.2 Intraocular therapy

Intracameral amphotericin (10 micrograms in 0.1 ml, unlicensed use) may be given in cases where treatment response is poor, particularly in the presence of a hypopyon. This should be performed after an anterior chamber washout, with the washings being sent for microbial culture.

Where a secondary endophthalmitis develops, intravitreal amphotericin (5–10 micrograms in 0.1 ml, unlicensed use) may be given, preceded by a vitreous biopsy where possible.

In cases of resistance to amphotericin, voriconazole may be used at a dose of 10 to 50 micrograms in 0.1ml (non-formulary) for both intracameral and intravitreal injection, unlicensed uses. (Voriconazole is restricted, contact Microbiology for advice).

Intrastromal voriconazole 50 micrograms in 0.1ml (non-formulary, unlicensed use). has been used in resistant cases. (Voriconazole is restricted, contact Microbiology for advice).

3.3 Systemic treatment

This is not obligatory, but should be strongly considered for cases of secondary endophthalmitis and penetrating keratomycosis, and given in addition to topical therapy. Adjunctive systemic therapy should be considered in all immunosuppressed hosts. It should be given in liaison with microbiologists and physicians. Liver and renal function must be monitored before and during treatment.

3.3.1 Yeast infection

Oral fluconazole should be given for 7–14 days where candidal infection is suspected or proven. A dosage of 50–100 mg once daily is required for those with a keratitis who are immunosuppressed. Where a secondary endophthalmitis is present, 400 mg once daily should be given. Liver function must be monitored before and during treatment, on a weekly basis.

Intravenous flucytosine (non-formulary) may be considered for invasive yeast infections, at a dosage of 200 mg/kg daily in four divided doses, for no more than 7 days. Contact Microbiology regarding plasma concentration monitoring.

3.3.2 Mould infection

Voriconazole is first-line systemic treatment for mould infections, but is restricted requiring microbiology approval. Voriconazole is also indicated for fluconazole-resistant *Candida* spp. For patients > 40 kg body weight this may be given orally (400 mg twice daily for 2 doses, then 200 mg twice daily, increasing if required to 300 mg twice daily), or intravenously (6 mg/kg twice daily for 2 doses, then 4 mg/kg twice daily). Children 2–12 years, oral (suspension recommended – the suspension is non-formulary) 200 mg every 12 hours; intravenous - 7 mg/kg every 12 hours (reduced to 4 mg/kg every 12 hours if not tolerated).

3.4 Antifungal therapy in pregnancy and lactation

Topical administration of clotrimazole, amphotericin and voriconazole is not considered to be harmful in pregnant and lactating women. There are however contraindications to the use of systemic antifungal therapy in pregnancy and lactation. It is therefore imperative to contact the microbiologists before starting systemic therapy for this patient group.