GUIDELINES FOR THE MANAGEMENT OF FUNGAL KERATITIS
## POLICY PROFILE

### Overview

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<td>Accountable Executive Director</td>
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<td>Lead Ophthalmic Pharmacist</td>
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### Consultation and referencing

| Key stakeholders consulted/involved in the development of the policy |
| Complementary Trust documents for cross reference |

### Approvals and monitoring

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<th>Divisional Governance Group – Surgery B Drugs and Therapeutic Committee</th>
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### DOCUMENT CONTROL AND HISTORY

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<tr>
<td>1</td>
<td>23-05-2011</td>
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<td>23-05-2014</td>
<td>e.g. full rewrite, amendment to reflect new legislation, updated flowchart, etc.</td>
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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: FBC, U+Es, LFTs, vasculitic screen, blood cultures if pyrexial, CXR and ECG.

Most patients with severe microbial keratitis need admission to hospital for intensive antimicrobial treatment. Some mild cases can be managed as an outpatient. The decision on whether to admit or not must be left to clinical judgement of the managing doctor.

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

3.1 Topical therapy

- Patients should be treated initially empirically with econazole 1% eye drops preservative-free, given hourly day and night for the first 24–48 hours. If
there is no response to econazole then non-formulary drugs may have to be used. Authorisation for the use of a non-formulary drug is obtained by contacting an officer of the Drug & Therapeutics committee.

- If the patient has existing ocular surface disease, amphotericin 0.15% eye drops preservative-free (non-formulary) may be used.

NB. Amphotericin 0.15% eye drops preservative-free are available from Moorfields Pharmaceuticals who prepare them one weekly on a Wednesday and delivered on a Thursday. Orders must be received by Thursday of the previous week for a Thursday delivery.

(Voriconazole eye drops 1% (non-formulary) have been used in the treatment of fungal keratitis, often with good effect. It is however not routinely available. Therefore, with Consultant permission, enquiries regarding availability should be made to pharmacy)

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

- Topical steroids should be added at the discretion of a senior Ophthalmologist – usually starting 48 hours after topical antifungal therapy: dexamethasone sodium phosphate 0.1% eye drops preservative-free, one drop daily.

3.2 Intraocular therapy

Intracameral amphotericin (10 micrograms in 0.1 ml) 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) 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. Contact Microbiology for advice.

Intrastromal voriconazole 50 micrograms in 0.1ml (non-formulary). has been used in resistant cases.

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 & 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 50–100mg daily is required for those with a keratitis who are immunosuppressed. Where a secondary endophthalmitis is present, 200–400mg 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 4 divided doses, for no more than 7 days. Contact Microbiology re plasma concentration monitoring.

3.3.2 Mould infection

Voriconazole is first-line systemic treatment for mould infections, Contact microbiology before using it. 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 econazole, 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.
Flowchart for the Management of Fungal Keratitis

Suspect Fungal Keratitis if risk factors
- Ocular trauma (organic)
- Immunosuppression
- Ocular surface disease
- Dry Eyes

Take a detailed history
- Check for systemic disease
- Immunosuppression (topical steroid use)
- Other opportunistic infections

Undertake slit-lamp examination for clinical signs suggestive of fungal keratitis
- Corneal epithelial defect + stromal infiltrates with feathery branching pattern
- Satellite lesions
- Hypopyon

Perform early and adequate corneal scrapes
- Urgent Gram stain
- Culture for bacteria, fungus and virus (HSV)
- Culture for Acanthamoeba if clinical suspicion

Admit patient and fill in-patient chart for intensive topical treatment

Consider systemic work-up
- Check for diabetes
- FBC, U&E, LFT

Topical antifungal therapy
- Initial treatment
  - Econazole 1% pres free eye drops hourly day and night for 48 hrs + atropine 1% eye drops or cyclopentolate 1% eye drops twice daily

If co-existing ocular surface disease
- Treatment required for many weeks and tapered based on clinical response
  - Replace econazole with amphotericin 0.15% pres free eye drops hourly (non-formulary – obtain authorisation from DTC)

If response to treatment is poor
- Consider voriconazole 1% eye drops (non-formulary)
  - Consider anterior chamber washout + intracameral amphotericin injection (10 micrograms in 0.1 ml). Send the washout for culture

If resistance to Amphotericin
- Consider intracameral voriconazole injection (10 to 50 micrograms in 0.1 ml) (non-formulary)
- Consider intrastromal voriconazole injection (50 micrograms in 0.1 ml) (non-formulary)

If secondary endophthalmitis
- Consider vitreous biopsy + intravitreal amphotericin injection (5 to 10 micrograms in 0.1 ml)

Adjunctive systemic antifungal treatment
- In cases of secondary endophthalmitis, penetrating keratomycosis and immunosuppressed patients.
- Liaise with Microbiologist and Physician
- Monitor liver and renal function

1. For yeast infection
- Oral fluconazole for 7-14 days:
  - Immunosuppressed patients (50 to 100 mg daily)
  - Secondary endophthalmitis (400mg daily)

2. For filamentous infections (Moulds)
- Intravenous flucytosine (non-formulary) for up to 7 days:
  - Penetrating keratomycosis (200 mg/kg daily in 4 divided doses)
  - Monitor plasma concentrations

Patients >40 kg
- Oral voriconazole: (400 mg twice daily for 2 doses, then 200 mg twice daily, increasing to 300 mg twice daily) OR
- Intravenous voriconazole: (6 mg/kg bd for 2 doses, then 4 mg/kg twice daily)

Children 2 to 12 years:
- Oral voriconazole (suspension): (200 mg twice daily)
- Intravenous voriconazole: (7 mg/kg every 12 hours, reduced to 4 mg/kg every 12 hours if not tolerated)

Guidelines for the management of fungal keratitis