CHAPTER 18

EYE DISORDERS

For many eye conditions early specialist consultation and advice is required. To mitigate delays in referral it is recommended that electronic consultation methods are utilised with transmission of appropriate images so that appropriate treatment can be initiated before referral.

18.1 CONJUNCTIVITIS

H10.9

DESCRIPTION

Inflammation of the conjunctiva, usually due to allergy or infection (viral or bacterial).
Conjunctivitis is usually bilateral. Other causes of a red eye are often unilateral.
The condition is self-limiting and usually resolves within 14 days.

GENERAL MEASURES

If it is due to an infection, counsel on the importance of:

» frequent hand washing,
» using separate linen, towels and washcloths, and
» avoiding direct contact with infected material or individuals.

Contact lenses should not be worn if conjunctivitis is present or during a course of topical therapy. Soft lenses should not be worn within 24 hours of instilling eye drops containing the preservative benzalkonium chloride.

18.1.1 CONJUNCTIVITIS, VIRAL

B30.1+ (H13.1*)

DESCRIPTION

Viral conjunctivitis is the commonest cause of infective conjunctivitis. It may be unilateral but often progresses to bilateral. Adenovirus is the commonest viral conjunctivitis, however other viral causes of conjunctivitis present in the same way.

Clinical features:

» Viral conjunctivitis may be associated with an upper respiratory tract infection.
» A burning, sandy, or gritty feeling in the eyes.
» Morning crusting followed by watery discharge.
» Preauricular lymphadenopathy may be present.
» The cornea, iris, and pupil are completely normal with normal visual acuity.

The condition is self-limiting, but eye irritation and discharge may get worse for the first week depending on the specific virus. Duration varies from 3-5 days to 2-3 weeks before resolution.

MEDICINE TREATMENT

- Sodium chloride 0.9%, eye washes or irrigation.

If sodium chloride 0.9% is not available, use cooled boiled water/sterile water.

- Oxymetazoline 0.025%, ophthalmic drops, instil 1 drop 6 hourly for a maximum of 7 days to reduce redness of eyes.

18.1.2 CONJUNCTIVITIS, ALLERGIC

See Primary Health Care Standard Treatment Guidelines and Essential Medicine List; Section 18.1.1 Conjunctivitis, allergic.

18.1.3 CONJUNCTIVITIS, BACTERIAL (NON-GONOCOCCAL)

H10.0

DESCRIPTION

Clinical features:

» It may be either unilateral or bilateral.
» There is matting of lashes in the morning with the eyelids stuck shut.
» There is a mucopurulent discharge throughout the day.
» The eyelids may be swollen.

MEDICINE TREATMENT

- Immediate irrigation of the eyes with sodium chloride 0.9%.

During the day:

- Chloramphenicol 1%, ophthalmic ointment 6 hourly for 7 days.

LoE: IVb[i]

OR

- Fluoroquinolone ophthalmic drops as second-line treatment (i.e. poor response to chloramphenicol or contra-indication/drug interactions with chloramphenicol) e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instil 1 drop 2 hourly for 2 days.
  - Then reduce frequency to 1 drop 4 hourly during waking hours, for 5 days.

LoE: IIb[ii]

REFERRAL

No response to treatment.

18.1.4 CONJUNCTIVITIS, BACTERIAL (GONOCOCCAL)

H10.0

Hyperacute bacterial conjunctivitis involves rapid onset and progression of conjunctivitis and is often caused by *N. gonorrhoeae*. **Gonococcal conjunctivitis requires immediate referral to an ophthalmologist to prevent corneal involvement and potential perforation.**

Clinical features:

» Hyperpurulent discharge.
» Diminished visual acuity.
» Eye tenderness.
» Swollen lymph nodes.

For conjunctivitis of the newborn, See Primary Health Care Standard Treatment Guidelines and Essential Medicine List; Section 18.1.3.

MEDICINE TREATMENT

- Ceftriaxone, IM, 250 mg as a single dose. W
  - For ceftriaxone IM injection: Dissolve ceftriaxone 250 mg in 0.9 mL lidocaine 1% without epinephrine (adrenaline).

AND

- Azithromycin, oral, 1 g as a single dose. W

For persistent infection, refer to Section 25.1 Male urethral syndrome or Section 25.2 Vaginal discharge syndrome.

REFERRAL

Refer all cases to an ophthalmologist immediately.

18.2 ENDOPHTHALMITIS, BACTERIAL

S05.4-6 + (Y43.99), H44.0

DESCRIPTION

Infection of the ocular cavity is an emergency as it can cause blindness. This may occur secondary to bacteraemia (endogenous infection) or, more commonly, after penetrating ocular injury or surgery.
In patients with endogenous endophthalmitis blood cultures should be done and the source of infection identified and treated.
In patients with endophthalmitis after penetrating injury/surgery culture should be done on specimens of aqueous or vitreous humour.

MEDICINE TREATMENT

Refer immediately to an ophthalmologist.

Endogenous endophthalmitis
Specialist initiated; vitrectomy often required:

- Ceftriaxone, IV, 2 g daily for 7 days. W

Adjust antibiotics according to culture and sensitivity results.
AND

- Ceftazidime, intravitreal, 2.25 mg. W

LoE:IIIb[iii]

AND

- Vancomycin, intravitreal, 1 mg. W
  - Administer antibiotics using separate tuberculin syringes.
  - Antibiotic doses may be repeated after 48 hours depending on culture results or clinical response.

LoE:IIIb[iv]

LoE:IIIb[v]

Post-surgical endophthalmitis
Specialist initiated; vitrectomy often required:

- Ceftazidime, intravitreal, 2.25 mg. W

AND

- Vancomycin, intravitreal, 1 mg. W
  - Administer antibiotics using separate tuberculin syringes.
  - Antibiotic doses may be repeated after 48 hours depending on culture results or clinical response.

LoE:IIIb[vi]

In addition, if there is soft tissue involvement or as prophylaxis after a penetrating eye injury:

- Ciprofloxacin, oral, 750 mg 12 hourly for 7 days. W

18.3 GLAUCOMA
H40.0-6/H40.8-9

DESCRIPTION
Glaucoma is characterised by damage to the optic nerve with associated visual field loss, for which raised intra-ocular pressure (IOP) is a primary risk factor. Glaucoma is classified as open-angle or angle-closure. Glaucoma may occur as a primary condition or secondary to other ocular conditions. The condition is usually bilateral but may be unilateral or asymmetrical (especially with secondary causes).

18.3.1 OPEN-ANGLE GLAUCOMA
H40.1

DESCRIPTION
» Mostly asymptomatic.
» History of gradual loss of vision in the affected eye or loss of visual field.

» Often suspected after seeing cupping of optic disc on routine fundoscopy or finding elevated intra-ocular pressure on screening.

MEDICINE TREATMENT

Refer to an ophthalmology unit for diagnosis and initiation of treatment.

First line

ß-blocker monotherapy:

- Non-selective β-blocker, e.g.: *LoE:IIb[vii]*
- Timolol 0.25%, ophthalmic drops, instil 1 drop 12 hourly.

OR

Selective β-blocker: *LoE:IVb*

- Betaxolol 0.25–0.5%, ophthalmic drops, instil 1 drop 12 hourly.

Second line *LoE:IIb[viii]*

- Prostaglandin analogue monotherapy, e.g.:
  - Latanoprost 0.005%, ophthalmic drops, instil 1 drop daily.
  - Use as first line if patient has contra-indication to ß-blocker.
  - Use in place of ß-blocker if patient has intolerable side effects with ß-blocker or if there is no significant reduction in IOP with ß-blocker.

OR

- Prostaglandin analogue in combination with non-selective ß-blocker if there is insufficient reduction in IOP with ß-blocker monotherapy, e.g.
  - Bimatoprost 0.03% + Timolol 0.5% *LoE:Ib[ix]*

OR

- Prostaglandin analogue in combination with selective ß-blocker if there a contraindication to a non-selective ß-blocker e.g.
  - Latanoprost 0,005% with betaxolol 0.25-0.5%

Third line

Intolerance to prostaglandin analogue, or poor response:

- Alpha-agonist, e.g.: *LoE:IIIb[x]*
  - Brimonidine 0.15–0.2%, ophthalmic drops, instil 1 drop 12 hourly.
  - Use as second line if patient is allergic to prostaglandin analogue.
  - Use in place of prostaglandin analogue if there is no significant further reduction in IOP when adding prostaglandin analogue to ß-blocker.
  - Use in combination with ß-blocker and prostaglandin analogue if the patient still has progression of disease or target IOP is not reached.

Failure to respond: *LoE:IVb*

Alternatives in consultation with a specialist:

Parasympathomimetic agent:

- Pilocarpine 1%, ophthalmic drops, instil 1 drop 6 hourly.

In severe cases, as a temporary measure before ocular surgery, in consultation with a specialist: *LoE:IIIb*[xi]

Carbonic anhydrase inhibitor:

- Acetazolamide, oral, 250 mg 6 hourly.

REFERRAL

All to an ophthalmology unit.

18.3.2 ACUTE ANGLE-CLOSURE GLAUCOMA

H40.2

DESCRIPTION

» Usually presents acutely with sudden onset of severe eye pain and redness, associated with nausea, vomiting and hemicranial headache.
» Loss of vision in the affected eye.
» Coloured haloes or bright rings around lights.
» Hazy-looking cornea.
» Fixed, semi-dilated pupil.
» Shallow anterior chamber.
» Severely elevated intra-ocular pressure. When measured with finger palpation, the affected eye feels hard, compared to the other eye.
» If intraocular pressure rises more slowly, the patients may be asymptomatic with gradual loss of vision.

MEDICINE TREATMENT

Institute initial therapy and then refer IMMEDIATELY to an ophthalmology unit.

Try to achieve immediate reduction in IOP:

- Acetazolamide, oral, 500 mg immediately as a single dose.
  - Followed by 250 mg 6 hourly.

AND

- Timolol 0.25–0.5%, ophthalmic drops, instil 1 drop 12 hourly.

Also treat patient for associated pain and nausea. See Sections 12.4.1: Perioperative analgesics and 12.6.5.2: Treatment of PONV.

Where those measures fail, for short-term use only:

- Mannitol, IV, 1.5–2 g/kg as a 20% solution over 30–60 minutes.

OR

Glycerol, oral, 1 g/kg of 50% solution as a single dose immediately.

REFERRAL

All to an ophthalmology unit.

18.4 HERPES ZOSTER OPHTHALMICUS

B02.3, G53.0

DESCRIPTION

Herpes zoster ophthalmicus (HZO) occurs when the varicella-zoster virus reactivates in the trigeminal ganglion and passes down the ophthalmic division of the trigeminal nerve. Patients present with a painful vesicular rash in the trigeminal V1 area – vesicles on the tip of the nose indicate nasociliary branch involvement, which indicates the risk of ocular involvement. A minority of patients may develop conjunctivitis, keratitis, uveitis, retinitis, and cranial nerve involvement (oculomotor or optic nerves). Permanent sequelae of ophthalmic zoster infection may include chronic ocular inflammation, loss of vision, and debilitating post-herpetic neuralgia. All patients should be offered HIV testing.

MEDICINE TREATMENT

- Aciclovir, oral, 800 mg 5 doses per day (4 hourly while awake) for 7–10 days.
    - Treatment should be initiated within the first three days of onset of symptoms, except in HIV-infected patients who should be treated if there are active skin lesions. *LoE:IVb*

For patients unable to take oral medication, severely immunocompromised patients and for patients with complicated HZO e.g. acute retinal necrosis (ARN), optic neuropathy or orbitopathy:

- Aciclovir, IV infusion over one hour, 10 mg/kg 8 hourly for 7-14 days.
    - Seek specialist advice for duration of treatment and for switching to oral aciclovir therapy.
    - Adjust dose based on renal clearance (See Appendix II for guidance on prescribing and monitoring). *LoE:IIIb*[xii]

Post-herpetic neuralgia:
Initiate treatment with adjuvant therapy (i.e. amitriptyline) early.
See Section 25.1.4: Neuropathic pain (Post-herpetic neuralgia).

LoE:IIIb[xiii]

REFERRAL

» Vesicles on the tip of the nose.
» Fluorescein staining of cornea shows corneal/ulceration.
» Decreased vision.
» Red eye (uveitis or keratitis).
» Cranial nerve palsies.

18.5 KERATITIS

18.5.1 KERATITIS, HERPES SIMPLEX

B00.5† + (H19.1*)

DESCRIPTION

Acute unilateral painful red eye with visual blurring and decreased corneal sensation. Characteristic dendritic corneal ulcer seen on staining with fluorescein.

MEDICINE TREATMENT

- Aciclovir, oral, 400 mg five times daily for 10–14 days. *LoE:Ib[xiv]*

Note: Topical corticosteroids are contraindicated for treating dendritic ulcers.

18.5.2 KERATITIS, SUPPURATIVE

H16.8

DESCRIPTION

Painful red eye with corneal lesion that stains with fluorescein and has creamy white appearance. Contact lenses are a major risk factor, especially for bacterial infections. Have a high index of suspicion for fungal infection in PLHIV, or there is a history of injury to eye with plant matter.

MEDICINE TREATMENT

Empiric therapy until culture results become available:

Bacterial infection:

- Fluoroquinolone ophthalmic drops, e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instil 1 drop hourly for 3 days.
  - Then reduce frequency to 1 drop 3–4 hourly until the ulcer is completely healed.
  - Patients requiring treatment for longer than 2 weeks should be on the advice of an ophthalmologist.

LoE: IVb[xv]

Fungal infection:

- Natamycin 5%, ophthalmic drops, instil 1 drop 1–2 hourly for 3–4 days. (Specialist prescribed).
  - Then reduce frequency to 1 drop 3–4 hourly.
  - Continue for 14–21 days until resolution of infection.

LoE: Ib[xvi]

REFERRAL

» All patients to be managed in consultation with an ophthalmologist.

18.6 RETINITIS, HIV CMV

H30.9 + (B20.2)

DESCRIPTION

Cytomegalovirus (CMV) retinitis is seen in advanced HIV infection, with CD4 count <100 cells/mm^3. The characteristic retinal appearance is that of necrosis, i.e. white exudates, and hemorrhages at the edges of the exudates. Visual loss is irreversible – the goal of therapy is to limit further loss.

MEDICINE TREATMENT

Limited CMV retinitis:

- Valganciclovir, oral, 900 mg 12 hourly for the first 3 weeks, then 900 mg daily until immune recovery (CD4 >100) and a minimum of 3 months of therapy with valganciclovir (if available). *LoE:IIIb*[xvii]
  - Monitor FBC weekly during induction, then monthly, as valganciclovir can cause bone marrow suppression. Avoid concomitant zidovudine use.
  - Initiate ART 2 weeks after starting induction therapy.

If valganciclovir is not available:

- Ganciclovir, intravitreal, 2 mg twice a week for three weeks then once a week (specialist).
  - Once immune function has been restored with antiretroviral therapy (CD4 >100) and the features of active retinitis has cleared, maintenance ganciclovir can be stopped but monitor for recurrence.

REFERRAL

To ophthalmologist for confirmation of diagnosis.
Patients with extensive or wide-spread CMV infection to be managed by an infectious disease specialist.

18.7 UVEITIS

H20.0

Uveitis can be associated with systemic diseases or infection, necessitating a careful history and review of presenting symptoms. Physical examination of the eye and pertinent organ systems should be performed to characterise the type of inflammation present and any concomitant systemic disease. Multimodal ophthalmic imaging has an important role in characterising certain types of intraocular inflammation. Determining the specific type of uveitis guides the selection of treatment. The goal of treatment is to control the disease activity and eliminate or reduce the risk of loss of vision. Uveitis is often classified anatomically based on the primary site of inflammation: anterior uveitis (iris and ciliary body), intermediate uveitis (vitreous), posterior uveitis (retina or choroid) and panuveitis (whole eye), with posterior segments of the eye generally associated with more severe disease.

18.7.1 INFECTIOUS UVEITIS
H20.0

Infectious uveitis may be caused by:
» Bacteria - (syphilis (refer to Section 6.8 syphilis, Section 14.6.3 meningovascular syphilis), tuberculosis (refer to Section 16.9 pulmonary TB, Section 16.10 Pleural TB), bartonellosis).
» Viruses - (herpes (refer to Section 4.11.2 Herpes zoster, Section 14.6.2 Herpes simplex encephalitis, Section 18.4 Herpes Zoster ophthalmicus, Section 18.5 Herpes simplex keratitis, Section 25.3 recurrent herpes simplex), cytomegalovirus (refer to Section 10.2.6 CMV, Section 18.6 retinitis, HIV CMV).
» Fungi - (histoplasmosis).
» Protozoa - (toxoplasmosis (refer to Section 10.2.10 Cerebral toxoplasmosis), toxocariasis, and cysticercosis (refer to Section 14.6.6 neurocysticercosis)).

Patients must be investigated for infectious causes. Further screening should be performed which should be informed by obtaining a full clinical history along with presenting signs and symptoms. Consider the following for further investigation:
» TB - Chest XR or TB.
» Syphilis – VDRL test.
» Toxoplasmosis - toxoplasma PCR.
» Herpes simplex and Herpes zoster: HSV or HZV PCR.
» Cat-scratch disease (bartonella): bartonella PCR.

If an infectious cause is found, treatment of the ocular disease is as for the systemic disease. Once the infection has been addressed, residual inflammation can be treated with adjuvant anti-inflammatory therapy.

18.7.2 NON-INFECTIOUS UVEITIS, ANTERIOR
H20.0

DESCRIPTION
The commonest form of non-infectious uveitis is acute anterior uveitis, which presents with pain and photophobia, variable loss of vision, circumcilliary injection, and a miotic pupil. Chronic anterior uveitis may lead to cystoid macular oedema with decreased central acuity, cataract formation, and secondary glaucoma.

MEDICINE TREATMENT
- Cycloplegic agent, e.g.:
- Atropine 1%, ophthalmic drops, instil 1 drop 12 hourly.

AND

- Corticosteroids, e.g.:
- Dexamethasone 0.1%, ophthalmic drops, instil 1–2 drops 4–6 hourly.

LoE:Ib[xviii]

REFERRAL

All, for management at an ophthalmology unit.

18.7.3 NON-INFECTIOUS POSTERIOR UVEITIS AND PANUVEITIS

H20.0

DESCRIPTION

Non-infectious posterior and panuveitis may be sight limiting if inflammation is not controlled. Both auto-inflammatory and autoimmune processes may be implicated. Posterior uveitis and panuvetis both present similarly with loss of vision, pain and photophobia, floaters and a red eye and are treated similarly as outlined below.

Indicators of severe inflammation include:

» Impairment of visual function.
» Bilateral disease.
» Vitreous haze.
» Macular or optic nerve disease.
» Retinal vascular inflammation.
» Exudative detachment.
» Ocular structural complications that threaten visual function.

LoE:IVb[xix]

MEDICINE TREATMENT

- Cycloplegic agent, e.g.:
- Atropine 1%, ophthalmic drops, instil 1 drop 12 hourly.

AND

- Corticosteroids, e.g.:

<u>Acute inflammation/flare</u>

- Prednisone, oral 1 mg/kg/day (max 80 mg/day) for one week
  - Use lowest possible dose for shortest possible duration to control inflammation.
  - Apply a dose tapering regimen over 3-6 weeks typically reducing doses every 1-2 days based on treatment response.

LoE:IIb[xx]

<u>Chronic inflammation</u>

- Prednisone, oral 1 mg/kg/day (max 80 mg/day) for no longer than one month.
  - Use lowest possible dose for shortest possible duration to control inflammation.

- Apply a dose tapering regimen typically reducing doses every 1-2 weeks based on treatment response.
- Monitor for infection, hypertension, fluid retention, diabetes mellitus, hyperlipidaemia, atherosclerosis, osteoporosis, glaucoma, and cataracts.

Patients requiring corticosteroid-sparing control or for persistent severe inflammation refractory to corticosteroid therapy:

Initiation of immunosuppressant therapy should be considered under the following conditions: LoE:IVb[xxi]

» Worsening of disease while on high dose corticosteroids
» No response to high dose corticosteroids after 2 to 4 weeks
» Lack of control of inflammation following treatment with high dose corticosteroids for 4 weeks.
» Patients requiring maintenance corticosteroid doses ≥7.5 mg/day for three or more consecutive months.
» Contra-indication or intolerance to corticosteroids. LoE:IVb[xxii]

- DMARDs (Disease-modifying antirheumatic drugs).
- Methotrexate, oral, 7.5 mg once weekly. LoE:IIb[xxiii]
  - Dose titration should be based on individual patient response using increments of 2.5 mg weekly to a maximum dose of 25 mg weekly.
  - As the onset of action is slow with a delayed time to full effect, commence dose tapering of concomitant corticosteroid therapy 2 weeks after initiating methotrexate therapy, based on treatment response.
  - Pre-treatment screening: exclude any infectious diseases that may be exacerbated by immunosuppression.
  - Monitoring: FBC and LFTs at baseline, 4 weeks after initiating treatment and 8 weekly thereafter.
  - Methotrexate is teratogenic - ensure women of child-bearing potential are counselled.

AND

- Folic acid, oral 5 mg daily

Patients presenting with concomitant anterior uveitis should also be managed with topical treatment (see Section 18.7.1: Infectious uveitis).

REFERRAL

All, for management at an ophthalmology unit.
If there is concomitant systemic disease refer to appropriate specialist.

18.8 SURGICAL AND DIAGNOSTIC PRODUCTS

Ocular peri-operative pharmaceutical products

- Sodium hyaluronate 10 mg/mL.
- Acetylcholine chloride (for intra-ocular irrigation).
- Sterile intraocular irrigating solution.
- Hyaluronidase 1500 IU injection (adjunct to anaesthesia for cataract surgery). *LoE:IIb*[xxiv]
- Mitomycin C 2 mg injection (for sponge application during trabeculectomy for glaucoma management). *LoE:IIb*[xxv]

Ocular diagnostic products

- Fluorescein 2%, ophthalmic drops.
- Fluorescein ophthalmic strips.
- Tropicamide 1%, ophthalmic drops.
- Cyclopentolate 2 mg/mL ophthalmic drops (for cycloplegic refraction).
- Cyclopentolate 2 mg/mL and phenylephrine 10 mg/mL (for fundoscopic examination).
- Polyacrylic acid 2 mg/g ophthalmic gel (as coupling liquid for diagnostic contact lenses).

▪ **Local anesthetics used on the eye**

- Oxybuprocaine hydrochloride 0.4%. *LoE:IIIb*[xxvi]

▪ **Preparations for tear deficiency**

- Hydroxypropyl methylcellulose 0.3–0.5%.

18.9 DRY EYE DISEASE

H04.1

DESCRIPTION

Dry eye occurs when there is inadequate tear volume or function. It is a multifactorial disease of the ocular surface.

The common symptoms include feelings of dryness, grittiness, burning and foreign body sensation, usually worse during the day. A stringy discharge, redness and transient blurring of vision are also common.
Allergic conjunctivitis should be excluded.

GENERAL MEASURES

The management of dry eye involves controlling the symptoms, since the disease is generally not curable.
Management encompasses both pharmacologic and non-pharmacologic approaches.

Relieve symptoms with warm compresses, i.e. a clean moistened cloth over the eyes for at least 1 minute two to three times per day.
Patients should be educated to avoid over the counter topical medications, many of which exacerbate dryness, and control their environmental factors (e.g. encourage frequent blinking during visually attentive tasks, avoid air conditioners or heating, use humidifiers).

MEDICINE TREATMENT

Tear substitutes:

- Hydroxypropyl methylcellulose, ophthalmic drops, 1 drop, 6 hourly.

OR *LoE:IVb*[xxvii]

Lanolin, anhydrous liquid, ophthalmic ointment, at night.

LoE:IVb[xxviii]

18.10 MEDICAL MANAGEMENT OF EYE INJURY

18.10.1 CHEMICAL BURN

This is a medical emergency.
See Primary Health Care Standard Treatment Guidelines Section 18.3.1: Eye injury, chemical burn.

18.10.2 EYE INJURY: BLUNT/PENETRATING/ FOREIGN BODY

See Primary Health Care Standard Treatment Guidelines Sections 18.3.2 Eye injury/foreign bodies and 18.3.3: Eye injury (blunt or penetrating).

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SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
AH CHAPTER 18: EYE CONDITIONS
NEMLC RECOMMEDATIONS FOR MEDICINE AMENDMENTS (2020-4 REVIEW CYCLE)

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the respective standard treatment guideline (STG).
All reviews and costing reports may be accessed at: https://www.health.gov.za/nhi-edp-stgs-eml/
Note that the associated EML chapter has been subjected to subsequent clinical editing. These editorial amendments may not be reflected in the report below.

A: NEW STGs

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED/NOT ADDED/RETAINED
18.1.4 Conjunctivitis, bacterial (gonococcal)	Ceftriaxone	New STG – *aligned to PHC Chp 12 STIs*
	Azithromycin	New STG– *aligned to PHC Chp 12 STIs*
18.7 Uveitis		
18.7.1 Non-infectious uveitis, anterior	STG guidance for non-infectious anterior uveitis separated from non-infectious posterior and panuveitis (new)	AMENDED
	Medicine treatment - homatropine:	DELETED - discontinued
	Medicine treatment – prednisolone acetate eye drops	NOT ADDED
18.7.2 Non-infectious uveitis, posterior uveitis and panuveitis	Medicine Treatment – Cycloplegic eye drops:	RETAINED
	Medicine treatment – prednisone oral	ADDED
	Medicine treatment – methotrexate oral	ADDED
	Medicine treatment – folic acid oral	ADDED
	Medicine treatment – azathioprine	Added to the therapeutic interchange database

B: MEDICINE AMENDMENTS

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED/NOT ADDED/RETAINED
Eye chapter	Consultation with specialists	Referral guidance - ADDED
18.1.1 Conjunctivitis, viral	Description	Amended
	Medicine treatment, oxymetazoline	Indication - CLARIFIED
18.1.2 Conjunctivitis, allergic	Medicine treatment– Epinastine hydrochloride 0.5mg/mL eye drops:	NOT ADDED
18.1.3 Conjunctivitis, bacterial (non-gonococcal)	Medicine treatment - Sodium chloride 0.9% irrigation	- ADDED
	Medicine treatment – fluoroquinolone ophthalmic drops:	Guidance CLARIFIED
18.3.1 Open-angle glaucoma	STG guidance separated for open-angle and angle closure glaucoma	Amended -Guidance separated
	Medicine treatment – bimatoprost:	DELETED - as example within therapeutic class
	Medicine treatment – Latanoprost:	ADDED – as example within therapeutic class
	Medicine treatment – Bimatoprost 0.03% + Timolol 0.5%:	ADDED - as example within therapeutic class
18.2 Endophthalmitis, bacterial	Endophthalmitis – vancomycin, intravitreal	Guidance AMENDED
18.3.2 Acute angle-closure glaucoma	STG guidance separated for open-angle and angle closure glaucoma	Amended -Guidance separated
18.4 Herpes zoster ophthalmicus	Description	Editorial amendment
	Aciclovir, IV	ADDED
	Valaciclovir, oral	NOT ADDED
18.5.1 Keratitis, herpes simplex	Medicine treatment – acyclovir 3% ophthalmic ointment	DELETED – *discontinued*
18.5.2 Keratitis, suppurative	Description	Editorial amendment
	Medicine treatment – chloramphenicol eye ointment:	NOT ADDED
	Medicine treatment – fluoroquinolone ophthalmic drops	Guidance CLARIFIED

	Referral	Amended
18.6 Retinitis, HIV CMV	Medicine treatment – ganciclovir, intravitreal	Dose CLARIFIED
	Referral	Guidance ADDED
18.8 Surgical and diagnostic products	Hyaluronidase 1500IU injection	ADDED
	Mitomycin C 2mg injection	ADDED
18.9 Dry Eye Disease	Description	Amended
	General measures	Amended

A. NEW STGs

18.1.4 CONJUNCTIVITIS, BACTERIAL (GONOCOCCAL)

Medicine treatment – ceftriaxone: *Added*

Medicine treatment – azithromycin: *Added*

The following guidance for the management of gonococcal conjunctivitis has been added to the chapter and is in alignment with the PHC Chp 12 STIs, Section 12.1 Vaginal discharge syndrome (VDS) and Section 12.3 Male urethritis syndrome (MUS)

8.1.4 CONJUNCTIVITIS, BACTERIAL (GONOCOCCAL)

H10.0

Hyperacute bacterial conjunctivitis involves rapid onset and progression of conjunctivitis and is often caused by N.gonorrhoeae. Gonococcal conjunctivitis requires immediate referral to an ophthalmologist to prevent corneal involvement and potential perforation.

Clinical features:
» Hyperpurulent discharge
» Diminished visual acuity
» Eye tenderness
» Swollen lymph nodes

For conjunctivitis of the newborn, See Primary Health Care Standard Treatment Guidelines and Essential Medicine List; section 18.1.3.

MEDICINE TREATMENT

- Ceftriaxone, IM, 250 mg as a single dose.
  - For ceftriaxone IM injection: Dissolve ceftriaxone 250 mg in 0.9 mL lidocaine 1% without epinephrine (adrenaline).

AND

- Azithromycin, oral, 1 g as a single dose.

For persistent infection, refer to Section 25.1 Male urethral syndrome or section 25.2 Vaginal discharge syndrome.

REFERRAL

Immediate referral to an ophthalmologist.

18.7 UVEITIS

The STG for the management of uveitis has undergone extensive revision. Guidance has been added on the screening of infectious uveitis. Furthermore, guidance for the management of non-infectious uveitis has been separated into Section 18.7.1 Infectious uveitis, 18.7.2 Non-infectious uveitis, anterior which is primarily managed with topical ophthalmic treatments and Section 18.7.2 Non-infectious uveitis, posterior and panuveitis which is managed with oral immunosuppressant therapies. STG guidance amended as follows:

AMENDED FROM:

18.7 UVEITIS

H20.0

DESCRIPTION

Inflammation of the uveal tract and adjacent structures. The commonest form is acute anterior uveitis, which presents with pain and photophobia, variable loss of vision, circumcilliary injection, and a miotic pupil. Chronic uveitis may lead to cystoid macular oedema with decreased central acuity, cataract formation, and secondary glaucoma. Numerous systemic diseases can cause uveitis.

MEDICINE TREATMENT
- Cycloplegic agent, e.g.:
- Homatropine 2 %, ophthalmic drops, instil 1–2 drops 3–4 hourly.

OR

Atropine 1%, ophthalmic drops, instil 1 drop 12 hourly.

AND
- Corticosteroids, e.g.:
- Dexamethasone 0.1%, ophthalmic drops, instil 1–2 drops 4–6 hourly.

REFERRAL

All, for management at an ophthalmology unit.

AMENDED TO:

18.7 UVEITIS

H20.0

Uveitis can be associated with systemic diseases or infection, necessitating a careful history and review of presenting symptoms. Physical examination of the eye and pertinent organ systems should be performed to characterise the type of inflammation present and any concomitant systemic disease. Multimodal ophthalmic imaging has an important role in characterising certain types of intraocular inflammation. Determining the specific type of uveitis guides the selection of treatment. The goal of treatment is to control the disease activity and eliminate or reduce the risk of loss of vision. Uveitis is often classified anatomically based on the primary site of inflammation: anterior uveitis (iris and ciliary body), intermediate uveitis (vitreous), posterior uveitis (retina or choroid) and panuveitis (whole eye), with posterior segments of the eye generally associated with more severe disease.

18.7.1 INFECTIOUS UVEITIS

H20.0

Infectious uveitis may be caused by:
» Bacteria - (syphilis (refer to Section 6.8 syphilis, section 14.6.3 meningovascular syphilis), tuberculosis (refer to Section 16.9 pulmonary TB , Section 16.10 Pleural TB), bartonellosis),
» Viruses - (herpes (refer to Section 4.11.2 Herpes zoster, Section 14.6.2 Herpes simplex encephalitis, Section 18.4 Herpes Zoster ophthalmicus, Section 18.5 Herpes simplex keratitis, Section 25.3 recurrent herpes simplex), cytomegalovirus (refer to Section 10.2.6 CMV, Section 18.6 retinitis, HIV CMV),
» Fungi - (histoplasmosis) and
» Protozoa - (toxoplasmosis (refer to Section 10.2.10 Cerebral toxoplasmosis), toxocariasis, and cysticercosis (refer to Section 14.6.6 neurocysticercosis)).

Patients must be investigated for infectious causes. Further screening should be performed which should be informed by obtaining a full clinical history along with presenting signs and symptoms. Consider the following for further investigation:
» TB - Chest XR or TB ,
» Syphilis – VDRL test
» Toxoplasmosis - toxoplasma PCR
» Herpes simplex and Herpes zoster: HSV or HZV PCR
» Cat-scratch disease (bartonella): bartonella PCR

If an infectious cause is found, treatment of the ocular disease is as for the systemic disease. Once the infection has been addressed, residual inflammation can be treated with adjuvant anti-inflammatory therapy.

18.7.2 NON-INFECTIOUS UVEITIS, ANTERIOR

STG Guidance: *Amended*

Guidance for the management of uveitis has been separated for non-infectious anterior uveitis which is primarily managed with topical ophthalmic treatments.

Medicine treatment - homatropine: *Deleted*

Homatropine 2% as an example of a cycloplegic agent has been removed from the EML as it is no longer available locally. Atropine 1% ophthalmic drops is retained in the EML as the recommended alternative.

Medicine treatment – prednisolone acetate eye drops: *Not added*

External comment to include prednisolone acetate eye drops as an alternative to dexamethasone eye drops was not supported by the Committee in accordance with a previous NEMLC decision[1] that there is no good evidence of

[1] NDoH Evidence Review. Prednisolone acetate versus dexamethasone 0.1% eye drops for uveitis. October 2017_v4.0

superiority to justify the price difference over dexamethasone. Refer to the Knowledge Hub or NHI webpage for the complete evidence review.

NDoH Evidence review: Prednisolone_Uveitis_October 2017_v4.0

Type of recommendation	We recommend against the option and for the alternative	We suggest not to use the option or to use the alternative	We suggest using either the option or the alternative	We suggest using the option	We recommend the option
	☐	☐	X	☐	☐

Recommendation: Dexamethasone 0.1% ophthalmic drops be retained in the Adult Hospital Level EML for uveitis.

Rationale: Much as corticosteroids are the main stay in the management of uveitis, there are no robust comparative studies to qualify the use of either prednisolone acetate or dexamethasone. However, prednisolone is widely used and it would be appropriate to consider as a second agent for treatment of acute non infectious uveitis, where the cheaper option dexamethasone is not available.

Level of Evidence: III Expert opinion, Guidelines

Other Factors and Considerations:

- Cost implication
- Efficacy in non-acute uveitis

,Review indicator:

Evidence of efficacy	Evidence of harm	Price reduction
x		X

VEN status:

Vital	Essential	Necessary
	X	

NEMLC MEETING OF 26 SEPTEMBER 2019
NEMLC accepted the medicine review and the proposed recommendations proposed by the Adult Hospital Level Committee.

Monitoring and evaluation considerations

Research priorities: Controlled head to head studies for topical steroids need to be prioritised especially prednisolone and dexamethasone

The STG has been amended as tabulated below:

18.7.2 NON-INFECTIOUS UVEITIS, ANTERIOR

H20.0

DESCRIPTION

~~Inflammation of the uveal tract and adjacent structures.~~ The commonest form of non-infectious uveitis is acute anterior uveitis, which presents with pain and photophobia, variable loss of vision, circumcilliary injection, and a miotic pupil. Chronic anterior uveitis may lead to cystoid macular oedema with decreased central acuity, cataract formation, and secondary glaucoma. ~~Numerous systemic diseases can cause uveitis.~~

MEDICINE TREATMENT

- Cycloplegic agent, e.g.:
- ~~Homatropine 2 %, ophthalmic drops, instil 1–2 drops 3–4 hourly.~~

~~OR~~

Atropine 1%, ophthalmic drops, instil 1 drop 12 hourly.

AND

- Corticosteroids, e.g.:
- Dexamethasone 0.1%, ophthalmic drops, instil 1–2 drops 4–6 hourly.

REFERRAL

All, for management at an ophthalmology unit.

18.7.3 NON-INFECTIOUS POSTERIOR UVEITIS AND PANUVEITIS

Medicine Treatment – Cycloplegic eye drops: *Retained*
Medicine Treatment- Prednisone oral: *Added*
Medicine Treatment- Methotrexate oral: *Added*
Medicine Treatment- Folic acid oral: *Added*

Prednisone oral has been added to the STG for the acute management of ocular inflammation and flare ups associated with non-infectious uveitis as well as short term treatment of chronic inflammation. Refer to the evidence summary included at the end of this report or alternatively, accessible on the Knowledge Hub or NHI webpage.

PHC/ADULT HOSPITAL LEVEL EXPERT REVIEW COMMITTEE RECOMMENDATION:

Type of recommendation	We recommend against the option and for the alternative **(strong)**	We suggest not to use the option **(conditional)**	We suggest using either the option or the alternative **(conditional)**	We suggest using the option **(conditional)**	We recommend the option **(strong)**
				X	

Recommendation: Oral prednisone/prednisolone is suggested as the first line standard of care for the management of non-infectious posterior or panuveitis in adults. Prescribing should be limited to specialists or ophthalmology medical officers in consultation with a specialist, where diagnosis of non-infectious uveitis is confirmed.

Rationale: Posterior uveiits and panuveitis are potentially sight-limiting conditions. International guidelines informed by expert opinion recommend oral corticosteroids as a first line treatment for posterior uveitis and panuveitis due to their perceived efficacy and well-established safety profile.

Level of Evidence: Very low certainty of evidence

Review indicator: Published evidence of benefit or harm.

NEMLC RECOMMENDATION 20 OCTOBER 2022:

The NEMLC supported the addition of oral prednisone/prednisolone to the EML as the first line standard of care for the management of non-infectious posterior or panuveitis in adults, pending editorial adjustments to the review document and the development of a new STG for the management of posterior uveitis and panuveitis.

Monitoring and evaluation considerations

Research priorities

Methotrexate has been added to the AH EML for the management of non-infectious posterior and panuveitis for patients requiring corticosteroid-sparing control or for persistent severe inflammation refractory to corticosteroid therapy. Refer to the evidence summary included at the end of this report or alternatively, accessible on the Knowledge Hub or NHI webpage.

PHC/ADULT HOSPITAL LEVEL EXPERT REVIEW COMMITTEE RECOMMENDATION:

Type of recommendation	We recommend against the option and for the alternative **(strong)**	We suggest not to use the option **(conditional)**	We suggest using either the option or the alternative **(conditional)**	We suggest using the option **(conditional)**	We recommend the option **(strong)**
				X	

Recommendation: The PHC/ Adult Hospital Level Committee suggests using methotrexate for the management of non-infectious posterior uveitis or panuveitis in patients who are refractory to corticosteroids or who require ongoing corticosteroids to maintain inflammation control. The recommendation is based on the limited observational data supporting the use of methotrexate for the management of non-infectious posterior uveitis or panuveitis.

Rationale: The potential harms with long term corticosteroid exposure is a concern as well as the risks of progression to blindness if inflammation is not controlled. Methotrexate is the cheapest of the DMARDs reviewed and is widely used for multiple indications already approved on the EML.

Level of Evidence: Low certainty

Review indicator: New RCT data for efficacy or safety.

NEMLC RECOMMENDATION (30 NOVEMBER 2023): NEMLC supports the recommendation by the ERC as above.

Monitoring and evaluation considerations

Therapeutic Interchange database

The following updates to the therapeutic interchange database were supported by the Committee:

Section - Heading	Indication	INN	strength	unit	formulation
Uveitis	Ocular inflammation	Methotrexate	2.5	mg	oral
Uveitis	Ocular inflammation	Azathioprine	50	mg	oral

Methotrexate oral

Dose: 7.5 mg to 25 mg per week

Azathioprine oral

Dose: 1mg – 4mg/kg/day

New guidance for the management of posterior and panuveitis has been added as tabulated below:

18.7.3 NON-INFECTIOUS UVEITIS, POSTERIOR UVEITIS AND PANUVEITIS

H20.0

DESCRIPTION

Non-infectious posterior and panuveitis may be sight limiting if inflammation is not controlled. Both auto-inflammatory and autoimmune processes may be implicated. Posterior uveitis and panuvetis both present similarly with loss of vision, pain and photophobia, floaters and a red eye and are treated similarly as outlined below.

Indicators of severe inflammation include:

- » Impairment of visual function
- » Bilateral disease
- » Vitreous haze
- » Macular or optic nerve disease
- » Retinal vascular inflammation
- » Exudative detachment
- » Ocular structural complications that threaten visual function

MEDICINE TREATMENT

- Cycloplegic agent, e.g.:
- Atropine 1%, ophthalmic drops, instil 1 drop 12 hourly.

- Corticosteroids, e.g.:

Acute inflammation/flare

- Prednisone, oral 1mg/kg/day (max 80mg/day) for one week
  - Use lowest possible dose for shortest possible duration to control inflammation.
  - Apply a dose tapering regimen over 3-6 weeks typically reducing doses every 1-2 days based on treatment response.

Chronic inflammation

- Prednisone, oral 1mg/kg/day (max 80mg/day) for no longer than one month
  - Use lowest possible dose for shortest possible duration to control inflammation.
  - Apply a dose tapering regimen typically reducing doses every 1-2 weeks based on treatment response.
  - Monitor for infection, hypertension, fluid retention, diabetes mellitus, hyperlipidemia, atherosclerosis, osteoporosis, glaucoma, and cataracts.

Patients requiring corticosteroid-sparing control or for persistent severe inflammation refractory to corticosteroid therapy:

Initiation of immunosuppressant therapy should be considered under the following conditions:

- Worsening of disease while on high dose corticosteroids
- No response to high dose corticosteroids after 2 to 4 weeks
- Lack of control of inflammation following treatment with high dose corticosteroids for 4 weeks.
- Patients requiring maintenance corticosteroid doses ≥7.5mg/day for three or more consecutive months
- Contra-indication or intolerance to corticosteroids

- DMARDs (Disease-modifying antirheumatic drugs)
- Methotrexate, oral 7.5 mg once weekly
  - Dose titration should be based on individual patient response using increments of 2.5 mg weekly to a maximum dose of 25mg weekly.
  - As the onset of action is slow with a delayed time to full effect, commence dose tapering of concomitant corticosteroid therapy 2 weeks after initiating methotrexate therapy, based on treatment response.
  - Pre-treatment screening: exclude any infectious diseases that may be exacerbated by immunosuppression.
  - Monitoring: FBC and LFTs at baseline, 4 weeks after initiating treatment and 8 weekly thereafter.
  - Methotrexate is teratogenic - ensure women of childbearing potential are counselled.

AND
- Folic acid, oral 5mg daily

Patients presenting with concomitant anterior uveitis should also be managed with topical treatment (See Section 18.7.1).

REFERRAL
All, for management at an ophthalmology unit.
If there is concomitant systemic disease refer to appropriate specialist

B. MEDICINE AMENDMENTS

18. EYE CHAPTER

Consultation with specialists: *Guidance added*

The following guidance has been added to the chapter to mitigate delays with referring patients for specialist care:

For many eye conditions early specialist consultation and advice is required.
To mitigate delays in referral it is recommended that electronic consultation methods are utilised with transmission of appropriate images so that appropiate treament can be initiated before referral.

18.1.1 CONJUNCTIVITIS, VIRAL

Description: A*mended*

Medicine treatment - oxymetazoline: *Guidance clarified*

The following amendments were made to the description of viral conjunctivitis which may be caused by a number of viruses, of which, adenovirus is the most common cause:

DESCRIPTION

~~Adenovirus is a~~ Viral conjunctivitis is the commonest cause of infective conjunctivitis. It may be unilateral but ~~is usually~~ often progresses to bilateral. Adenovirus is the commonest viral conjunctivitis, however other viral causes of conjunctivitis present in the same way.

Clinical features:
» Viral conjunctivitis may be associated with an upper respiratory tract infection.
» A burning, sandy, or gritty feeling in the eyes.
» Morning crusting followed by watery discharge.
» Preauricular lymphadenopathy may be present.
» The cornea, iris and pupil are completely normal with normal visual acuity.

The condition is self-limiting but eye irritation and discharge may get worse~~ for 3-5 days before getting better and symptoms can persist~~ for the first week depending on the specific virus. Duration varies from 3-5 days to 2-3 weeks before resolution.

The following statement was amended to clarify that the use of oxymetazoline (a vasoconstrictor), is intended as symptomatic management of redness of the eye only: *"Oxymetazoline 0.025%, eye drops, instil 1–2 drops 6 hourly for a maximum of 7 days to reduce redness of eyes.'*

Long term use of vasoconstrictors may cause rebound congestion and should be avoided.

18.1.2 CONJUNCTIVITIS, ALLERGIC

Medicine treatment– Epinastine hydrochloride 0.5mg/mL eye drops: *Not added*

External comment received for the inclusion of epinastine hydrochloride 0.5mg/mL eye drops for the management of allergic conjunctivitis. Epinastine eye drops is already included on the therapeutic interchange database and has therefore not been added to the EML. Guidance on the management of allergic conjunctivitis is included in the PHC Chp 18 Eye chapter Section 18.1.1 and is cross referenced in the Adult Hospital EML.

NEMLC report 2019

Medicine	Directions for use	Price (ZAR)*	ml	Daily dose (ml)**	Price for 30 days (ZAR)
cromoglicic acid 2%,	1 drop 6 hourly	75.59	13	0.2	34.89
lodoxamide 0.01%	1 drop 6 hourly	288.63	10	0.2	173.18
olopatadine 0.1%	1 drop 12 hourly	251.74	5	0.1	151.04
epinastine 0.05%	1 drop 12 hourly	225.61	5	0.1	135.37
ketotifen 0.025%,	1 drop 12 hourly	253.74	5	0.1	152.24
azelastine 0.05%	1 drop 12 hourly	88.70	10	0.1	39.92

* Cheapest product listed on SEP database, accessed 26 June 2019

** 1 drop = 0.05mL

Level of Evidence: II Systematic review and meta-analysis of low to moderate quality RCTs, Guidelines

18.1.3 CONJUNCTIVITIS, BACTERIAL (NON-GONOCOCCAL)

Medicine treatment - Irrigation with sodium chloride 0.9%*: Added*

The use of sodium chloride 0.9% for irrigation of the eyes has been added to the list of topical therapies for the management of non-gonococcal bacterial conjunctivitis. Furthermore, the management of bacterial conjunctivitis has been separated into non-gonococcal and gonococcal (refer to section 18.1.4) conjunctivitis.

Medicine treatment – fluoroquinolone ophthalmic drops: *Guidance clarified*

Guidance has been clarified as to when the use of fluoroquinolone ophthalmic drops as a second line option would be applicable i.e. contraindications to chloramphenicol or where drug interactions may be a concern. Chloramphenicol ophthalmic ointment is inactivated in the liver and may interact with medicines that are metabolised by hepatic microsomal enzymes[2]. Amendments to the STG are as tabulated below:

AMENDED FROM:

MEDICINE TREATMENT

During the day:

- Chloramphenicol 1%, ophthalmic ointment 6 hourly for 7 days.

OR

- Fluoroquinolone ophthalmic drops as second-line treatment, e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instil 1 drop 2 hourly for 2 days.
  - Then reduce frequency to 1 drop 4 hourly during waking hours, for 5 days.

AMENDED TO:

MEDICINE TREATMENT

- Immediate irrigation of the eyes with sodium chloride 0.9%.

During the day:

- Chloramphenicol 1%, ophthalmic ointment 6 hourly for 7 days.

OR

- Fluoroquinolone ophthalmic drops as second-line treatment (i.e. poor response to chloramphenicol or contra-indication/drug interactions with chloramphenicol) e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instil 1 drop 2 hourly for 2 days.
  - Then reduce frequency to 1 drop 4 hourly during waking hours, for 5 days.

18.2 ENDOPHTHALMITIS, BACTERIAL

Endophthalmitis – vancomycin, intravitreal: *Guidance amended*

[2] Product information. Chloramex® Ophthalmic Ointment. PHARMACARE LIMITED. Date of the most recent amendment to the professional information as approved by the Authority: 29 September 2017

Doses on intravitreal vancomycin when used for endogenous or post-surgical endophthalmitis, may be repeated after 48 hours depending on culture results or clinical response[3]. Amendments to the STG are as tabulated below:

AMENDED FROM:

Endogenous endophthalmitis

Specialist initiated, vitrectomy often required:

- Ceftriaxone, IV, 2 g daily for 7 days.
  - Adjust antibiotics according to culture and sensitivity results.

AND

- Ceftazidime, intravitreal, 2.25 mg.

AND

- Vancomycin, intravitreal, 1 mg.
  - Administer using separate tuberculin syringes.

Post-surgical endophthalmitis

Specialist initiated, vitrectomy often required:

- Ceftazidime, intravitreal, 2.25 mg.

AND

- Vancomycin, intravitreal, 1 mg.
  - Administer using separate tuberculin syringes.

AMENDED TO:

Endogenous endophthalmitis

Specialist initiated, vitrectomy often required:

- Ceftriaxone, IV, 2 g daily for 7 days.
  - Adjust antibiotics according to culture and sensitivity results.

AND

- Ceftazidime, intravitreal, 2.25 mg.

AND

- Vancomycin, intravitreal, 1 mg.
  - Administer antibiotics using separate tuberculin syringes.
  - Antibiotic doses may be repeated after 48 hours depending on culture results or clinical response.

Post-surgical endophthalmitis

Specialist initiated, vitrectomy often required:

- Ceftazidime, intravitreal, 2.25 mg.

AND

- Vancomycin, intravitreal, 1 mg.
  - Administer antibiotics using separate tuberculin syringes.
  - Antibiotic doses may be repeated after 48 hours depending on culture results or clinical response.

18.3.1 OPEN-ANGLE GLAUCOMA

STG Guidance: *Amended -Guidance separated*
Medicine treatment – bimatoprost: *Deleted*
Medicine treatment – Latanoprost: *Added*
Medicine treatment – Bimatoprost 0.03% + Timolol 0.5%: *Added*

Guidance on the management of glaucoma has been separated into two subsections, namely 18.3.1 Open-angle glaucoma and 18.3.2 Angle-closure glaucoma.

The EML has been updated to reflect the latest prostaglandin analogues allocated on tender including latanoprost 0.005% and the combination eye drop, Bimatoprost 0.03% + Timolol 0.5%. Updates are as tabulated below. The Committee acknowledged the availability of multiple generic formulations of prostaglandin analogues which does warrant prioritisation of this STG during the next review cycle.

AMENDED FROM:	AMENDED TO:
18.3.1OPEN-ANGLE GLAUCOMA	**18.3.1 OPEN-ANGLE GLAUCOMA** H40.1

[3] Durand ML.Endophthalmitis. Clinical Microbiology and Infection 2013;19(3):227-34. As cited in Cochrane review Emami S, Kitayama K, Coleman AL. Adjunctive steroid therapy versus antibiotics alone for acute endophthalmitis a#er intraocular procedure. Cochrane Database of Systematic Reviews 2022, Issue 6. Art. No.: CD012131. DOI: 10.1002/14651858.CD012131.pub3

MEDICINE TREATMENT

Open-angle glaucoma

Refer to an ophthalmology unit for diagnosis and initiation of treatment.

First line

ß-blocker:

- Non-selective β-blocker, e.g.:
- Timolol 0.25%, ophthalmic drops, instil 1 drop 12 hourly.

OR

Selective β-blocker:

- Betaxolol 0.25–0.5%, ophthalmic drops, instil 1 drop 12 hourly.

Poor response despite adequate adherence:

ADD

- Prostaglandin analogues, e.g.:
- Bimatoprost 0.01%, ophthalmic drops, instil 1 drop daily.
  - As first line if patient has contra-indication to ß-blocker.
  - In place of ß-blocker if patient has intolerable side effects with ß-blocker or if there is no significant reduction in IOP with other medicines.
  - In combination with ß-blocker if there is significant reduction in IOP with ß-blocker.

Intolerance to prostaglandin analogue, or poor response:

- Alpha-agonist, e.g.:
- Brimonidine 0.15–0.2%, ophthalmic drops, instil 1 drop 12 hourly.
  - Second line if patient allergic to prostaglandin analogue.
  - In place of prostaglandin analogue if there is no significant further reduction in IOP when adding prostaglandin analogue to ß-blocker.
  - In combination with ß-blocker and prostaglandin analogue if the patient still has progression of disease or target IOP is not reached.

Failure to respond:

Alternatives in consultation with a specialist:

Parasympathomimetic agent:

- Pilocarpine 1%, ophthalmic drops, instil 1 drop 6 hourly.

In severe cases, as a temporary measure before ocular surgery in consultation with a specialist:

Carbonic anhydrase inhibitor:

- Acetazolamide, oral, 250 mg 6 hourly.

MEDICINE TREATMENT

Refer to an ophthalmology unit for diagnosis and initiation of treatment.

First line

ß-blocker monotherapy:

- Non-selective β-blocker, e.g.:
- Timolol 0.25%, ophthalmic drops, instil 1 drop 12 hourly.

OR

Selective β-blocker:

- Betaxolol 0.25–0.5%, ophthalmic drops, instil 1 drop 12 hourly.

Second line

- Prostaglandin analogue monotherapy, e.g.:
  - Latanoprost 0.005%, ophthalmic drops, instill 1 drop daily.
  - Use as first line if patient has contra-indication to ß-blocker.
  - Use in place of ß-blocker if patient has intolerable side effects with ß-blocker or if there is no significant reduction in IOP with ß-blocker.

OR

- Prostaglandin analogue in combination with non-selective ß-blocker if there insufficient reduction in IOP with ß-blocker monotherapy, e.g.
  - Bimatoprost 0.03% + Timolol 0.5%

OR

- Prostaglandin analogue in combination with selective ß-blocker if there a contraindication to a non-selective ß-blocker e.g.
  - Latanoprost 0,005% with betaxolol 0.25-0.5%

Third line

Intolerance to prostaglandin analogue, or poor response:

- Alpha-agonist, e.g.:
  - Brimonidine 0.15–0.2%, ophthalmic drops, instil 1 drop 12 hourly.
  - Use as second line if patient is allergic to prostaglandin analogue.
  - Use in place of prostaglandin analogue if there is no significant further reduction in IOP when adding prostaglandin analogue to ß-blocker.
  - Use in combination with ß-blocker and prostaglandin analogue if the patient still has progression of disease or target IOP is not reached.

Failure to respond:

Alternatives in consultation with a specialist:

Parasympathomimetic agent:

- Pilocarpine 1%, ophthalmic drops, instil 1 drop 6 hourly.

In severe cases, as a temporary measure before ocular surgery, in consultation with a specialist:

Carbonic anhydrase inhibitor:

- Acetazolamide, oral, 250 mg 6 hourly.

REFERRAL

All to an ophthalmology unit.

18.3.2 ACUTE ANGLE-CLOSURE GLAUCOMA

STG Guidance: *Amended - Guidance separated*

Guidance on the management of glaucoma has been separated into two subsections, namely 18.3.1 Open-angle glaucoma and 18.3.2 Angle-closure glaucoma. For angle-closure glaucoma, initial therapy should be instituted with immediate referral to an ophthalmology unit.
As for Section 18.3.1 Open-angle glaucoma, the Committee supported that this STG be prioritized for review during the next review cycle.

18.4 HERPES ZOSTER OPHTHALMICUS

Description: *Editorial amendment*
The following statement as included in the description was amended: '*Patients present with a painful vesicular rash in the trigeminal V1 area – vesicles on the tip of the nose indicate nasociliary branch involvement, which i~~ncreases~~ indicates the risk of ocular involvement*

Medicine treatment – Acyclovir, IV: Added
Medicine treatment – Valacyclovir, oral: Not added
Aciclovir IV was added to the AH chp 18 Section 18.4 herpes zoster ophthalmicus (HZO) for patients unable to take oral medication, severely immunocompromised patients and for patients with complicated HZO e.g. acute retinal necrosis (ARN), optic neuropathy or orbitopathy. This addition has been aligned to guidance in the AH Chp 9 Infections Section 9.13: Zoster (shingles).

While oral valacyclovir does offer a theoretical advantage of improved compliance with its TDS dosing regimen relative to oral acyclovir's 4 hourly dosing regimen, the Committee did not support the inclusion of valacyclovir on the EML. Authors of a Cochrane review[4] comparing valacyclovir versus acyclovir for the treatment of herpes zoster ophthalmicus in immunocompetent patients concluded that there is uncertainty of the relative benefits and harms of valacyclovir over acyclovir in HZO. The certainty of evidence was rated by the study authors as low to very low which was downgraded for both imprecision and study limitations. Valacyclovir is also significantly more expensive than oral acyclovir. Note that studies comparing oral antiviral therapies for the management of HZO in immunocompromised patients are lacking and a Cochrane protocol by Olusanya et al published in 2010[5], specifically in PLHIV was subsequently withdrawn in 2018 due to insufficient progress having been made with the review.
Updates to the STG are as tabulated below:

AMENDED FROM:
MEDICINE TREATMENT
- Acyclovir, oral, 800 mg 4 hourly (4 hourly while awake for 7–10 days).
    - Treatment should be initiated within the first three days of onset of symptoms, except in HIV-infected patients who should be treated if there are active skin lesions.

AMENDED TO:
MEDICINE TREATMENT
- Acyclovir, oral, 800 mg 5 doses per day (4 hourly while awake) for 7–10 days.
    - Treatment should be initiated within the first three days of onset of symptoms, except in HIV-infected patients who should be treated if there are active skin lesions.

For patients unable to take oral medication, severely immunocompromised patients and for patients with complicated HZO e.g. acute retinal necrosis (ARN), optic neuropathy or orbitopathy:
- Acyclovir, IV infusion over one hour, 10 mg/kg 8 hourly for 7-14 days.
    - Seek specialist advice for duration of treatment and for switching to oral acyclovir therapy.
    - Adjust dose based on renal clearance (See Appendix II for guidance on prescribing and monitoring).

18.5.1 KERATITIS, HERPES SIMPLEX

Medicine treatment – acyclovir 3% topical eye ointment: *deleted*

[4] Schuster AK, et al. (2016). Valacyclovir versus acyclovir for the treatment of herpes zoster ophthalmicus in immunocompetent patients. Cochrane Database of Systematic Reviews.

[5] Olusanya BA, Oshun PO. Management of herpes zoster ophthalmicus in people with HIV infection. *Cochrane Database of Systematic Reviews* 2010, Issue 10. [DOI: 10.1002/14651858.CD008770

The recommendation for the use of acyclovir 3% topical eye ointment for the management of herpes simplex keratitis has been removed as the eye ointment has been discontinued locally. Oral acyclovir 400mg five times daily for 10-14 days has been retained in the STG for the management of herpes simplex keratitis.

18.5.2 KERATITIS, SUPPURATIVE

Description: *Editorial amendment*

The description has been amended to include bacterial infections as a major risk factor for contact lens wearers. Fungal infections as a risk factor for PLHIV has been retained with editorial amendments as tabulated below:

AMENDED FROM:

DESCRIPTION

Painful red eye with corneal lesion that stains with fluorescein and has creamy white appearance. Contact lenses are a major risk factor, especially for fungal infections. Have a high index of suspicion for fungal infection if HIV positive or there is a history of injury to eye with plant matter.

AMENDED TO:

DESCRIPTION

Painful red eye with corneal lesion that stains with fluorescein and has creamy white appearance. Contact lenses are a major risk factor, especially for bacterial infections. Have a high index of suspicion for fungal infection in PLHIV, or there is a history of injury to eye with plant matter.

Medicine treatment – chloramphenicol eye ointment: *Not added*

External comment received to include chloramphenicol eye ointment in addition to ciprofloxacin 03% eye drops for the management of bacterial keratitis to cover for gram positive organisms. Based on a small retrospective study in a tertiary hospital in the KZN province, the susceptibility patterns for most patients with culture-positive keratitis suggests that empiric therapy with ciprofloxacin monotherapy is appropriate for local consideration[6]. The Committee did not support the addition of chloramphenicol eye ointment for empiric therapy, but suggested that a review on the empiric treatment of bacterial keratitis be considered for the next review cycle.

Medicine treatment – fluoroquinolone ophthalmic drops: *Guidance clarified*

Guidance on the use of empiric fluoroquinolone ophthalmic drops has bene clarified as tabulated below:

AMENDED FROM:

MEDICINE TREATMENT

Empiric therapy until culture results become available:

Bacterial infection:

- Fluoroquinolone ophthalmic drops, e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instil 1 drop hourly for 3 days.
  - Then reduce frequency to 1 drop 3–4 hourly.

AMENDED TO:

MEDICINE TREATMENT

Empiric therapy until culture results become available:

Bacterial infection:

- Fluoroquinolone ophthalmic drops, e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instil 1 drop hourly for 3 days.
  - Then reduce frequency to 1 drop 3–4 hourly until the ulcer is completely healed.
  - Patients requiring treatment for longer than 2 weeks should be on the advice of an ophthalmologist.

Referral: *Amended*

[6] Proxenos CJ et al. Bacterial keratitis at a tertiary hospital in KwaZulu-Natal: a retrospective study. **South African Ophthalmology JournalVol. 16, No. 4**. 26 Jan 2022. https://hdl.handle.net/10520/ejc-nm_saoj_v16_n4_a5

The criteria for referral has been removed as tabulated below. The Committee noted that there is a risk of blindness if patients are not managed appropriately hence the recommendation to seek expert advice for all patients diagnosed with suppurative keratitis.

AMENDED FROM:

REFERRAL

» Hypopyon (pus in the anterior chamber)
» No facilities for microscopy, culture and sensitivity.

AMENDED TO:

REFERRAL

» All patients to be managed in consultation with an ophthalmologist.

18.6 RETINITIS, HIV CMV

Medicine treatment – ganciclovir, intravitreal: Dose clarified

The dose of intravitreal ganciclovir has been clarified and is aligned to dosing guidance included in the SAMF, as tabulated below:

AMENDED FROM:

If valganciclovir is not available:

- Ganciclovir, intravitreal, 2 mg once a week (specialist)
  - Once immune function has been restored with antiretroviral therapy (CD4 >100) and the features of active retinitis has cleared, maintenance ganciclovir can be stopped but monitor for recurrence.

AMENDED TO:

If valganciclovir is not available:

- Ganciclovir, intravitreal, 2 mg twice a week for three weeks then once a week (specialist)
  - Once immune function has been restored with antiretroviral therapy (CD4 >100) and the features of active retinitis has cleared, maintenance ganciclovir can be stopped but monitor for recurrence.

Referral: *Guidance added*

Guidance to refer patients with extensive or widespread CMV infection for management by an infectious disease specialist, has been added to the STG.

18.8 SURGICAL AND DIAGNOSTIC PRODUCTS

Ocular peri-operative pharmaceutical products – hyaluronidase 1500 IU injection: *ADDED*

Mitomycin C 2mg injection: *ADDED*

Hyaluronidase 1500IU injection has been added to the EML as an adjunct to anaesthesia for cataract surgery. Refer to the evidence summary included at the end of this report or alternatively, accessible on the Knowledge Hub or NHI webpage.

PHC/ADULT HOSPITAL LEVEL EXPERT REVIEW COMMITTEE RECOMMENDATION:

Type of recommendation	We recommend against the option and for the alternative **(strong)**	We suggest not to use the option **(conditional)**	We suggest using either the option or the alternative **(conditional)**	We suggest using the option **(conditional)**	We recommend the option **(strong)**
				X	

Recommendation: The Committee suggests a conditional recommendation for the use of hyaluronidase as an adjunct to anaesthesia for peri-orbital block. Its potential for improved akinesia may be beneficial in certain clinical settings, (extracapsular cataract surgery or manual small incision cataract surgery is still the predominant method used at many sites locally). As the technique uses larger incisions and it is difficult to stabilize the eye with one

instrument, movement of the eye increases the risk of posterior capsule rupture with vitreous loss resulting in poor visual outcomes.

Rationale: Operating with good akinesia is of utmost importance for trainee and inexperienced surgeons performing extracapsular surgery which is of lesser importance when phacoemulsification is used with smaller incisions and two hands available to stabilize the eye. Hyaluronidase also assists with spreading fluid in the tissues, which reduces the risk of elevated intraocular pressure. A high coincidence rate exists between sharp rise of IOP and undesirable intraoperative complications such as: shallowing of anterior chamber, herniation of iris through incision site and stromal corneal oedema. Javrishvili (2021)).

Level of Evidence: Low quality evidence

Review indicator:

NEMLC RECOMMENDATION (MEETING OF 23 FEBRUARY 2023):

NEMLC supports the recommendation of the Expert Review Committee as detailed above.

Monitoring and evaluation considerations

Research priorities

Mitomycin C 2mg injection

Mitomycin 2mg injection has been added to the EML for the management of glaucoma, as a sponge application during trabeculectomy. Refer to the evidence summary included at the end of this report or alternatively, accessible on the Knowledge Hub or NHI webpage.

PHC/ADULT HOSPITAL LEVEL EXPERT REVIEW COMMITTEE RECOMMENDATION:

Type of recommendation	We recommend against the option and for the alternative **(strong)**	We suggest not to use the option **(conditional)**	We suggest using either the option or the alternative **(conditional)**	We suggest using the option **(conditional)**	We recommend the option **(strong)**
				X	

Recommendation: The committee suggests that adult patients with glaucoma undergoing filtration surgery (trabeculectomy) should receive intraoperative mitomycin compared to No mitomycin-C, No 5-fluorouracil, placebo or sham *(conditional, low certainty of evidence).*

Rationale: Intraoperative sponge application of MMC results in fewer surgical failures at 12 months compared to No mitomycin-C, No 5-fluorouracil, placebo or sham. The benefits of 5-FU versus placebo or control is limited to low risk patients only. Furthermore, while the cost per unit of MMC is greater than 5-FU, utilizing an ARR 5%, (NNT 20) for MMC versus 5-FU, the cost of treating 20 patients with intraoperative sponge application of MMC is R5000 to prevent 1 additional surgical failure that would result in a cost of R5500-7200 being averted for an Ahmed valve which is used in follow up surgery, as the current standard of care for patients with failed trabeculectomies.

Level of Evidence: MMC vs placebo or no antimetabolite (moderate certainty evidence) and MMC v 5-FU (low certainty of evidence

Review indicator: New evidence on efficacy or safety of MMC

NEMLC RECOMMENDATION (MEETING OF 30 November 2023): NEMLC supports the ERC's recommendation as stated above.

Monitoring and evaluation considerations

Research priorities

Additions to the STG are as tabulated below:

18.8 SURGICAL AND DIAGNOSTIC PRODUCTS

Ocular peri-operative pharmaceutical products

- Sodium hyaluronate 10 mg/mL
- Acetylcholine chloride (for intra-ocular irrigation)
- Sterile intraocular irrigating solution
- Hyaluronidase 1500IU injection (adjunct to anaesthesia for cataract surgery)
- Mitomycin C 2mg injection (for sponge application during trabeculectomy for glaucoma management)

18.9 DRY EYE DISEASE

Description: *Amended*
General measures: *Amended*
The description of dry eye disease has been amended as follows: '*Dry eye occurs when there is inadequate tear volume or function. It is a multifactorial disease of the ocular surface.'*

The section on general measures for the management of dry eye disease has been amended with additions as tabulated below:

GENERAL MEASURES
The management of dry eye involves controlling the symptoms, since the disease is generally not curable. Management encompasses both pharmacologic and non-pharmacologic approaches. Relieve symptoms with warm compresses, i.e. a clean moistened cloth over the eyes for at least 1 minute two to three times per day. Patients should be educated to avoid over the counter topical medications, many of which exacerbate dryness, and control their environmental factors (e.g. encourage frequent blinking during visually attentive tasks, avoid air conditioners or heating, use humidifiers

REQUEST FOR NEW STGs

External comments have been received motivating for the development of new STGs for both the PHC and AH Eye chapters. The Eye chapters have been identified for priority review in the next review cycle. The following will be considered for prioritization in the PHC Eye chapter:

- Vernal Keratoconjunctivitis (VKC)
- Keratoconus
- Ocular Surface squamous neoplasia
- Peripheral ulcerative keratitis
- Stevens-Johnson syndrome (with ocular involvement)

Existing STGs to be considered for prioritization include:

- Section 18.2 Prevention of post-surgical endopthalmitis
- Section 18.3 Glaucoma management
- Section 18.5.2 Bacterial keratitis – empiric antibiotic therapy
- Section 18.8 Surgical and diagnostic products such as:
  - Viscoelastics
  - Local anaesthetics
  - Phenylephrine hydrochloride 10% minims to dilate the pupil in floppy iris syndrome (for intra-ocular injection)
  - Tropicamide 1% minims for intra-ocular use (to dilate the pupil during surgery)
  - Cyclopentolate hydrochloride 1% minims for intra-ocular use (to dilate pupil during surgery)
  - Preservative free moxifloxacin 0.5%, 0.1ml injected intra-ocular at the end of intra-ocular surgery (for prophylaxis of endophthalmitis)
  - Riboflavin 0.1% for use during collagen cross linking for keratoconus (isotonic and hypotonic)
  - Trypan blue 0.06 - 0.15% for staining the anterior capsule during cataract surgery
  - Preservative free triamcinolone for staining the vitreous during cataract and retinal surgery
  - MMC or 5FU as adjuvant treatment for conjunctival carcinoma.