SESLHD GUIDELINE COVER SHEET

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SUMMARY	This guideline describes the staff responsibilities and assessment required when monitoring patients for ocular toxicity when undergoing ethambutol treatment.

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Assessment of Ethambutol Optic Nerve Toxicity

Section 1 - Background

Ethambutol is a common medicine used in the treatment of tuberculosis (TB) and non-tuberculosis mycobacterial disease. Ocular toxicity has been associated with the drug, in some cases causing *Ethambutol-induced Optic Neuropathy (EON)*, which is rare, however is the most common side-effect of the drug[1].

Ocular toxicity is dose-related with an incidence of approximately 1% at standard TB doses (15 mg/kg/day or less)[1]. The risk of ocular toxicity increases substantially in patients who require higher doses and/or prolonged therapy, with poor renal function, smokers and those who take concurrent anti-retroviral therapy[1].

EON typically presents within 2-5 months following commencement of ethambutol but may occur within days[2]. Symptoms can be highly variable and may initially be unilateral[2].

Common signs of EON can include reduction of visual acuity, colour vision impairment either red-green dyschromatopsia or blue yellow dyschromatopsia with the latter being most common[3]. EON also causes visual field loss including central/paracentral scotoma (centrocecal scotomas), however bitemporal visual field defects have also been reported due to the drug's effects on the optic chiasm[2], and peripheral constriction of visual fields have also been reported[2].

Subclinical toxicity has been reported to occur and can be detected by loss of retinal nerve fibre layer (RNFL) and increased latency of visually evoked potentials (VEP)[4]. Medication duration, age and cumulative dose have been reported as a strong risk factor for subclinical EON[4].

If EON is suspected, patients should be referred to the specialist who prescribed the medication for immediate cessation or reduction in dosing[1]. Visual recovery may occur taking from weeks to months, however cessation of ethambutol still carries of risk of toxicity up to 3 months following cessation of the drug. Between 30 – 64% of patients will show some recovery of EON if detected early and ethambutol is ceased[1].

Section 2 - Definitions

Term	Definition
Orthoptist	Orthoptists are allied health professionals who specialise in the study of ocular motility and visual development. Their primary role is to investigate and diagnose visual system dysfunctions involving vision, eye movement, eye alignment and binocularity in children and adults. Orthoptics focuses on the non-surgical treatment of amblyopia and strabismus. They specialise in visual function assessment and neuromuscular anomalies.
Anti-Retroviral Therapy	Drugs that inhibit the multiplication of retroviruses such as HIV
Ethambutol (Myambutol)	Ethambutol hydrochloride (Myambutol®) is a broad spectrum antibiotic; commonly used in the treatment of tuberculosis (Mycobacterium *tuberculosis*) and, other infectious agents including Mycobacterium *avium* complex and Mycobacterium *kansasii*. There is a risk that ethambutol can cause toxic effects to the optic nerve potentially causing irreversible vision impairment.
Ethambutol-induced Optic Neuropathy (EON)	This refers to the neurotoxic effect ethambutol has on the optic nerve. It is a form of toxic optic neuropathy.
Humphrey Visual field test (HVF)	A non-invasive test for assessing a patients' peripheral vision using automated quantitative threshold testing.
Nontuberculous mycobacteria	Does not cause tuberculosis, it can cause changes in the lungs but can resemble tuberculosis.
Spectral Domain Optical Coherence Topography (SD-OCT)	Is a non-invasive high resolution imaging test used to take cross section images of the retina
Subclinical toxicity	Lack of development signs and symptoms of toxicity/EON but with changes on ophthalmic examination or diagnostic assessment.
Toxic Optic Neuropathy	Refers to impairment due to optic nerve damage caused by a toxin. Toxic Optic Neuropathy is characterised by bilateral, usually symmetric vision loss, papillo-macular bundle damage, central or centrocecal scotoma and reduced colour vision.
Tuberculosis	A bacterial disease that can affect the lungs, brain, kidneys, spine and skin.

Section 3 - Responsibilities

Orthoptists are responsible for:

- Ensuring the assessment they perform for patients on ethambutol treatment align with this guideline and when visual assessments are modified or not consistent with this guideline, to ensure documentation in the healthcare record reflects this.
- Triaging referrals for patients on ethambutol requiring investigation for ocular toxicity (SSEH only). This includes ensuring patients do not attend for assessment unless they are no longer considered a public health risk as outlined in this guideline.
- Orthoptic assessments meeting the standard outlined in the Orthoptic Competency Standards[7].
- Orthoptists are to perform patient identification in accordance to protocol outlined in the NSW Health Policy Directive PD2017_032 - Clinical Procedure Safety, and document that this has occurred in the patient's healthcare record/eMR.
- Documentation of clinical assessments in patients' healthcare record complies with NSW Health Policy Directive PD2012_069 – Health Care Records - Documentation and Management and SESLHDPDR/336 – Documentation in the Health Care Record.
- Clinical handover to appropriate ophthalmology team for any incidental findings on assessment.

Nurses are responsible for:

- Ensuring the assessment they perform for patients on ethambutol treatment align with this guideline and when visual assessments are modified or not consistent with this guideline, to ensure documentation in the healthcare record reflects this.
- Triaging referrals for patients on ethambutol requiring investigation for ocular toxicity. This includes ensuring patients do not attend for assessment unless they are no longer considered a public health risk as outlined in this guideline.
- Performing history and visual acuity where appropriate.
- Clinical handover to orthoptists or ophthalmologists when required.
- Performing patient identification in accordance to protocol outlined in the NSW Health Policy Directive PD2017_032 - Clinical Procedure Safety, and document that this has occurred in the patient's healthcare record/eMR.
- Documentation of clinical assessments in patients' healthcare record complies with NSW Health Policy Directive PD2012_069 – Health Care Records - Documentation and Management and SESLHDPDR/336 – Documentation in the Health Care Record.
- Clinical handover to ophthalmology team and orthoptists when required.

Medical staff are responsible for:

- Ensuring the assessment they perform for patients on ethambutol treatment align with this guideline and when visual assessments are modified or not consistent with this guideline, to ensure documentation in the healthcare record reflects this.
- Performing patient identification in accordance to protocol outlined in the NSW Health Policy Directive PD2017_032 - Clinical Procedure Safety, and document that this has occurred in the patient's healthcare record/eMR.
- Documentation of clinical assessments in patients' healthcare record complies with NSW Health Policy Directive PD2012_069 – Health Care Records - Documentation and Management and SESLHDPDR/336 – Documentation in the Health Care Record.
- Clinical handover when required.
- Medical staff to document recommended review or follow up plan, including relevant referrals for further investigation.

Section 4 – Training Requirements

Orthoptists must have completed competency assessments for the following:

- Optical Coherence Tomography (OCT)
- Humphrey Visual Field (HVF)

Section 5 – Clinical Assessment Guidelines

Patients referred for baseline and follow up monitoring for require assessment by an orthoptist followed by review with Ophthalmologist/ registrar.

For infection prevention and control reasons, baseline assessment should not occur until the patient no longer requires airborne precautions/TB isolation (i.e. no longer considered a public health risk) by the TB Coordinator or treating physician, which is typically following at least 14 days of treatment[8, 9].

If a patient requires a baseline assessment but has not yet been identified as non-infectious and is still considered a public health risk by the TB Coordinator or treating physician, a risk assessment should be completed. The risk assessment requires input from the TB Coordinator, TB treating physician, local Infection control team, and ophthalmology team.

If baseline assessment is deemed necessary following risk assessment, all infection control procedures should be adhered to as per NSW Health Policy Directive PD2017_013 - Infection Prevention and Control Policy. Patients with pulmonary Tuberculosis who are deemed infectious are not to have a HVF assessment due to risk of infection transmission[9] and inability to disinfect the bowl on the machine (as per manufacturer recommendations).

Baseline assessments and follow up assessments and should include (unless otherwise indicated by ophthalmologist team)[4,5]:

- History – including ethambutol dose, duration of use, previous ocular history and any recent vision changes*
- Best-corrected visual acuity (BCVA)*
  - If BCVA is less than 6/6, VA should be then tested using a pinhole. If there is an improvement of VA of 2 lines or more with pinhole, a subjective refraction should be performed to determine potential BCVA
- Colour vision assessment – Farnsworth Munsell test (15 or 28 Hue) or City University colour vision test
- Humphrey Visual Field assessment– 24-2 threshold testing
- Spectral Domain (SD) OCT – Macula and Retinal Nerve Fibre Layer (RNFL) scan
- Pupil Assessment (prior to dilation)

Following assessment with the Orthoptist, the patient requires a dilated fundus examination with the relevant ophthalmic team/clinic to exclude other causes of visual loss including retinal disease[10].

Timeline for baseline and review assessments

Patient require baseline assessment within 2 months of commencing ethambutol, given that EON doesn't typically present until 2-5 months after starting treatment[2].

Follow up is recommended every 3 months whilst the patient remains on a low dose treatment. However, monthly reviews are recommended for patients with doses above 15 mg/kg/day[11].

If there are signs of EON or visual symptoms, patients require urgent visual assessment. Patients should be reviewed for the duration they are on treatment, for 3 months following cessation of ethambutol unless otherwise indicated by the ophthalmology team[11].

Factors to be considered in determining appropriate review period include:

- Medication dose and duration of treatment
- Renal function
- concurrent anti-retroviral treatment
- smoker
- Pre-existing visual or ocular conditions

Section 6 - Documentation

All documentation must comply with the NSW Health Policy Directive PD2012_069 - Health Care Records – Documentation and Management and SESLHDPDR/336 – Documentation in the Health Care Record.

Prior to commencing a patient assessment the clinician is required to perform patient identification in accordance to protocol outlined in the NSW Health Policy Directive PD2017_032 - Clinical Procedure Safety, and document that this has occurred in the patient's healthcare record/eMR.

In the event there is deviation from the recommendations in this guideline, it is expected that the clinician clearly documents the reason for this.

Section 7 – References

1. Chamberlain et al (2017) Ethambutol optic neuropathy, Current Opinion in Ophthalmology, 28(6), p545-551.

2. Royal College of Ophthalmologists Statement on Ethambutol toxicity; Quality and Safety Group, 31st October 2017 - https://www.rcophth.ac.uk/2017/10/rcophth-statement-on-ethambutol-toxicity/ (Accessed on 24 August 2021)

3. Koul P. A. (2015). Ocular toxicity with ethambutol therapy: Timely recaution. Lung India : official organ of Indian Chest Society, 32(1), 1–3

4. Mandal, S., Saxena, R., Dhiman, R., Mohan, A., Padhy, S.K., Phuljhele, S., Sharma, P., & Guleria, R. (2021, July). Prospective study to evaluate incidence and indicators for early detection of ethambutol toxicity. British Journal of Ophthalmology, 105(7), 1024-1028

5. Lin, K. W., Lee, J. Y., Rhiu, S., & Choi, D. G. (2019). Longitudinal evaluation of visual function and structure for detection of subclinical Ethambutol-induced optic neuropathy. PloS one, 14(4), e0215297.

6. Orthoptic Scope of Practice; Orthoptics Australia

7. Australian Orthoptic Board Competency Standards for Orthoptists, 20th July 2015

8. SESLHDPR/502 - Tuberculosis: Patient Management

9. Tuberculosis – CDNA National Guidelines for Public Health Units (3 March 2022)

10. Ethambutol Optic Neuropathy (last updated March 2021) - https://eyewiki.aao.org/Ethambutol_Optic_Neuropathy

11. The ocular adverse effects of oral drugs; Aust Prescr 2021;44:129-36; 2 August 2021 DOI: 10.18773/austprescr.2021.028; NPS medicinewise; Publications https://www.nps.org.au/australian-prescriber/articles/the-ocular-adverse-effects-of-oral-drugs#r20

Version and Approval History

Date	Version	Version and approval notes
July 2023	1	New document. Endorsed at SSEH Medication Safety Committee, District Drug and Therapeutic Committee and District Clinical and Quality Council.