A GUIDE TO

deprescribing

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GLAUCOMA EYE DROPS

KEY POINTS

- **Glaucoma treatment is considered lifelong; the treating ophthalmologist should be included in the process of considering deprescribing of glaucoma treatment.**
- **Patients who have mild glaucoma or ocular hypertension would be at minimal risk if they cease their medications in the short to medium term.**
- **For a patient who is completely asymptomatic (or who has a mild, asymptomatic visual field defect) from glaucoma, it would probably take quite some time before they would experience symptomatic vision loss even without treatment - unless the pressure is very high.**
- **Consider discontinuation in patients who have significant difficulty with medication administration and whose life expectancy may be limited.**
- **Patients who have advanced glaucoma may lose vision if they cease their medications.**
- **If patients have symptomatic vision loss from glaucoma (i.e. the patient is aware that vision is fading) this would indicate that the glaucoma is advanced, and medications should be continued**

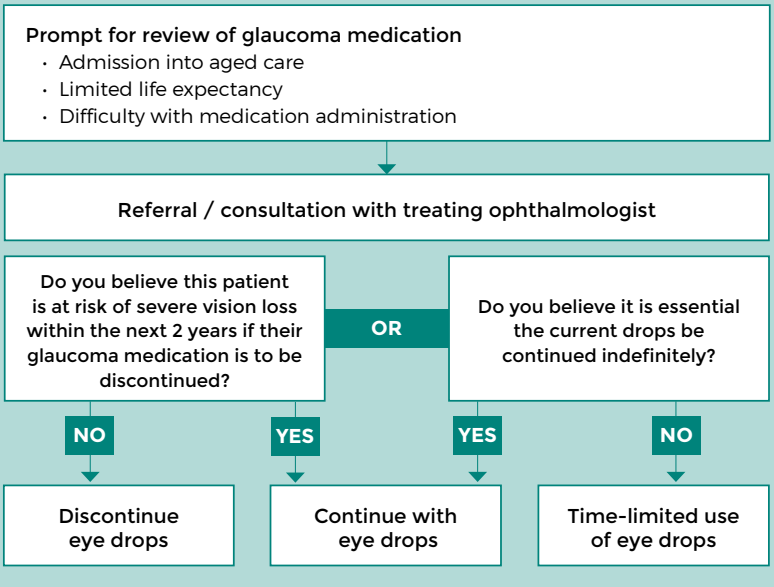
CONTEXT

This guide considers the use of topical ophthalmic agents for open-angle glaucoma, particularly in patients with a limited life expectancy and those with difficulties relating to administration of eye drops.

RECOMMENDED DEPRESCRIBING STRATEGY

- Review of glaucoma medications should be considered when a person has limited life expectancy and/or is having issues with the drops. In particular, topical side-effects from glaucoma medications can adversely affect quality of life in many cases.
- When glaucoma drops are ceased, it is likely the intraocular pressure (IOP) will rise to pre-treatment levels. This is asymptomatic and may not be vision-threatening for people with mild glaucoma or ocular hypertension, assuming a limited life expectancy. People who have advanced glaucoma, may lose vision if medications are ceased. Thus it is important to assess the degree of optic nerve damage.
- If a person goes into residential care it may become impractical to monitor the IOP and glaucoma progression, however this is likely to be relatively gradual. Where other medical and cognitive comorbidities predominate ongoing glaucoma management may be a lower priority.

DEPRESCRIBING ALGORITHM



BACKGROUND

Glaucoma is the most common neurodegenerative disease of the optic nerve, with a prevalence of about 3%.[1] This means that about 150,000 Australians, about 75% of whom are aged over 70, have glaucoma. This number will double over the next 30 years as our population ages.[2]

Glaucoma is characterised by optic neuropathy, optic disc changes and irreversible, progressive visual field loss caused by progressive degeneration of retinal ganglion cells. Degeneration results in cupping, a characteristic appearance of the optic disc and visual loss.[3] Increased intraocular pressure (IOP) or ocular hypertension (although not a defining characteristic) is the only modifiable risk factor for glaucoma.

Although the pathogenesis of glaucoma is not fully understood, the level of intraocular pressure is related to retinal ganglion cell death. The balance between secretion of aqueous humor by the ciliary body and its drainage through 2 independent pathways—the trabecular meshwork and uveoscleral outflow pathway—determines the IOP. In patients with open-angle glaucoma, there is increased resistance to aqueous outflow through the trabecular meshwork. In contrast, the access to the drainage pathways is obstructed typically by the iris in patients with angle-closure glaucoma (see **Figure 1**).

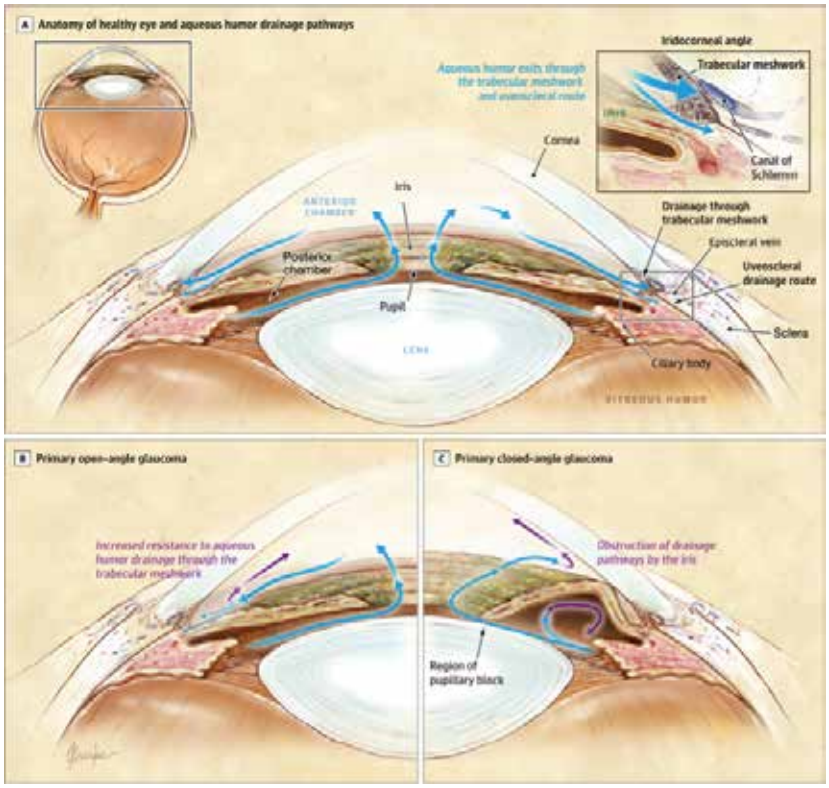


Figure 1: Aqueous Humor Drainage Pathways of Healthy and Glaucomatous Eyes.[3]

Although elevated IOP is a consistent risk factor for the presence of glaucoma, several population-based studies found IOP was lower than 22mmHg in 25-50% of individuals with glaucoma.[3] Despite the strong association between elevated IOP and glaucoma, substantial numbers of people with elevated IOP never develop glaucoma.[3] Presence of characteristic visual field defects can confirm the diagnosis, but as many as 30-50% of retinal ganglion cells may be lost before defects are detectable by standard visual field testing.[3]

TARGET IOPs[4]

- A minimum target IOP reduction of 20% in patients with suspected primary open angle glaucoma with high-risk status. It is advised that IOP remains under 24mmHg. Those without high-risk factors can simply be observed.
- A minimum target IOP reduction of 20% in patients with early and established primary open angle glaucoma without high-risk status. It is advised that IOP remains under 16-19mmHg.
- A minimum target IOP reduction of 30% in patients with established primary open angle glaucoma with high-risk status, and patients with advanced primary open angle glaucoma.
- Maintenance of IOP below 18mmHg in patients with established primary open angle glaucoma, and even lower to below 15mmHg in patients with advanced primary open angle glaucoma.

RISK FACTORS

The risk of glaucoma is highest when examination reveals an increased cup-disk ratio (CDR), CDR asymmetry, disc haemorrhage, or elevated intraocular pressure. Other risk factors that may warrant referral to optometry / ophthalmological review include the following: [3]

- Older age
- Family history of glaucoma
- Black race
- Use of systemic or topical corticosteroids
- High intraocular pressure

EFFICACY

Topical drugs are first-line treatment (either alone or in combination). They reduce IOP by decreasing production of aqueous humor and/or by increasing its outflow. The ultimate objective of glaucoma treatments is to preserve the remaining visual field (i.e., to stop visual field defect progression).

The Ocular Hypertension Treatment Study randomized patients with ocular hypertension (high IOP but no clinical signs of glaucomatous damage to the optic nerve or visual field) to treatment vs no treatment. At the end of 5 years of follow-up, 4.4% of patients in the medication group vs 9.5% in the untreated group developed signs of glaucoma.[5] The Early Manifest Glaucoma Trial also randomized patients to treatment vs no treatment; with all patients having a clear diagnosis of glaucoma at the baseline visit. After a median follow-up of 6 years, progression was less frequent in the treatment group (45%) than in the control group (62%).[6]

This highlights that progression can be slow for some individuals and that review of medication treatment is appropriate in individuals whose life expectancy might be limited, or in whom adverse effects of difficulty with medication administration may be a problem.

A target IOP for treatment is determined based upon the patient's risk factors for glaucoma progression, the amount of initial damage, rate of deterioration, risk factors for progression, life expectancy, and potential for adverse effects from treatment. In general, the initial target aims for 20% to 50% reduction in pressure; however, the target pressure needs to be continuously reassessed during patient follow-up, depending on the evolution of the disease.

The target IOP should be achieved with the fewest medications and minimum adverse effects. Several different classes of pressure-lowering medications are available (**Table 1**). Medication choice may be influenced by cost, adverse effects, and dosing schedules. In general, prostaglandin analogues are the first line of medical therapy. These drugs reduce IOP by reducing outflow resistance resulting in increased aqueous humor flow through the uveoscleral pathway.

Other classes of topical medications are less effective in lowering IOP than prostaglandin analogues. They are used as second-line agents or when there is a contraindication or intolerance to the use of prostaglandin analogues. Laser or surgical interventions are considered if drug treatment is inadequate or intolerable.

Please refer to **Table 1** on page 4 for more information about topical medications for glaucoma.

ADVERSE EFFECTS

The prostaglandin analogues are administered once nightly and generally have few systemic adverse effects. However, they can cause local adverse effects such as conjunctival hyperaemia, elongation and darkening of eyelashes, loss of orbital fat (so-called prostaglandin-associated periorbitopathy), induced iris darkening, and periocular skin pigmentation. Some of these other agents, such as β-adrenergic blockers, may have significant systemic adverse effects and can be contraindicated in patients with history of chronic pulmonary obstructive disease, asthma, or bradycardia.

Eye drops contain main therapeutic agents, along with various additives, including preservatives. It is worth noting that benzalkonium, purite and polyquad preservative are considered gentler. Most preservatives also act as surfactants which destabilize bacterial cell membranes. This causes destruction of the cell membrane, inhibition of cell growth, and reduction of cell adhesiveness. However, preservatives also exert these effects on normal corneal and conjunctival cells, resulting in ocular surface disorders. These include superficial punctate keratitis, corneal erosion, conjunctival allergy, conjunctival injection, and anterior chamber inflammation.[7]

Correct instillation technique has been identified as a problem for patients using glaucoma medications. Many patients do not wait a sufficient time between instilling their different medications, with approximately 5 minutes considered necessary. Over-administration of drops can also become a problem when multiple attempts are needed to deliver one drop to each eye. One study revealed that more than 37% of patients instilled more than two drops per eye, when the intent was to instill just one. In the same study, more than 20% of patients instilled more than three drops per eye.[8]

DRUG CLASS	MECHANISM OF ACTION/ DOSING	OPHTHALMIC SIDE EFFECTS	SYSTEMIC SIDE EFFECTS
prostaglandin analogues (bimatoprost, latanoprost, tafluprost, travoprost)	▪ once daily at night, though can be used in the morning but are less effective (less effective if given more than once daily) ▪ increase in uveoscleral outflow of aqueous humor ▪ first line therapy – the most effective class of medications	▪ conjunctival hyperaemia (less with latanoprost) ▪ lengthening and darkening of eyelashes ▪ brown discoloration of the iris ▪ uveitis ▪ macular oedema ▪ orbital fat atrophy ▪ periocular skin pigmentation ▪ blurred vision ▪ burning, stinging ▪ foreign body sensation	▪ unlikely
beta-blockers (betaxolol, timolol)	▪ 1-2 times daily ▪ reduction of aqueous humor production	▪ burning & stinging ▪ photophobia ▪ itching ▪ tearing ▪ decreased corneal sensitivity ▪ hyperaemia ▪ diplopia	▪ bronchospasm ▪ hypotension ▪ bradycardia ▪ heart block ▪ mask hypoglycaemia ▪ impotence ▪ fatigue ▪ depression ▪ alopecia ▪ confusion
alpha2 agonists (apraclonidine, brimonidine)	▪ 2-3 times daily ▪ initial reduction of aqueous humor production with subsequent effect of increase in outflow ▪ second line treatment ▪ tachyphylaxis can develop	▪ allergic reaction is relatively common ▪ ocular irritation ▪ dry eyes ▪ foreign-body sensation ▪ hyperaemia ▪ lid retraction ▪ conjunctival blanching ▪ photophobia	▪ dry mouth ▪ headache ▪ fatigue ▪ drowsiness ▪ bradycardia ▪ hypotension ▪ apnoea ▪ taste disturbance ▪ syncope
carbonic anhydrase inhibitors (brinzolamide, dorzolamide, acetazolamide)	▪ 2-3 times daily ▪ reduction of aqueous humor production ▪ second line treatment ▪ acetazolamide used in more acute and serious glaucoma	▪ burning & stinging ▪ itching ▪ blepharoconjunctivitis ▪ dry eyes	▪ bitter taste ▪ headache ▪ nausea ▪ fatigue ▪ dry mouth ▪ dizziness ▪ anaphylaxis
cholinergic (pilocarpine)	▪ 3-4 times daily ▪ increase in aqueous humor outflow	▪ eye pain ▪ decrease in night vision ▪ blurred vision ▪ myopic shift ▪ miosis ▪ retinal detachment ▪ lacrimation	▪ headache ▪ salivation ▪ urinary frequency ▪ diarrhoea ▪ abdominal cramps ▪ bronchospasm ▪ hypotension ▪ bradycardia ▪ nausea & vomiting

Table 1: Topical ophthalmic medications for glaucoma

FACTORS TO CONSIDER

IN FAVOUR OF DEPRESCRIBING

The stage of disease can be graded considering the amount of disc damage. The optic discs may be graded in three zones: green, yellow or red. In the green zone, the patients do not have definite damage. When a patient is in the yellow zone, the optic nerve is damaged, but the person may still be asymptomatic. Finally, when a person is already in the red zone, there is already moderate to advanced damage and the person has visual disability. The patient may have decreased quality of life or impaired ability to perform daily activities.[9] Review of medication treatment may be appropriate in individuals whose life expectancy might be limited, or in whom adverse effects or difficulty with medication administration may be a problem.

ISSUES IN PREDICTING VISUAL FIELD PROGRESSION[10]

- The predictive value of IOP in determining whether the optic disc and/or visual field will deteriorate is almost non-existent unless the IOP is in a range which is always abnormal, that is above 35mmHg.[11]
- There is virtually no predictive value of an individual's IOP in determining who will become disabled;
- It is possible to prevent visual field loss in patients with glaucoma, yet many patients with glaucoma still get progressive visual field loss;
- Visual field changes are often misleading;
- The significance of glaucoma is a function of the severity of the disease and the duration of the disease

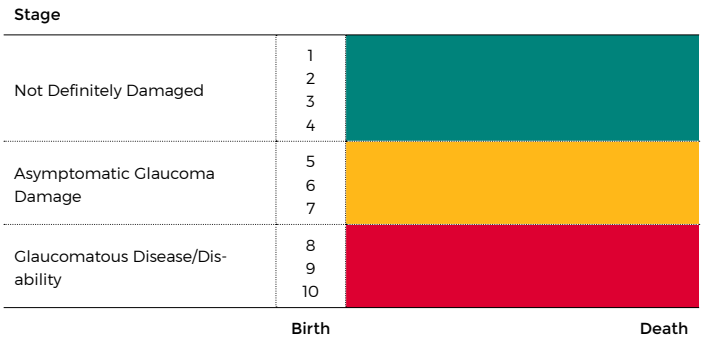


Figure 2: Glaucoma Colour Graph 'The Glaucoma Process'

AGAINST DEPRESCRIBING

Generally, glaucoma treatment is considered to be life-long unless there are changes to an individual's circumstances that prompt a review. Evidence indicates that factors associated with greater risk of glaucoma progression include[12]

- Elevated/ fluctuating IOP
- Optic disc haemorrhage
- An increased CDR or CDR asymmetry
- Increased severity of glaucomatous disc damage and
- Very low blood pressure.

These patients require greater reduction in IOP. It is worth noting that in a recent NHMRC review of the diagnosis and management of glaucoma it was concluded, "There is a paucity of information regarding the management of glaucoma in elderly patients such as those in nursing homes and aged care facilities. For example, beta-blockers have been shown to increase the risk of falls in the elderly, more research may be available to inform subsequent revisions of this guideline." [4]

FACTORS AGAINST DEPRESCRIBING GLAUCOMA MEDICATION:

- advanced disc cupping as documented by ophthalmologist
- advanced visual field loss (MD on humphrey static perimetry less than or equal to -15 dB)
- visual field defect involving the central part of the vision in one or both eyes
- loss of vision in one eye from glaucoma already
- known very high pre-treatment IOP (over 35mmHg)

Glaucoma medications should be continued where a person continues to:

- be able to read
- use their vision to perform tasks that improve their quality of life
- be able to articulate visual symptoms
- attend for ophthalmic investigations and examinations despite entrance into settings such as residential care.

DISCONTINUATION SYNDROMES

An increase in the patient's IOP would be asymptomatic however, the patient may experience visual field loss if the glaucoma is advanced. Cessation of glaucoma medications would not result in pain, though an elderly patient may have difficulty with expressing any changes to their vision in the setting of multiple comorbidities.

RESOURCES

- QUICK REFERENCE GUIDE
- GENERAL INFORMATION
- ALLOPURINOL
- ANTIHYPERTENSIVES
- ANTIPLATELET AGENTS
- ANTIPSYCHOTICS
- BENZODIAZEPINES
- BISPHOSPHONATES
- CHOLINESTERASE INHIBITORS
- GLAUCOMA EYE DROPS
- NSAIDS
- OPIOIDS
- PROTON PUMP INHIBITORS
- STATINS
- SULPHONYLUREAS
- VITAMIN D AND CALCIUM

AUTHORSHIP

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