OPEN ANGLE GLAUCOMA

CHI Formulary Development Project

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM- November 2023

To the CHI Original Open Angle Glaucoma Clinical Guidance- Issued May 2020

Contents

Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

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Abbreviations

5-FU	5-Fluorouracil
AAF	Acute Angle Closure
ACG	Angle Closure Glaucoma
AH	Aqueous Humor
ALT	Argon Laser Trabeculoplasty
BAC	Benzalkonium Chloride
CCT	Central Corneal Thickness
CHI	Council of Health Insurance
COAG	Chronic Open Angle Glaucoma
EGS	European Glaucoma Society
EMA	European Medicines Agency
IOP	Intra-Ocular Pressure
MMC	Mitomycin C
NICE	National Institute for Health and Care Excellence
OHT	Ocular Hypertension
PG	Pigmentary Glaucoma
PGA	Prostaglandin Analogue
POAG	Primary Open-Angle Glaucoma
PXFG	Pseudo Exfoliative Glaucoma
RNFL	Retinal Nerve Fiber Layer
SLT	Selective Laser Trabeculoplasty

Executive Summary

Open-angle glaucoma is a chronic and progressive optic neuropathy with multiple contributing factors, featuring an open angle in the anterior chamber of the eye, alterations in the optic nerve head, a gradual decline in peripheral vision, ultimately leading to central visual field impairment, which is irreversible[1].

Open angle glaucoma is divided into two big subcategories: **primary** open-angle glaucoma is a distinct category of glaucoma characterized by a normal-appearing open anterior chamber angle and elevated intraocular pressure, and it doesn't result from any other underlying condition. In cases where an identifiable underlying cause leads to elevated intraocular pressure, it is referred to as **secondary** glaucoma[2].

Factors that increase the risk of primary open-angle glaucoma encompass advancing age, African or Latino/Hispanic ethnicity, elevated intraocular pressure, a family history of glaucoma, reduced ocular perfusion pressure, type 2 diabetes mellitus, myopia, and a thin central cornea[3].

The characteristic of open-angle glaucoma is a slow, painless decline in vision[4].

Both primary and secondary glaucoma can be managed with medication, typically involving the prescription of eye drops and oral drugs. When dealing with secondary glaucoma, it's essential to address the underlying condition as well. If medication proves ineffective, alternative approaches such as laser therapy or minimally invasive glaucoma surgery may be considered to enhance fluid drainage[5].

Glaucoma stands as one of the prominent causes of blindness worldwide. The estimated worldwide prevalence of open-angle glaucoma is approximately 3.5% in individuals aged 40 to 80. In 2020, it was estimated that approximately 76 million people were affected by glaucoma, with projections suggesting this number will rise to 112 million by 2040. Additionally, the prevalence of glaucoma is influenced by racial factors, with open-angle glaucoma being more prevalent among black populations[6].

A study conducted in the Central Province of Saudi Arabia indicated a glaucoma prevalence of 5.6%, a rate consistent with findings reported in other Middle Eastern nations[7].

For the prevention of open angle glaucoma, it is advisable to have an eye check-up every 3-5 years once you reach the age of 40, and then annually after turning 60. Managing elevated eye pressure is crucial in reducing the risk of glaucoma. Maintaining a well-balanced diet and ensuring that blood pressure remains within the healthy range are essential. To prevent severe eye injuries, it is advised to always wear protective glasses[4].

CHI issued open angle glaucoma clinical guidance after thorough review of renowned international and national clinical guidelines in May 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI open angle glaucoma clinical guidance and seeks to offer guidance for the effective management of open angle glaucoma. It provides an **update on the open angle glaucoma guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update are summarized, by being the **update** of these guidelines: **NICE** guidelines for the diagnosis and management of glaucoma (**2022**), the American Academy of Ophthalmology Preferred Practice Patterns for primary open-angle glaucoma (**2020**) and for primary open-angle glaucoma suspect patients (**2020**), and the 5th edition of the European glaucoma society terminology and guidelines for glaucoma (**2021**), as well as the addition of a **new guideline** to the report such the Australian clinical practice guide for the diagnosis and management of open-angle glaucoma (**2020**)**.**

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is advisable to make sure that 5-fluorouracil and mannitol do not need "prior authorization (PA)" as a prescribing edit. Additionally, it is important to note that acetazolamide, levobunolol and befunolol have been withdrawn from SFDA and other alternatives are present on the market.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in Open angle glaucoma management.

Below is a table summarizing the major changes based on the different Open angle glaucoma guidelines used to issue this report:

Table 1. General Recommendations for the Management of Open Angle Glaucoma

Management of Open angle glaucoma	
General Recommendations	**Level of Evidence/Grade of Recommendation and Reference**
<u>Treatment for people with suspected chronic open-angle glaucoma (COAG)</u> Do not offer treatment to people with suspected COAG and intraocular pressure (IOP) less than 24	Not graded NICE (2022)[8]

mmHg unless they are at risk of visual impairment within their lifetime.	
Prostaglandin analogs are the most frequently prescribed eye drops for lowering IOP in patients with glaucoma because they are most efficacious and well tolerated, and they need to be instilled only once daily. Therefore, prostaglandin analogs are often selected as initial medical therapy unless other considerations, such as contraindications, cost, side effects, intolerance, or patient refusal preclude this.	Not graded American Academy of Ophthalmology (2020)[3,9]
Pregnancy In general, most ophthalmologists avoid the use of prostaglandins during pregnancy because of the theoretical risk of premature labor, but these medications may be considered for use in the breastfeeding mother. Oral carbonic anhydrase inhibitors have been shown to cause teratogenicity when delivered in high doses to animals.	Not graded American Academy of Ophthalmology (2020)[3,9]
Breastfeeding Some topical glaucoma medications have been detected in breast milk, such as timolol, carbonic anhydrase inhibitors, and brimonidine. The data are inconsistent as to whether timolol poses a threat to the breastfeeding infant. The American Academy of Pediatrics has approved the use of both oral and topical forms of carbonic anhydrase inhibitors during lactation, although the infant should be carefully monitored when the former are used. Brimonidine is known to cross the blood-brain barrier and can cause apnea in infants. For this reason, it is usually recommended that the medication not be used in mothers who are breastfeeding.	Not graded American Academy of Ophthalmology (2020)[3,9]
Laser trabeculoplasty Laser trabeculoplasty may be used as initial or adjunctive therapy in patients with POAG. Laser trabeculoplasty lowers IOP by improving aqueous outflow and can be performed using argon or solid-state lasers.	Not graded American Academy of Ophthalmology (2020)[3,9]

A target IOP should be set as a treatment goal at diagnosis. Target IOP should be updated at each monitoring visit on the basis of changes in glaucoma or other ocular or systemic diseases.	Level of evidence: Low Strength of recommendation: Strong European Glaucoma Society (2021)[6]
Selective laser trabeculoplasty (SLT) can be offered as a first-choice treatment for open angle glaucoma.	Level of evidence: Moderate (only one high quality trial, LiGHT) Strength of recommendation: Strong European Glaucoma Society (2021)[6]
Trabeculectomy augmented with antifibrotic agents is recommended as an initial surgical treatment for open angle glaucoma.	Level of evidence: Low Strength of recommendation: Strong European Glaucoma Society (2021)[6]
Secondary open angle glaucoma due to ocular trauma treatment: • Anti-inflammatory medication • Topical and systemic IOP lowering medication • Long-term IOP lowering and follow up in the presence of permanent anterior segment damage • Glaucoma surgery	Not graded European Glaucoma Society (2021)[6]
Topical pharmacotherapy is generally considered the mainstay of glaucoma treatment, particularly for optometrists. Medications for treating glaucoma are divided into several classes, depending on their mechanisms of action. Currently, these include: • Prostaglandin analogues • Beta-blockers • Alpha2-agonists • Carbonic anhydrase inhibitors • Parasympathomimetics	Not graded Australian Glaucoma Clinical Practice Guide (2020)[10]
Netarsudil 0.02% is an antiglaucoma medication in the rho kinase class. It primarily acts on trabecular	Not graded

meshwork cells, preventing assembly and stabilization of actin fibers, to increase the pore size and outflow and subsequently reduce IOP. However, they also increase blood vessel diameter reducing resistance to aqueous outflow and inhibit norepinephrine (which is thought to mimic alpha 2 agonists) and reduce aqueous production.	Australian Glaucoma Clinical Practice Guide (2020)[10]

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **Open angle glaucoma clinical and therapeutic management.**

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Open angle glaucoma report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This section contains the **updated versions** of the guidelines mentioned in the May 2020 CHI Open angle glaucoma Report and the corresponding recommendations:

Table 2. Guidelines Requiring Revision

Guidelines requiring revision	
Old versions	**Updated versions**
Glaucoma: diagnosis and management **NICE** guideline Published: 1 November **2017**	Glaucoma: diagnosis and management NICE (published 2017, updated **2022**)[8]
2016 by the **American Academy of Ophthalmology** Primary Open-Angle Glaucoma.	**American Academy of Ophthalmology**: Primary Open-Angle Glaucoma Preferred Practice Pattern (**2020**)[9] and Primary Open-Angle Glaucoma Suspect Preferred Practice Pattern (**2020**)[3]
2014 European society of glaucoma: Terminology and guidelines for glaucoma	**European Glaucoma Society**- Terminology and Guidelines for Glaucoma, 5th Edition (**2021**)[6]

1.1.1 NICE Guidance – Glaucoma: Diagnosis and Management (Published 2017, Updated 2022)

The National Institute for Health and Care Excellence (NICE) issued a 2022 update of the original 2017 guidance on the diagnosis and management of glaucoma[8]. The recommendations concerning glaucoma are the following:

Initial treatment for people with ocular hypertension (OHT):

- Offer 360° selective laser trabeculoplasty (SLT) to people with newly diagnosed OHT with IOP of 24 mmHg or more (excluding cases associated with pigment dispersion syndrome) if they are at risk of visual impairment within their lifetime. To help inform their decision, tell people:
    - That having 360° SLT can delay the need for eye drops and can reduce but does not remove the chance they will be needed at all
    - How long it may take for their IOP to improve after the procedure
    - About 360° SLT-specific side effects and complications and how long they are likely to last
    - That a second 360° SLT procedure may be needed at a later date.
- Consider a second 360° SLT for people with OHT if the effect of an initial successful SLT has subsequently reduced over time.
- Offer a generic prostaglandin analogue (PGA) to people with OHT with IOP of 24 mmHg or more if they are at risk of visual impairment within their lifetime and:
    - They choose not to have 360° SLT or
    - 360° SLT is not suitable or
    - They are waiting for 360° SLT and need an interim treatment or
    - They have had 360° SLT but need additional treatment to reduce their IOP sufficiently to prevent the risk of visual impairment.

➔ Demonstrate correct eye drop installation technique and observe the person using the correct technique when eye drops are first prescribed.

Ongoing treatment for people with OHT

- Offer another pharmacological treatment to people with an IOP of 24 mmHg or more who cannot tolerate their current treatment. The first choice should be an alternative generic PGA, and if this is not tolerated, offer a beta-blocker. If neither of these options is tolerated, offer a non-generic PGA, carbonic

anhydrase inhibitor, sympathomimetic, miotic or a combination of treatments.

- Refer people to a consultant ophthalmologist to discuss other options if their IOP cannot be reduced sufficiently with 360° SLT or pharmacological treatment or both to prevent the risk of progression to sight loss.
- Offer preservative-free eye drops to people who have an allergy to preservatives or people with clinically significant and symptomatic ocular surface disease, but only if they are at high risk of conversion to chronic open-angle glaucoma (COAG).

Treatment for people with suspected COAG

- Do not offer treatment to people with suspected COAG and IOP less than 24 mmHg unless they are at risk of visual impairment within their lifetime. Advise people to continue regular visits to their primary eye care professional, at clinically appropriate intervals.

Treatment for people with COAG

- Offer people with advanced COAG, glaucoma surgery with pharmacological augmentation (MMC) as indicated. Give them information on the risks and benefits of surgery. MMC is here off label.
- Offer people who present with advanced COAG and who are listed for glaucoma surgery, interim treatment with a generic PGA.

Initial treatment for people with COAG

- Offer 360° selective laser trabeculoplasty (SLT) to people with newly diagnosed COAG with IOP of 24 mmHg or more (excluding cases associated with pigment dispersion syndrome) if they are at risk of visual impairment within their lifetime. To help inform their decision, tell people:
    - That having 360° SLT can delay the need for eye drops and can reduce but does not remove the chance they will be needed at all
    - How long it may take for their IOP to improve after the procedure
    - About 360° SLT-specific side effects and complications and how long they are likely to last
    - That a second 360° SLT procedure may be needed at a later date.
- Consider a second 360° SLT for people with COAG if the effect of an initial successful SLT has subsequently reduced over time. (same recommendations as OHT)

- Offer a generic PGA to people with COAG if:
    - They choose not to have 360° SLT or
    - 360° SLT is not suitable or
    - They are waiting for an 360° SLT and need an interim treatment or
    - They have previously had 360° SLT but need additional treatment to reduce their IOP sufficiently to prevent the risk of visual impairment.

➔ Demonstrate correct eye drop installation technique and observe the patient using the technique when eye drops are first prescribed.

Ongoing treatment for people with COAG

- Ask about adherence to treatment and check the eye drop instillation technique in people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss, despite pharmacological treatment with a generic PGA.
- Offer 1 of the following to people with satisfactory adherence to treatment and eye drop instillation technique whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss:
    - a medicine from another therapeutic class (a beta-blocker, carbonic anhydrase inhibitor or sympathomimetic); topical medicines from different therapeutic classes may be needed at the same time to control IOP or
    - 360° SLT or
    - glaucoma surgery with pharmacological augmentation (MMC) as indicated. (MMC is off label here)
- Consider 360° SLT or glaucoma surgery with pharmacological augmentation (MMC) as indicated for people with COAG who are at risk of progressing to sight loss despite treatment with medicines from 2 therapeutic classes. Give them information on the risks and benefits of surgery.
- Consider 1 of the following for people with COAG who cannot tolerate a pharmacological treatment:
    - a medicine from another therapeutic class (a beta-blocker, carbonic anhydrase inhibitor or sympathomimetic) or
    - preservative-free eye drops if there is evidence that the person is allergic to the preservative or has clinically significant and symptomatic ocular surface disease.

    - After treatment with medicines from 2 therapeutic classes, consider 360° SLT or glaucoma surgery with pharmacological augmentation (MMC) as indicated. MMC is off label here.
- Offer 1 of the following to people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss after glaucoma surgery:
    - pharmacological treatment; topical medicines from different therapeutic classes may be needed at the same time to control IOP or
    - further glaucoma surgery or
    - 360° SLT or
    - cyclodiode laser treatment.
- Offer 1 of the following to people with COAG (including advanced COAG) who prefer not to have glaucoma surgery or for whom glaucoma surgery is not suitable:
    - pharmacological treatment; topical medicines from different therapeutic classes may be needed at the same time to control IOP or
    - 360° SLT (for example in people with systemic comorbidities) or
    - cyclodiode laser treatment.

1.1.2 American Academy of Ophthalmology Preferred Practice Patterns (2020)

In 2020, the American Academy of Ophthalmology published two preferred practice guidelines (PPP). One tackles the treatment of patients with confirmed primary open-angle glaucoma, while the second reviews the management of suspect patients[3,9]. The main recommendations from both guidelines are summarized below:

Table 3. SIGN-Based Scale

Level of Evidence	Definition
I++	High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias
I+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
I-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
II++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a

	very low risk of confounding or bias and a high probability that the relationship is causal
II+	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
II-	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
III	Nonanalytic studies (e.g., case reports, case series)

Table 4. GRADE Body of Evidence Rating

Evidence Quality	Definition
Good quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Insufficient quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate Any estimate of effect is very uncertain

Table 5. GRADE Key Recommendations for Care

Strength of Recommendation	Interpretation
Strong recommendation	Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not
Discretionary recommendation	Used when the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced

- The IOP can be lowered by medical treatment, laser therapy, or incisional surgery (alone or in combination).
- Medical therapy is presently the most common initial intervention to lower IOP.

Table 6. Glaucoma Medications. Adapted from the 2020 American Academy of Ophthalmology Preferred Practice Pattern.

Drug Classification	Agents	Methods of Action	IOP Reduction	Potential Side Effects	Potential Contraindications	FDA Pregnancy Safety Category
Prostaglandin analogs	Bimatoprost Latanoprost Latanoprostene bunod Tafluprost Travoprost	Increase uveoscleral and/or trabecular outflow	25%-33%	• Increased and misdirected eyelash growth • Periocular hyperpigmentation • Conjunctival injection • Allergic conjunctivitis/ contact dermatitis • Keratitis • Possible herpes virus activation • Increased iris pigmentation • Uveitis • Cystoid macular edema • Peri orbitopathy • Migraine-like headache • Flu-like symptoms	• Macular edema • History of herpetic keratitis • Active uveitis	C

Beta-adrenergic antagonists (beta-blockers)	Nonselective Carteolol Levobunolol Metipranolol Timolol Selective Betaxolol	Decrease aqueous production	20%-25%	• Allergic conjunctivitis/ contact dermatitis • Keratitis • Bronchospasm • Bradycardia • Hypotension • CHF • Reduced exercise tolerance • Depression • Impotence	• Chronic obstructive pulmonary disease • Asthma • CHF • Bradycardia • Hypotension • Greater than first-degree heart block	C
Alpha-adrenergic agonists	Apraclonidine Brimonidine	Decrease aqueous production; decrease episcleral venous pressure or increase uveoscleral outflow	20%-25%	• Allergic conjunctivitis/ contact dermatitis • Follicular conjunctivitis • Dry mouth and nose • Hypotension • Headache • Fatigue • Somnolence	• Monoamine oxidase inhibitor therapy • Infants and children (for brimonidine)	B
Parasympathomimetic agents	Cholinergic agonist Pilocarpine Anticholinesterase agent Echothiophate	Increase trabecular outflow	20%-25%	• Increased myopia • Decreased vision • Cataract • Periocular contact dermatitis	• Areas of peripheral retina that predispose to breaks	C

				• Allergic conjunctivitis/ contact dermatitis • Conjunctival scarring • Conjunctival shrinkage • Keratitis • Paradoxical angle closure • Retinal tears/detachment • Eye or brow ache/pain • Increased salivation • Abdominal cramps	• The need to regularly assess the fundus • Neovascular, uveitic, or malignant glaucoma	
Rho kinase inhibitors	Netarsudil	Increase trabecular outflow Decrease episcleral venous pressure Decrease aqueous production	10%–20%	• Conjunctival hyperemia • Corneal verticillata • Instillation site pain • Conjunctival hemorrhage • Keratitis	None	-
Topical carbonic	Brinzolamide Dorzolamide	Decrease aqueous production	15%–20%	• Allergic dermatitis/ conjunctivitis • Corneal edema	• Sulfonamide allergy	C

anhydrase inhibitors				• Keratitis • Metallic taste	• Sickle cell disease with hyphema	
Oral carbonic anhydrase inhibitors	Acetazolamide Methazolamide	Decrease aqueous production	20%–30%	• Stevens-Johnson syndrome • Malaise, anorexia, depression • Serum electrolyte imbalance • Renal calculi • Blood dyscrasias (aplastic anemia, thrombocytopenia) • Metallic taste • Enuresis • Parasthesia • Diarrhea • Abdominal cramps	• Sulfonamide allergy • Kidney stones • Aplastic anemia • Thrombocytopenia • Sickle cell disease	C
Hyperosmotic agents	Glycerol Mannitol	Dehydration of vitreous	No data	• Headache • CHF • Nausea, vomiting • Diarrhea • Renal failure • Diabetic complications • Mental confusion	• Renal failure • CHF • Potential CNS pathology	C

- Prostaglandin analogs are the most frequently prescribed eye drops for lowering IOP in patients with glaucoma because they are most efficacious and well tolerated, and they need to be instilled only once daily. Therefore, prostaglandin analogs are often selected as initial medical therapy unless other considerations, such as contraindications, cost, side effects, intolerance, or patient refusal preclude this.
- Topical beta-adrenergic antagonists are commonly prescribed to treat glaucoma and have demonstrated good efficacy and tolerability. Nonselective beta-adrenergic antagonists (e.g., timolol) block both beta-1 (primarily cardiac) and beta-2 (primarily pulmonary) receptors. Cardio selective beta-blockers (e.g., betaxolol) target beta-1 receptors and minimize, but do not completely eliminate, the risk of pulmonary adverse effects in patients with obstructive airway disease. Topical beta-blockers may be dosed once or twice daily. However, nighttime dosing of beta-blockers is associated with limited efficacy and may contribute to visual field progression via nocturnal reduction of systemic blood pressure. Other glaucoma medications include alpha2 adrenergic agonists, parasympathomimetic, rho-kinase inhibitors, and topical and oral carbonic anhydrase inhibitors.
- Adequate treatment of glaucoma requires a high level of adherence to therapy.
- Multiple dosing requirements or side effects (such as depression, exercise intolerance, and impotence that might occur with topical beta-blockers) may impact adherence to therapy.
- Even with instruction, free medication, once-daily administration, use of a dosing aid, and electronic monitoring of adherence, nearly 45% of patients in one study took fewer than 75% of their prescribed doses. Fixed combinations of two medications may improve patient adherence by reducing the number of drops required for therapy.
- Simplified drug regimens also could be of benefit but again the current published studies do not provide conclusive evidence. Thus, adherence interventions are left to the judgment of the treating ophthalmologist. (I-, Insufficient Quality, Strong Recommendation)

Special circumstances in pregnancy and during breastfeeding:

Managing glaucoma in the pregnant or lactating patient involves an interdisciplinary approach to prevent disease progression in the mother while minimizing risks to the fetus and nursing infant. Laser trabeculoplasty may be considered as an alternative or adjunct to medical therapy in select patients during pregnancy and breastfeeding.

- **Pregnancy:**

In general, most ophthalmologists avoid the use of prostaglandins during pregnancy because of the theoretical risk of premature labor, but these medications may be considered for use in the breastfeeding mother. Oral carbonic anhydrase inhibitors have been shown to cause teratogenicity when delivered in high doses to animals. Rho-kinase inhibitors are therefore not assigned a pregnancy category. No data exist on the use of netarsudil in pregnant women. Animal studies did not demonstrate adverse effects on the developing fetus with clinically relevant intravenous exposures.

- **Breastfeeding:**

Some topical glaucoma medications have been detected in breast milk, such as timolol, carbonic anhydrase inhibitors, and brimonidine. The data are inconsistent as to whether timolol poses a threat to the breastfeeding infant. The American Academy of Pediatrics has approved the use of both oral and topical forms of carbonic anhydrase inhibitors during lactation, although the infant should be carefully monitored when the former are used. Brimonidine is known to cross the blood-brain barrier and can cause apnea in infants, P101 Primary Open-Angle Glaucoma PPP 28 toddlers, and children. For this reason, it is usually recommended that the medication not be used in mothers who are breastfeeding.

Laser trabeculoplasty

Laser trabeculoplasty may be used as initial or adjunctive therapy in patients with POAG. Laser trabeculoplasty lowers IOP by improving aqueous outflow and can be performed using argon or solid-state lasers. Laser trabeculoplasty may be performed to 180 degrees or to 360 degrees of the angle.

Several types exist: argon and diode laser trabeculoplasty and selective laser trabeculoplasty.

- **Perioperative care for laser trabeculoplasty**

Medications that are not being used chronically may be used perioperatively to avert temporary IOP elevations, particularly in those patients with severe disease. A 2017 Cochrane Systematic Review found that perioperative medications are superior to no medication to prevent the occurrence of spikes in IOP but it was unclear whether one medication was better than other medications in this class of drugs. Therefore, in consultation with the individual patient, treating ophthalmologists should use perioperative medications if temporary IOP elevations are a concern. (I+, Moderate Quality, Strong Recommendation) Brimonidine has been shown to be as effective as apraclonidine in preventing immediate IOP elevation after laser trabeculoplasty. Treating 180 degrees reduces the incidence and magnitude of postoperative IOP elevation compared with 360- degree treatment.

- **Incisional glaucoma surgery**

Trabeculectomy:

Trabeculectomy is effective in lowering IOP; it is generally indicated when medications and appropriate laser therapy are insufficient to control disease and can be considered in selected cases as initial therapy.

Trabeculectomy provides an alternative path for the escape of aqueous humor into subconjunctival space, and it often reduces IOP and the need for medical treatment. Estimates of success rates over time range from 31% to 88% in different populations. Medical treatment with benzalkonium chloride-preserved drugs may be a risk factor for surgical failure.

- **Aqueous shunts**

All aqueous shunts (also known as tube shunts, glaucoma drainage devices, and setons) consist of a tube that diverts aqueous humor to an end plate located within the subconjunctival space in the equatorial region of the eye. The primary resistance to flow through these devices occurs across the fibrous capsule that develops around the end plate. Aqueous shunts have traditionally been used to manage medically uncontrolled glaucoma when trabeculectomy has failed to control IOP or is deemed unlikely to succeed. This includes eyes with neovascular glaucoma, uveitic glaucoma, conjunctival scarring from previous ocular surgery or cicatrizing diseases of the conjunctiva, and congenital glaucoma in which angle surgery has failed. However, the indications for using aqueous shunts have been broadening, and these devices are being increasingly used in the surgical management of glaucoma. the selection of aqueous shunts or trabeculectomy should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient. (I-, Insufficient Quality, Strong Recommendation).

- **Combined surgeries**

Patients with POAG who have visually significant cataracts have a range of options available. If IOP control is at target on one or two medications, cataract surgery alone may be adequate, with the additional benefit that it may lower IOP slightly. If IOP is poorly controlled on several medications or there is evidence of glaucomatous progression in a patient with a moderate cataract, glaucoma surgery may be indicated initially, with the plan to perform cataract surgery once IOP is adequately controlled. In between these two extremes, the decision of which procedure(s) to perform first or whether to combine cataract and glaucoma surgery is determined by the ophthalmologist and patient after discussion of the risks and benefits of each course of action. the selection of a combined surgery or cataract surgery alone can be left to the discretion of the treating ophthalmologist in consultation with the individual patient. (I-, Insufficient Quality, Strong Recommendation)

- **Other incisional glaucoma surgeries**

Several other glaucoma surgeries exist as alternatives to trabeculectomy and aqueous shunt implantation. The precise role of these procedures in the surgical management of glaucoma continues to evolve.

- **Nonpenetrating glaucoma surgery**

The rationale for nonpenetrating glaucoma surgery is that by avoiding a continuous passageway from the anterior chamber to the subconjunctival space, the incidence of complications such as bleb-related problems and hypotony can be reduced. The nonpenetrating procedures have a higher degree of surgical difficulty compared with trabeculectomy and they require special instrumentation.

    - **Deep sclerectomy**: Deep sclerectomy involves excision of sclerocorneal tissue under a partial thickness scleral flap, leaving a thin window of trabecular meshwork and Descemet membrane to provide some resistance to aqueous outflow. Antifibrotic agents are frequently used as adjuncts to deep sclerectomy, and it has been suggested that placement of collagen drainage devices under the scleral flap can improve aqueous humor filtration.
    - **Viscocanalostomy:** Viscocanalostomy includes deep sclerectomy along with expansion of Schlemm's canal using an ophthalmic viscoelastic device. The procedure is intended to allow passage of aqueous humor through the trabeculodescemetic membrane window and into the physiologic outflow pathway through Schlemm's canal. The selection of viscocanalostomy and deep sclerectomy over trabeculectomy should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient. (I-, Insufficient Quality, Strong Recommendation)
    - **Canaloplasty:** In canaloplasty, circumferential viscodilation of Schlemm's canal using a flexible microcatheter is performed in combination with deep sclerectomy. Dilating the entire canal aims to give aqueous humor access to a greater number of collector channels.

- **Minimally invasive glaucoma surgery:**

Limited long-term data are currently available for MIGS, given its relatively recent introduction. Modest IOP reduction has been reported following MIGS, and postoperative pressures are typically in the middle to upper teens. Although less effective in lowering IOP than trabeculectomy and aqueous shunt surgery, MIGS appears to have a more favorable safety profile in the short term. Currently available MIGS includes procedures targeting the trabecular meshwork/Schlemm's canal and the subconjunctival space. They are commonly combined with phacoemulsification;

some are only FDA approved to be performed concurrently with phacoemulsification.

- Trabecular meshwork/Schlemm's canal-based MIGS: Trabecular MIGS includes the excision or cleavage, dilation, or stenting of varying extents of the trabecular meshwork and inner wall of Schlemm's canal under gonioscopic guidance. These procedures enhance aqueous access to collector channels and increase outflow. The IOP-lowering effect of trabecular MIGS is limited by resistance in distal outflow pathways and the episcleral venous pressure. Ab interno trabeculectomy involves the removal of a strip of trabecular meshwork and inner wall of Schlemm's canal.
- The first-generation trabecular microbypass stent, or iStent, is a single snorkel-shaped device manufactured from heparin-coated titanium that is implanted into Schlemm's canal using a preloaded inserter. The iStent is FDA approved for implantation in combination with cataract surgery in patients with mild to moderate OAG. Studies suggest that implantation of multiple stents may provide better IOP lowering than a single stent; however, placement of more than one first-generation iStent is considered off-label use in the United States.
- The second-generation iStent inject® system includes two conical implantable stents in its preloaded injector and has the same indications as its predecessor. Thus, the selection of iStent or medications should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient. (I-, Insufficient Quality, Strong Recommendation)
- Hydrus microstent in the short term is more effective when compared to iStent for lowering IOP in patients with OAG. (I, Moderate Quality, Strong Recommendation)
- Subconjunctival MIGS: the selection of the Xen gel stent should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient. (I-, Insufficient Quality, Discretionary Recommendation)
- Suprachoroidal MIGS is an ab interno suprachoroidal shunt that was FDA approved for implantation at the time of cataract surgery in patients with mild to moderate POAG.

- **Perioperative care in incisional glaucoma surgery**

Cyclodestructive surgery: Cyclodestructive procedures reduce the rate of aqueous production. There are several ways to reduce ciliary body function, including cyclocryotherapy, transscleral and noncontact Nd: YAG laser, and transscleral and

noncontact endodiode laser cyclophotocoagulation. Therefore, the selection of cyclophotocoagulation over other procedures should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient. (I-, Insufficient Quality, Discretionary Recommendation)

- **Follow-up evaluation**

Table 7. Follow-up Evaluation for Open-Angle Glaucoma

Target IOP achieved	Progression of damage	Duration of control (mos)	Approximate follow-up interval (mos)
Yes	No	≤ 6	6
Yes	No	≤ 6	6-12
Yes	Yes	NA	1-2
No	Yes	NA	1-2
No	No	NA	3-6

1.1.3 European Glaucoma Society: Terminology and Guidelines for Glaucoma, Fifth Edition (2021)

The European Glaucoma Society published in 2021 its fifth edition of clinical guidelines with the aim of supporting ophthalmologists in managing people with, or at risk of, glaucoma[6]. Recommendations are proposed using GRADE methodology, according to the level of evidence: high, moderate, low, very low; as well as strength of recommendation: strong or weak. A strong recommendation should be interpreted as “we recommend” and/or “very relevant in clinical practice”, and a weak recommendation as “we suggest” and/or “less relevant in clinical practice”. The main recommendations are detailed below:

- A target IOP should be set as a treatment goal at diagnosis. Target IOP should be updated at each monitoring visit on the basis of changes in glaucoma or other ocular or systemic diseases. (Level of evidence: low -Strength of recommendation: strong)
- Prostaglandin analogues (PGAs) are the most effective medication and they are usually recommended as first choice treatment for open angle glaucoma. (Level of evidence: High for IOP reduction but very low for other outcomes. Strength of recommendation: strong)
- SLT can be offered as a first-choice treatment for open angle glaucoma. (Level of evidence: moderate (only one high quality trial, LiGHT) Strength of recommendation: strong)

- Trabeculectomy augmented with antifibrotic agents is recommended as an initial surgical treatment for open angle glaucoma. (Level of evidence: low Strength of recommendation: strong)
- **Primary congenital glaucoma: from birth to the first years of life:**
    - Neonatal or newborn onset (0-1 month)
    - Infantile onset (>1 until 24 months)
    - Late onset or late recognized (>2 years)
    - Spontaneously non-progressing cases with normal IOP but typical signs of PCG may be classified as self-healed PCG.
    - Management of these cases is particularly challenging. Initial surgery is indicated in nearly all cases with primary congenital glaucoma. Medical treatment is usually neither effective nor practicable in long term. Medications, including oral CAIs can be used while decision is made on a surgical approach and in case of failed surgery while waiting for further options. Primary surgery: early goniotomy, trabeculotomy, filtration surgery; long-tube drainage devices may be indicated if these are unsuccessful. Repeat surgery is relatively frequent.
- **Late-onset childhood open angle glaucoma with onset from more than two years of age to puberty**
    - Cases with later manifestation usually do not have enlargement of the globe and may have a more favorable outcome with surgery.
    - The treatment of pediatric glaucoma cases is particularly challenging due to the nature of the disease and to the intrinsic difficulties in examining patients at this age and operating on them. Treatment has to be adapted to the primary anomaly, and the mechanism of IOP elevation. Whenever possible these cases should be referred to tertiary care centers.
- **Secondary childhood glaucoma**
    - Management to be adapted to the primary anomaly, the mechanism of IOP elevation and the QoL of the patient. These cases require highly specialized care.
- **Primary open angle glaucoma (POAG)**

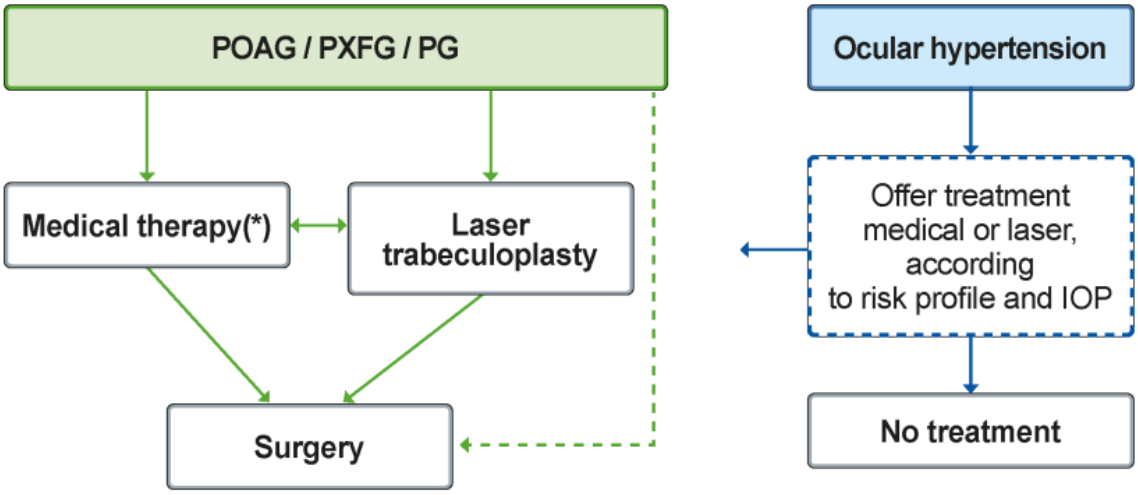

Figure 1. *Treatment of Primary Angle Glaucoma. Retrieved from the European Glaucoma Society 2021 Guidelines.*

- **Ocular hypertension:**
    - Treatment may be advisable in people with high risk of conversion to glaucoma. Increased IOP should be confirmed before starting treatment unless it is very high. In general offer treatment in patients with repeated IOPs in the high twenties, even without additional risk factors. Treatment principles and choices will be similar to those for POAG. The initial approach is to offer either medical treatment or laser trabeculoplasty. Follow-up at intervals of 6-12 months initially, to be prolonged if all parameters remain stable.
- **Secondary open angle glaucoma**
    - **Pseudo exfoliative or exfoliative glaucoma (PXFG)**
        - Treatment options of PXFG are similar to those of POAG although there is higher risk of progression in PXFG. Laser trabeculoplasty and medical treatment are equally effective but both lose efficacy after some years. In clinically unilateral PXFG the fellow eye also needs to be regularly checked for IOP elevation and glaucoma since the conversion rate is high.
    - **Pigmentary glaucoma (PG)**
        - Treatment of PG is similar to that of POAG. No PG-specific treatment is available. Laser trabeculoplasty and medical treatment are equally effective, but spikes of IOP are common after laser trabeculoplasty and so should be performed

cautiously with low power settings and with prophylactic treatment to prevent IOP spikes.

- **Lens-induced open angle glaucoma**
    - Extraction of lens or lens fragments followed by topical anti-inflammatory medication, vitrectomy if needed.
- **Glaucoma associated with intraocular hemorrhage**
    - Topical and systemic IOP lowering medication as needed. It is recommended to avoid carbonic anhydrase inhibitors and hyperosmotic agents in patients with sickle cell disease
    - Conservative treatment, bed rest, topical cycloplegics and steroids, can be considered for uncomplicated hyphaema. Antifibrinolytic agents such as tranexamic acid can reduce the risk of rebleeding. However, it is not clear whether any of the interventions have an effect on visual acuity.
    - Wash-out through a paracentesis of the anterior chamber and/or vitrectomy to remove RBCs from vitreous if IOP remains high with the risk of corneal blood staining and/or optic neuropathy.
- **Uveitic glaucoma**
    - Topical and systemic anti-inflammatory therapy according to the underlying disease.
    - Topical and systemic IOP lowering medication.
    - Traditionally topical β-blockers and CAIs have been used as first-line treatment.
    - PGAs can be used therapy in eyes with well controlled uveitis.
    - Glaucoma surgery suited for the type of inflammatory disease.
    - Laser trabeculoplasty should be avoided.
- **Glaucoma due to intraocular tumors**
    - Treatment of underlying tumor (irradiation, surgical tumor excision, enucleation) Topical and systemic IOP lowering medication; medical therapy is often first-line treatment while awaiting definitive treatment.
- **Secondary open angle glaucoma due to ocular trauma:**
    - Anti-inflammatory medication
    - Topical and systemic IOP lowering medication

        - Long-term IOP lowering and follow up in the presence of permanent anterior segment damage
        - Glaucoma surgery
    - **Iatrogenic secondary open angle glaucoma:**
        - Discontinuation of corticosteroid therapy is recommended if possible; steroid-sparing therapy of underlying condition should be considered. If this is not possible, consider switching to weaker steroid (e.g., loteprednol, fluorometholone)
        - Topical and systemic IOP lowering medication
        - Laser trabeculoplasty
        - Glaucoma surgery may be performed in intractable cases
    - **Secondary open angle glaucoma due to ocular surgery and laser:**
        - Topical and systemic IOP-lowering medication
        - Anti-inflammatory treatment
        - Removal of silicone oil may be considered in eyes with IOP elevation secondary to silicon oil emulsification. However current data suggest that removal of silicon oil is not effective in all cases and the risk of re-detachment increases. Transscleral cyclo-photocoagulation and aqueous drainage devices seem to represent more effective options, although the latter are associated with the risk of silicon oil escape into subconjuctival space. Endoscopic cyclophotocoagulation in eyes requiring silicon oil removal and glaucoma treatment is another option. Conventional filtration surgery is associated with poor prognosis.
        - Removal of the intraocular lens may be needed in case of UGH syndrome
        - Glaucoma surgery according to the specific condition
    - **Glaucoma associated with vitreoretinal surgery:**
        - Topical and systemic IOP-lowering medication
        - Surgery for retinal detachment
        - Consider glaucoma surgery if IOP not controlled
    - **Secondary open angle glaucoma caused by extraocular disease:**
        - Treatment of the underlying disease
        - Topical and systemic IOP-lowering medication

- Glaucoma surgery

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Open angle glaucoma report, along with their recommendations.

Table 8. Additional Guidelines

Additional Guidelines
Optometry Australia Clinical Practice Guide for the Diagnosis and Management of Open Angle Glaucoma (**2020**)[10]

1.2.1 Optometry Australia Clinical Practice Guide for the Diagnosis and Management of Open Angle Glaucoma (2020)

This Clinical Practice Guide provides evidence-based information about current best practice in the management of glaucoma. It is a general guide for optometrists, and while it is not a formal management protocol, its aim is to aid clinicians in their diagnosis and management[10]. The main recommendations are listed below.

- Topical pharmacotherapy is generally considered the mainstay of glaucoma treatment, particularly for optometrists. Medications for treating glaucoma are divided into several classes, depending on their mechanisms of action. Currently, these include:
    - Prostaglandin analogues
    - Beta-blockers
    - Alpha2-agonists
    - Carbonic anhydrase inhibitors
    - Parasympathomimetics

Table 9. Medications for the Treatment of Open-Angle Glaucoma on the Australian Market. Adapted from the 2020 Optometry Australia Guidelines.

Preparations by class	Mechanism of action	Efficacy	Daily dosage	Order of treatment choices
Prostaglandin analogues • Latanoprost 0.005% • Travoprost 0.004% • Bimatoprost 0.03% • Tafluprost 0.0015%	Increase aqueous outflow	25-35% Maximum effect: 8-12 hours	Once daily (night)	First
Beta-blockers Non-selective agents: • Timolol 0.25%, 0.5%, 1% Selective agents: • Betaxolol 0.25%, 0.5%	Decrease aqueous production	20-25% Maximum effect: 2 hours	One to two times daily	First
Alpha2-agonists • Brimonidine 0.2%, 0.15% • Apraclonidine* 0.5%	Increase aqueous outflow and decrease aqueous production	10-25% Maximum effect: 1-4 hours	two to three times daily	Second
Carbonic anhydrase inhibitors Topical: • Dorzolamide 2% • Brinzolamide 1%	Decrease aqueous production	15-25% Maximum effect: 2 hours	Two to three times daily	Second
Systemic: • Acetazolamide 250mg	Decrease aqueous production	25-30%	Two to four times daily	Third

Cholinergics (miotics) • Pilocarpine 1%, 2%	Increase aqueous outflow	15-20% Maximum effect: 3-4 hours	Three to four times daily	Third
Combination therapies • Combigan (brimonidine 0.2%/timolol 0.5%) • Cosopt (dorzolamide 2%/timolol 0.5%) • DuoTrav (travoprost 0.004%/timolol 0.5%) • Xalacom (latanoprost 0.005%/timolol 0.5%) • Ganfort (bimatoprost 0.03%/timolol 0.5%) • Azarga (brinzolamide 1%/timolol 0.5%) • Simbrinza (brinzolamide 1%/brimonidine 0.2%)	As for individual components	20-35%	Combigan: Twice daily Cosopt: Twice daily DuoTrav: Once daily Xalacom: Once daily Ganfort: Once daily Azarga: Twice daily Simbrinza: Twice daily	Second

Prostaglandin analogues:

There are a number of reasons why prostaglandin analogues are considered a first-line therapy for glaucoma. As monotherapy, it is generally the most efficacious at reducing IOP and also flattening the diurnal variation curve (i.e. controlling IOP fluctuations). The IOP lowering effect is also sustained over time, unlike some alternatives that may result in development of tachyphylaxis. Adverse effects of prostaglandin analogues are primarily cosmetic in nature. However, this may be a source of non-compliance, so patients need to be appropriately warned prior to treatment initiation. If the initial prostaglandin is partially effective but does not reach target IOP, consider switching within the prostaglandin analogue class, as individual patients may respond to each medication differently. There is some evidence that prostaglandins may thin corneas over time, which should be considered when reviewing for effective glaucoma control.

Beta blockers:

Prior to the discovery of prostaglandin analogue therapy, beta-blockers were the first-line therapy for topical glaucoma therapy. Beta-blockers still have a role as a first-line topical therapy particularly in the following cases:

- Intolerance to prostaglandin analogues (including its cosmetic effects)
- Unilateral treatment (to avoid unilateral cosmetic effects of prostaglandin analogues)
- Concerns regarding the presence or potential presence of ocular inflammation.

Beta-blockers in gel-forming solutions may be best suited for therapy, due to the maintenance of efficacy (25% reduction) at only once daily dosing. Specifically, timolol gel-forming solution is a commonly prescribed and well-studied beta-blocker and its once daily dosing is an attractive clinical choice.

Beta-blockers are unlikely to be the first line treatment for most patients, even the cardio-selective medications, given the availability of alternative, safer medications. Beta-blockers should not be used in early or mid-pregnancy periods or in asthma and COPD, or if already taken systemically.

Alpha 2 agonists:

Alpha-2 agonists are primarily considered to be **second-line** therapy or adjunctive medication in the management of glaucoma.

Indications for monotherapy using an alpha-2 agonist include:

- Intolerance to prostaglandin analogues plus contraindication to beta-blocker use

- Short-term use in the presence of inflammation of the eye (such as uveitis) or as an interim treatment prior to undergoing laser or surgical glaucoma treatment.

Although aqueous production is also reduced by beta-blockers, the alpha-2 agonist acts on a different receptor and should therefore be considered to be complementary to a beta-blocker. Alpha-2 agonist use is often limited in long-term glaucoma management due to the frequent development of follicular conjunctivitis, lower efficacy than prostaglandin analogues and more frequent dosing schedule.

Carbonic anhydrase inhibitors:

Carbonic anhydrase inhibitors, like alpha-2 agonists, are also considered to be second-line therapy for glaucoma. Carbonic anhydrase is an enzyme that catalyzes the hydration of carbon dioxide and thus inhibition decreases aqueous production from active filtration in the non-pigmented epithelium of the pars plicata. As it decreases aqueous production via an alternative pathway to beta-blockers, it acts synergistically with other antiglaucoma medications. Brinzolamide is typically recommended over dorzolamide due to better efficacy and tolerability.

Parasympathomimetics:

Pilocarpine is the only sympathomimetic available for use by optometrists in Australia and is rarely used in modern glaucoma management.

Laser therapy:

Argon laser trabeculoplasty is an older technique that is no longer used, being largely replaced by selective laser trabeculoplasty (SLT). The mechanism of SLT is thought to be an increase in aqueous outflow. Practically, the procedure is short, typically performed as an in-office, out-patient procedure, has a quick recovery and excellent safety profile. Complications are typically transient and self-limiting.

Although topical therapies are usually considered a first line treatment, SLT may be considered a first line treatment in open angle glaucoma (either primary or, less commonly, secondary). Some indications include:

- Young patients
- Medication-sparing therapy (avoiding adverse effects), either as monotherapy or medication-reducing treatment
- Medication non-compliance or intolerance (less reduction in quality of life)
- Additive/adjunctive treatment on top of existing topical therapy

Surgical treatment options for glaucoma:

Table 10. Surgical Treatment Options for Glaucoma. Adapted from the 2020 Optometry Australia Guidelines.

Technique	Notes
Lens extraction	IOP reduction following lens extraction is debated in the literature but may be associated with higher preoperative IOP and narrow angles. As it is still a surgical procedure, it is typically used as a surgical treatment of convenience, when it will be performed anyway, rather than as a first-line treatment for glaucoma.
MIGS: minimally invasive glaucoma surgery	The aim of MIGS is to enhance aqueous outflow and can be further classified into trabecular, suprachoroidal or subconjunctival. MIGS may be beneficial in a subset of patients who require concurrent cataract surgery or top-up for IOP reduction; there is insufficient evidence at this stage for its use as a first-line treatment option. The current role of the optometrist is primarily for identifying individuals suitable for this type of intervention. Indications include issues with medical therapy (adverse effects, quality of life, compliance), a less invasive alternative to incisional surgery and/or concurrent cataract surgery. Most commonly, IOP spikes following the procedure have been reported and mild transient hyphemia.
Filtration/incisional surgery	It is currently the gold standard for glaucoma surgery, especially when a low IOP is required and is typically reserved for advanced cases of glaucoma. Essentially, the surgical procedure creates a new channel (fistula) between the anterior chamber and subconjunctival space. Thus, the IOP reduction obtained using filtration surgery tends to be dramatic and much higher compared to other treatment modalities. The current role of the optometrist is primarily in identification of complications from filtration surgery. These should

	be promptly referred to the operating surgeon for review.
Tube shunts	Growing in popularity in the surgical management of glaucoma. Tube, with a valve, is inserted in the eye and shunts aqueous. The current role of the optometrist is to identify complications from the surgery, such as infection or hypotony, diplopia, tube shunt erosion or tube failure.

Emerging therapies:

The role of agents to support neural health or provide neuroprotection to the retinal ganglion cells has been a topic of interest complementing conventional intraocular pressure lowering therapies. Dietary supplementation with vitamin B3 (nicotinamide) has been shown by a variety of animal studies to reduce vulnerability to glaucoma by supporting the neural elements of the eye.

Nitric oxide is thought to directly trigger relaxation of the trabecular meshwork. Nitric oxide is also suggested to relax the vessel within the canal of Schlemm.

Latanoprostene bunod, incorporates nitric oxide by being a nitric oxide donor, releasing it to the trabecular meshwork upon metabolism. By adding another mechanism of action to reduce intraocular pressure, nitric oxide may complement existing anti-glaucoma medications, thereby further lowering intraocular pressure.

Netarsudil 0.02% (Rhopressa) is a new antiglaucoma medication in the new rho kinase class. It primarily acts on trabecular meshwork cells, preventing assembly and stabilization of actin fibers, to increase the pore size and outflow and subsequently reduce IOP. However, they also increase blood vessel diameter reducing resistance to aqueous outflow and inhibit norepinephrine (which is thought to mimic alpha 2 agonists) and reduce aqueous production.

Section 2.0 Drug Therapy

This section comprises four subsections: the first one contains the newly recommended drugs SFDA registered, the second one covers drug modifications, the third one outlines the drugs that have been withdrawn from the market and the fourth one includes new drugs FDA/EMA approved but not SFDA registered.

2.1 Additions

After May 2020, there have been no new drugs that have received FDA and EMA approval and are SFDA registered for open angle glaucoma disease treatment.

2.2 Modifications

Please refer to section 2.7.7 and 2.8.7 of the old report on open angle glaucoma:

5-fluorouracil and mannitol do not need “Prior Authorization (PA)” as a prescribing edit.

2.3 Delisting

Table 11. Delisted Medications

Delisted medications	Reason	Medication status	Alternative
Acetazolamide (ophthalmic drops)	Withdrawn from SFDA	The guidelines recommend carbonic anhydrase inhibitors as a class as a second line therapy if prostaglandin analogues do not work. According to the American guidelines on open angle glaucoma, the two mentioned carbonic anhydrase inhibitors are: dorzolamide and brinzolamide which are present on the SFDA market	Ophthalmic drops: Brinzolamide Dorzolamide
Befunolol (ophthalmic drops)	Withdrawn from SFDA	The guidelines recommend beta blockers as a class as a second line therapy if prostaglandin analogues do not work. According to the American guidelines on open angle glaucoma, the beta	Ophthalmic drops: Carteolol Timolol

		blockers mentioned are: Carteolol Levobunolol Metipranolol and Timolol. There are already two alternatives available on the SFDA market (timolol and carteolol). They belong to the same class of non-selective beta blockers and can be used interchangeably.	
Levobunolol (ophthalmic drops)	Withdrawn from SFDA	The guidelines recommend beta blockers as a class as a second line therapy if prostaglandin analogues do not work. According to the American guidelines on open angle glaucoma, the beta blockers mentioned are: Carteolol Levobunolol Metipranolol and Timolol. There are already two beta blockers available on the SFDA market (timolol and carteolol). They belong to the same class of non-selective beta blockers and can be used interchangeably with levobunolol.	Ophthalmic drops: Carteolol Timolol

2.4 Other Drugs

Netarsudil (Rhopressa) was FDA approved in 2017 and EMA approved in 2019[12].

According to the American and Australian guidelines regarding open angle glaucoma treatment, Netarsudil 0.02% (Rhopressa) is a new antiglaucoma medication in the new rho kinase class. It primarily acts on trabecular meshwork cells, preventing assembly and stabilization of actin fibers, to increase the pore size and outflow and subsequently reduce IOP. However, they also increase blood vessel diameter reducing resistance to aqueous outflow and inhibit norepinephrine (which is thought to mimic alpha 2 agonists) and reduce aqueous production[3,9,10].

It is usually dosed as: Ophthalmic: Instill 1 drop into affected eye(s) once daily in the evening (maximum: 1 drop into affected eye(s) once daily)[13].

Latanoprostene bunod (Vyzulta) was FDA approved in November 2017[14].

It is usually dosed as: Ophthalmic: Instill 1 drop into affected eye(s) once daily in the evening; do not exceed the once daily dosage (may decrease the IOP-lowering effect)[15].

According to the American guidelines regarding open angle glaucoma, latanoprostene bunod is one of the prostaglandin analogues that can be used for treatment of open glaucoma. It makes part of the same class as: latanoprost, bimatoprost, travoprost and tafluprost already on the SFDA market[3,9].

Apraclonidine (Iopidine) was FDA approved in 1987[16].

It is usually dosed as: Open-angle glaucoma: 0.5%: Instill 1 to 2 drops into the affected eye(s) 3 times daily[18].

According to the European guidelines regarding open angle glaucoma, apraclonidine is one of the alpha adrenergic that can be used for treatment of open glaucoma. It makes part of the same class as: brimonidine which is already on the SFDA market[3,9].

Omidenepag was FDA approved on September 2022[19].

It is usually dosed as One drop in the affected eye(s) once daily in the evening for open angle glaucoma[20].

According to FDA labeled indication, OMLONTI® (Omidenepag Isopropyl Ophthalmic Solution) 0.002% is approved for the Reduction of Elevated Intraocular Pressure in Patients with Primary Open-Angle Glaucoma or Ocular Hypertension[19].

Section 3.0 Key Recommendations Synthesis

- Prostaglandin analogues (PGAs) are the most effective medication and they are usually recommended as first choice treatment for open angle glaucoma. (Level of evidence: High for IOP reduction but very low for other outcomes. Strength of recommendation: strong)[6].
- SLT can be offered as a first-choice treatment for open angle glaucoma. (Level of evidence: moderate (only one high quality trial, LiGHT) Strength of recommendation: strong)[6].
- Trabeculectomy augmented with antifibrotic agents is recommended as an initial surgical treatment for open angle glaucoma. (Level of evidence: low Strength of recommendation: strong)[6].
- Netarsudil 0.02% (Rhopressa) is a new antiglaucoma medication in the new rho kinase class. It primarily acts on trabecular meshwork cells, preventing

assembly and stabilization of actin fibers, to increase the pore size and outflow and subsequently reduce IOP. However, they also increase blood vessel diameter reducing resistance to aqueous outflow and inhibit norepinephrine (which is thought to mimic alpha 2 agonists) and reduce aqueous production[10].

- **Prostaglandin analogues:** they are considered a first-line therapy for glaucoma. As monotherapy, it is generally the most efficacious at reducing IOP and also flattening the diurnal variation curve. Adverse effects of prostaglandin analogues are primarily cosmetic in nature. However, this may be a source of non-compliance, so patients need to be appropriately warned prior to treatment initiation[10].
- **Beta blockers:** Prior to the discovery of prostaglandin analogue therapy, beta-blockers were the first-line therapy for topical glaucoma therapy. Beta-blockers still have a role as a first-line topical therapy particularly in the following cases:
    - Intolerance to prostaglandin analogues (including its cosmetic effects)
    - Unilateral treatment (to avoid unilateral cosmetic effects of prostaglandin analogues)
    - Concerns regarding the presence or potential presence of ocular inflammation[10].
- Beta-blockers are unlikely to be the first line treatment for most patients, even the cardio-selective medications, given the availability of alternative, safer medications. Beta-blockers should not be used in early or mid-pregnancy periods or in asthma and COPD, or if already taken systemically[10].
- **Alpha 2 agonists:** they are primarily considered to be second-line therapy or adjunctive medication in the management of glaucoma. Indications for monotherapy using an alpha-2 agonist include: intolerance to prostaglandin analogues plus contraindication to beta-blocker use, short-term use in the presence of inflammation of the eye (such as uveitis) or as an interim treatment prior to undergoing laser or surgical glaucoma treatment. Although aqueous production is also reduced by beta-blockers, the alpha-2 agonist acts on a different receptor and should therefore be considered to be complementary to a beta-blocker[10].
- **Carbonic anhydrase inhibitors:** Carbonic anhydrase inhibitors, like alpha-2 agonists, are also considered to be second-line therapy for glaucoma[10].

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Open Angle Glaucoma report** and aims to provide recommendations to aid in the management of Open angle glaucoma. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with open angle glaucoma. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules, or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses, and sequence of therapy

Appendix B. Open-Angle Glaucoma Scope

Section	Rationale/Updates
Glaucoma: diagnosis and management NICE 2022[8]	• **Initial treatment for people with Ocular hypertension (OHT):** o Offer 360° selective laser trabeculoplasty (SLT) to people with newly diagnosed OHT with IOP of 24 mmHg or more (excluding cases associated with pigment dispersion syndrome) if they are at risk of visual impairment within their lifetime. To help inform their decision, tell people: ▪ That having 360° SLT can delay the need for eye drops and can reduce but does not remove the chance they will be needed at all ▪ How long it may take for their IOP to improve after the procedure ▪ About 360° SLT-specific side effects and complications and how long they are likely to last ▪ That a second 360° SLT procedure may be needed at a later date. o Consider a second 360° SLT for people with OHT if the effect of an initial successful SLT has subsequently reduced over time. o Offer a generic prostaglandin analogue (PGA) to people with OHT with IOP of 24 mmHg or more if they are at risk of visual impairment within their lifetime and: ▪ They choose not to have 360° SLT or ▪ 360° SLT is not suitable or ▪ They are waiting for 360° SLT and need an interim treatment or ▪ They have had 360° SLT but need additional treatment to reduce their IOP sufficiently to prevent the risk of visual impairment. ➔ Demonstrate correct eye drop installation technique and observe the person using the correct technique when eye drops are first prescribed. • **Ongoing treatment for people with OHT** o Offer another pharmacological treatment to people with an IOP of 24 mmHg or more who cannot tolerate their current treatment. The first choice should be an

	alternative generic PGA, and if this is not tolerated, offer a beta-blocker. If neither of these options is tolerated, offer a non-generic PGA, carbonic anhydrase inhibitor, sympathomimetic, miotic or a combination of treatments. o Refer people to a consultant ophthalmologist to discuss other options if their IOP cannot be reduced sufficiently with 360° SLT or pharmacological treatment or both to prevent the risk of progression to sight loss. • **Treatment for people with suspected COAG** o Do not offer treatment to people with suspected COAG and IOP less than 24 mmHg unless they are at risk of visual impairment within their lifetime. Advise people to continue regular visits to their primary eye care professional, at clinically appropriate intervals. • **Treatment for people with COAG** o Offer people with advanced COAG, glaucoma surgery with pharmacological augmentation (MMC) as indicated. Give them information on the risks and benefits of surgery. MMC is here off label. o Offer people who present with advanced COAG and who are listed for glaucoma surgery, interim treatment with a generic PGA. • **Initial treatment for people with COAG** o Offer 360° selective laser trabeculoplasty (SLT) to people with newly diagnosed COAG with IOP of 24 mmHg or more (excluding cases associated with pigment dispersion syndrome) if they are at risk of visual impairment within their lifetime. To help inform their decision, tell people: ▪ That having 360° SLT can delay the need for eye drops and can reduce but does not remove the chance they will be needed at all ▪ How long it may take for their IOP to improve after the procedure ▪ About 360° SLT-specific side effects and complications and how long they are likely to last ▪ That a second 360° SLT procedure may be needed at a later date.

	○ Consider a second 360° SLT for people with COAG if the effect of an initial successful SLT has subsequently reduced over time. (same recommendations as OHT) ○ Offer a generic PGA to people with COAG if: ▪ They choose not to have 360° SLT or ▪ 360° SLT is not suitable or ▪ They are waiting for an 360° SLT and need an interim treatment or ▪ They have previously had 360° SLT but need additional treatment to reduce their IOP sufficiently to prevent the risk of visual impairment. ➔ Demonstrate correct eye drop installation technique and observe the patient using the technique when eye drops are first prescribed. • **Ongoing treatment for people with COAG** ○ Ask about adherence to treatment and check the eye drop instillation technique in people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss, despite pharmacological treatment with a generic PGA. ○ Offer 1 of the following to people with satisfactory adherence to treatment and eye drop instillation technique whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss: ▪ a medicine from another therapeutic class (a beta-blocker, carbonic anhydrase inhibitor or sympathomimetic); topical medicines from different therapeutic classes may be needed at the same time to control IOP or ▪ 360° SLT or ▪ glaucoma surgery with pharmacological augmentation (MMC) as indicated. (MMC is off label here) ○ Consider 360° SLT or glaucoma surgery with pharmacological augmentation (MMC) as indicated for people with COAG who are at risk of progressing to sight loss despite treatment with medicines from 2 therapeutic classes. Give them information on the risks and benefits of surgery.

	○ Consider 1 of the following for people with COAG who cannot tolerate a pharmacological treatment: ▪ a medicine from another therapeutic class (a beta-blocker, carbonic anhydrase inhibitor or sympathomimetic) or ▪ preservative-free eye drops if there is evidence that the person is allergic to the preservative or has clinically significant and symptomatic ocular surface disease. ▪ After treatment with medicines from 2 therapeutic classes, consider 360° SLT or glaucoma surgery with pharmacological augmentation (MMC) as indicated. MMC is off label here. ○ Offer 1 of the following to people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss after glaucoma surgery: ▪ pharmacological treatment; topical medicines from different therapeutic classes may be needed at the same time to control IOP or ▪ further glaucoma surgery or ▪ 360° SLT or ▪ cyclodiode laser treatment. ○ Offer 1 of the following to people with COAG (including advanced COAG) who prefer not to have glaucoma surgery or for whom glaucoma surgery is not suitable: ▪ pharmacological treatment; topical medicines from different therapeutic classes may be needed at the same time to control IOP or ▪ 360° SLT (for example in people with systemic comorbidities) or ▪ cyclodiode laser treatment.
American academy of ophthalmology: Primary Open-Angle Glaucoma	• Special circumstances in pregnancy and during breastfeeding • Pregnancy • Breastfeeding • Laser trabeculoplasty

Preferred Practice Pattern 2020[9] and Primary open-angle glaucoma suspect preferred practice pattern 2020[3]	• Perioperative care for laser trabeculoplasty
	• Incisional glaucoma surgery
	Trabeculectomy:
	• Aqueous shunts
	• Combined surgeries
	• Other incisional glaucoma surgeries
	• Nonpenetrating glaucoma surgery
	  o Deep sclerectomy
	  o Viscocanalostomy
	  o Canaloplasty
	• Minimally invasive glaucoma surgery
	• Perioperative care in incisional glaucoma surgery
	Cyclodestructive surgery

European glaucoma society-terminology and guidelines for glaucoma 2021-5th edition[6]	• A target IOP should be set as a treatment goal at diagnosis. Target IOP should be updated at each monitoring visit on the basis of changes in glaucoma or other ocular or systemic diseases. (Level of evidence: low Strength of recommendation: strong) • Prostaglandin analogues (PGAs) are the most effective medication and they are usually recommended as first choice treatment for open angle glaucoma. (Level of evidence: High for IOP reduction but very low for other outcomes. Strength of recommendation: strong) • SLT can be offered as a first-choice treatment for open angle glaucoma. Level of evidence: moderate (only one high quality trial, LiGHT) Strength of recommendation: strong • Trabeculectomy augmented with antifibrotic agents is recommended as an initial surgical treatment for open angle glaucoma. (Level of evidence: low Strength of recommendation: strong) • **Primary open angle glaucoma (POAG)** • **Ocular hypertension:**

	○ Treatment may be advisable in people with high risk of conversion to glaucoma. Increased IOP should be confirmed before starting treatment unless very high. In general offer treatment in patients with repeated IOPs in the high twenties, even without additional risk factors. Treatment principles and choices will be similar to those for POAG. The initial approach is to offer either medical treatment or laser trabeculoplasty. Follow-up at intervals of 6-12 months initially, to be prolonged if all parameters remain stable. • **Secondary open angle glaucoma** ○ **Pseudoexfoliative or exfoliative glaucoma (PXFG)** ▪ Treatment options of PXFG are similar to those of POAG although there is higher risk of progression in PXFG. Laser trabeculoplasty and medical treatment are equally effective but both lose efficacy after some years. In clinically unilateral PXFG the fellow eye also needs to be regularly checked for IOP elevation and glaucoma since the conversion rate is high. ○ **Pigmentary glaucoma (PG)** ▪ Treatment of PG is similar to that of POAG. No PG-specific treatment is available. Laser trabeculoplasty and medical treatment are equally effective, but spikes of IOP are common after laser trabeculoplasty and so should be performed cautiously with low power settings and with prophylactic treatment to prevent IOP spikes. ○ **Lens-induced open angle glaucoma** ▪ Extraction of lens or lens fragments followed by topical anti-inflammatory medication, vitrectomy if needed. ○ **Glaucoma associated with intraocular haemorrhage** ▪ Topical and systemic IOP lowering medication as needed. It is recommended to avoid carbonic anhydrase inhibitors and hyperosmotic agents in patients with sickle cell disease ▪ Conservative treatment, bed rest, topical cycloplegics and steroids, can be considered for uncomplicated hyphaema. Antifibrinolytic agents such as

	tranexamic acid can reduce the risk of rebleeding. However it is not clear whether any of the interventions have an effect on visual acuity. ▪ Wash-out through a paracentesis of the anterior chamber and/or vitrectomy to remove RBCs from vitreous if IOP remains high with the risk of corneal blood staining and/or optic neuropathy. o **Uveitic glaucoma** ▪ Topical and systemic anti-inflammatory therapy according to the underlying disease. ▪ Topical and systemic IOP lowering medication. ▪ Traditionally topical β-blockers and CAIs have been used as first-line treatment. ▪ PGAs can be used therapy in eyes with well controlled uveitis. ▪ Glaucoma surgery suited for the type of inflammatory disease. ▪ Laser trabeculoplasty should be avoided o **Glaucoma due to intraocular tumors** ▪ Treatment of underlying tumour (irradiation, surgical tumour excision, enucleation) Topical and systemic IOP lowering medication; medical therapy is often first-line treatment while awaiting definitive treatment. o **SECONDARY open angle glaucoma due to ocular trauma:** ▪ Anti-inflammatory medication ▪ Topical and systemic IOP lowering medication ▪ Long-term IOP lowering and follow up in the presence of permanent anterior segment damage ▪ Glaucoma surgery o **Iatrogenic secondary open angle glaucoma:** ▪ Discontinuation of corticosteroid therapy is recommended if possible; steroid-sparing therapy of underlying condition should be considered. If this is not possible, consider switching to weaker steroid (e.g. loteprednol, fluorometholone)

	▪ Topical and systemic IOP lowering medication ▪ Laser trabeculoplasty ▪ Glaucoma surgery may be performed in intractable cases ○ **Secondary open angle glaucoma due to ocular surgery and laser:** ▪ Topical and systemic IOP-lowering medication ▪ Anti-inflammatory treatment ▪ Removal of silicone oil may be considered in eyes with IOP elevation secondary to silicon oil emulsification. However current data suggest that removal of silicon oil is not effective in all cases and the risk of re-detachment increases. Transscleral cyclo-photocoagulation and aqueous drainage devices seem to represent more effective options, although the latter are associated with the risk of silicon oil escape into subconjuctival space. Endoscopic cyclophotocoagulation in eyes requiring silicon oil removal and glaucoma treatment is another option. Conventional filtration surgery is associated with poor prognosis. ▪ Removal of the intraocular lens may be needed in case of UGH syndrome ▪ Glaucoma surgery according to the specific condition ○ **Glaucoma associated with vitreoretinal surgery:** ▪ Topical and systemic IOP-lowering medication ▪ Surgery for retinal detachment ▪ Consider glaucoma surgery if IOP not controlled ○ **Secondary open angle glaucoma caused by extraocular disease:** ▪ Treatment of the underlying disease ▪ Topical and systemic IOP-lowering medication ▪ Glaucoma surgery
The Australia glaucoma clinical practice guide contents: Clinical	• **Light trial:** • The results from a large multicentre study (LiGHT) examining laser versus medications as first line therapy for primary open angle glaucoma and ocular hypertension suggests

Practice Guide for the Diagnosis and Management of Open Angle Glaucoma 2020[10]	some benefit in offering selective laser trabeculoplasty to patients first. Selective laser trabeculoplasty is a safe procedure and has been suggested to be similar in its cost-effectiveness compared to first-line prostaglandin therapy. Clinicians should recognise though that the LiGHT study included patients with high baseline intraocular pressure (on average 24 mmHg), and many studies have shown that selective laser trabeculoplasty works best on patients with higher pressures, compared to those with lower pressures (such as low or normal tension glaucoma). Clinicians should also recognise that many patients still required topical medications due to pressure spikes or increases. Therefore, whilst selective laser trabeculoplasty may be an effective option, clinicians should maintain close follow up of their ocular hypertensive or primary open angle glaucoma patients. • Topical pharmacotherapy is generally considered the mainstay of glaucoma treatment, particularly for optometrists. Medications for treating glaucoma are divided into several classes, depending on their mechanisms of action. Currently, these include: ▪ Prostaglandin analogues ▪ Beta-blockers ▪ Alpha2-agonists ▪ Carbonic anhydrase inhibitors ▪ Parasympathomimetics **Prostaglandin analogues:** There are a number of reasons why prostaglandin analogues are considered a first-line therapy for glaucoma. As monotherapy, it is generally the most efficacious at reducing IOP and also flattening the diurnal variation curve (i.e. controlling IOP fluctuations). The IOP lowering effect is also sustained over time, unlike some alternatives that may result in development of tachyphylaxis. Adverse effects of prostaglandin analogues are primarily cosmetic in nature. However, this may be a source of non-compliance, so patients need to be appropriately warned prior to treatment initiation. If the initial prostaglandin is partially effective but does not reach target IOP, consider switching within the prostaglandin analogue class, as individual patients may respond to each medication differently. There is some evidence that prostaglandins may

	thin corneas over time, which should be considered when reviewing for effective glaucoma control. **Beta blockers:** Prior to the discovery of prostaglandin analogue therapy, beta-blockers were the first-line therapy for topical glaucoma therapy. Beta-blockers still have a role as a first-line topical therapy particularly in the following cases: ▪ Intolerance to prostaglandin analogues (including its cosmetic effects) ▪ Unilateral treatment (to avoid unilateral cosmetic effects of prostaglandin analogues) ▪ Concerns regarding the presence or potential presence of ocular inflammation Beta-blockers in gel-forming solutions may be best suited for therapy, due to the maintenance of efficacy (25% reduction) at only once daily dosing. Specifically, timolol gel-forming solution is a commonly prescribed and well-studied beta-blocker and its once daily dosing is an attractive clinical choice. Beta-blockers are unlikely to be the first line treatment for most patients, even the cardio-selective medications, given the availability of alternative, safer medications. Beta-blockers should not be used in early or mid-pregnancy periods or in asthma and COPD2, or if already taken systemically. **Alpha 2 agonists:** Alpha-2 agonists are primarily considered to be second-line therapy or adjunctive medication in the management of glaucoma. Indications for monotherapy using an alpha-2 agonist include: intolerance to prostaglandin analogues plus contraindication to beta-blocker use, short-term use in the presence of inflammation of the eye (such as uveitis) or as an interim treatment prior to undergoing laser or surgical glaucoma treatment. Although aqueous production is also reduced by beta-blockers, the alpha-2 agonist acts on a different receptor and should therefore be considered to be complementary to a beta-blocker. Alpha-2 agonist use is often limited in long-term glaucoma management due to the frequent development of follicular conjunctivitis, lower efficacy than prostaglandin analogues and more frequent dosing schedule. **Carbonic anhydrase inhibitors:**

	Carbonic anhydrase inhibitors, like alpha-2 agonists, are also considered to be second-line therapy for glaucoma. Carbonic anhydrase is an enzyme that catalyses the hydration of carbon dioxide and thus inhibition decreases aqueous production from active filtration in the non-pigmented epithelium of the pars plicata. As it decreases aqueous production via an alternative pathway to beta-blockers, it acts synergistically with other antiglaucoma medications. Brinzolamide is typically recommended over dorzolamide due to better efficacy and tolerability. **Parasympathomimetics:** Pilocarpine is the only sympathomimetic available for use by optometrists in Australia and is rarely used in modern glaucoma management. **Laser therapy** **Surgical treatment options for glaucoma:** refer to table **Emerging therapies:** The role of agents to support neural health or provide neuroprotection to the retinal ganglion cells has been a topic of interest complementing conventional intraocular pressure lowering therapies. Dietary supplementation with vitamin B3 (nicotinamide) has been shown by a variety of animal studies to reduce vulnerability to glaucoma by supporting the neural elements of the eye. Nitric oxide is thought to directly trigger relaxation of the trabecular meshwork. Nitric oxide is also suggested to relax the vessel within the canal of Schlemm. Latanoprostene bunod, incorporates nitric oxide by being a nitric oxide donor, releasing it to the trabecular meshwork upon metabolism. By adding another mechanism of action to reduce intraocular pressure, nitric oxide may complement existing anti-glaucoma medications, thereby further lowering intraocular pressure. Netarsudil 0.02% (Rhopressa) is a new antiglaucoma medication in the new rho kinase class. It primarily acts on trabecular meshwork cells, preventing assembly and stabilization of actin fibers, to increase the pore size and outflow and subsequently reduce IOP. However, they also increase blood vessel diameter reducing resistance to aqueous outflow, and inhibit norepinephrine (which is thought to mimic alpha 2 agonists) and reduce aqueous production.

Optometric clinical practice guideline 2020- care of the patient with open angle glaucoma[11]	• The treatment of OAG includes the use of topical or orally administered agents that enhance aqueous outflow or reduce aqueous production or both. – refer to the table.

Appendix C. MeSH Terms PubMed

Query	Filters	Search Details	Results
((((((((((((((((((((Glaucoma, Open-Angle[MeSH Terms]) OR (Open-Angle Glaucomas[Title/Abstract])) OR (Glaucoma, Compensated[Title/Abstract])) OR (Compensated Glaucoma[Title/Abstract])) OR (Open-Angle Glaucoma[Title/Abstract])) OR (Glaucoma, Open Angle[Title/Abstract])) OR (Open Angle Glaucoma[Title/Abstract])) OR (Open Angle Glaucomas[Title/Abstract])) OR (Glaucoma, Pigmentary[Title/Abstract])) OR (Pigmentary Glaucoma[Title/Abstract])) OR (Glaucoma, Simple[Title/Abstract])) OR (Simple Glaucoma[Title/Abstract])) OR (Glaucoma Simplex[Title/Abstract])) OR (Simplex, Glaucoma[Title/Abstract])) OR (Simplices, Glaucoma[Title/Abstract])) OR (Glaucoma, Compensative[Title/Abstract])) OR (Compensative Glaucoma[Title/Abstract])) OR (Glaucoma, Primary Open Angle[Title/Abstract])) OR (Primary Open Angle Glaucoma[Title/Abstract])) OR (Chronic Primary Open Angle Glaucoma[Title/Abstract])) OR (Secondary Open Angle Glaucoma[Title/Abstract])) OR (Glaucoma, Secondary Open Angle[Title/Abstract])	Guideline, in the last 5 years	("glaucoma, open angle"[MeSH Terms] OR "open angle glaucomas"[Title/Abstract] OR (("Glaucoma"[MeSH Terms] OR "Glaucoma"[All Fields] OR "Glaucomas"[All Fields] OR "glaucomas"[All Fields]) AND "Compensated"[Title/Abstract]) OR "compensated glaucoma"[Title/Abstract] OR "open angle glaucoma"[Title/Abstract] OR "glaucoma open angle"[Title/Abstract] OR "open angle glaucoma"[Title/Abstract] OR "open angle glaucomas"[Title/Abstract] OR "glaucoma pigmentary"[Title/Abstract] OR "pigmentary glaucoma"[Title/Abstract] OR "glaucoma simple"[Title/Abstract] OR "simple glaucoma"[Title/Abstract] OR "glaucoma simplex"[Title/Abstract] OR "simplex glaucoma"[Title/Abstract] OR ("Simplices"[All Fields] AND "Glaucoma"[Title/Abstract]) OR (("Glaucoma"[MeSH Terms] OR "Glaucoma"[All Fields] OR "Glaucomas"[All Fields] OR "glaucomas"[All Fields]) AND "Compensative"[Title/Abstract]) OR (("Compensative"[All Fields] OR "compensatively"[All Fields]) AND "Glaucoma"[Title/Abstract]) OR "glaucoma primary open angle"[Title/Abstract] OR "primary open angle glaucoma"[Title/Abstract] OR "chronic primary open angle glaucoma"[Title/Abstract] OR "secondary open angle glaucoma"[Title/Abstract] OR "glaucoma secondary open angle"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	2

Appendix D. Treatment Algorithm

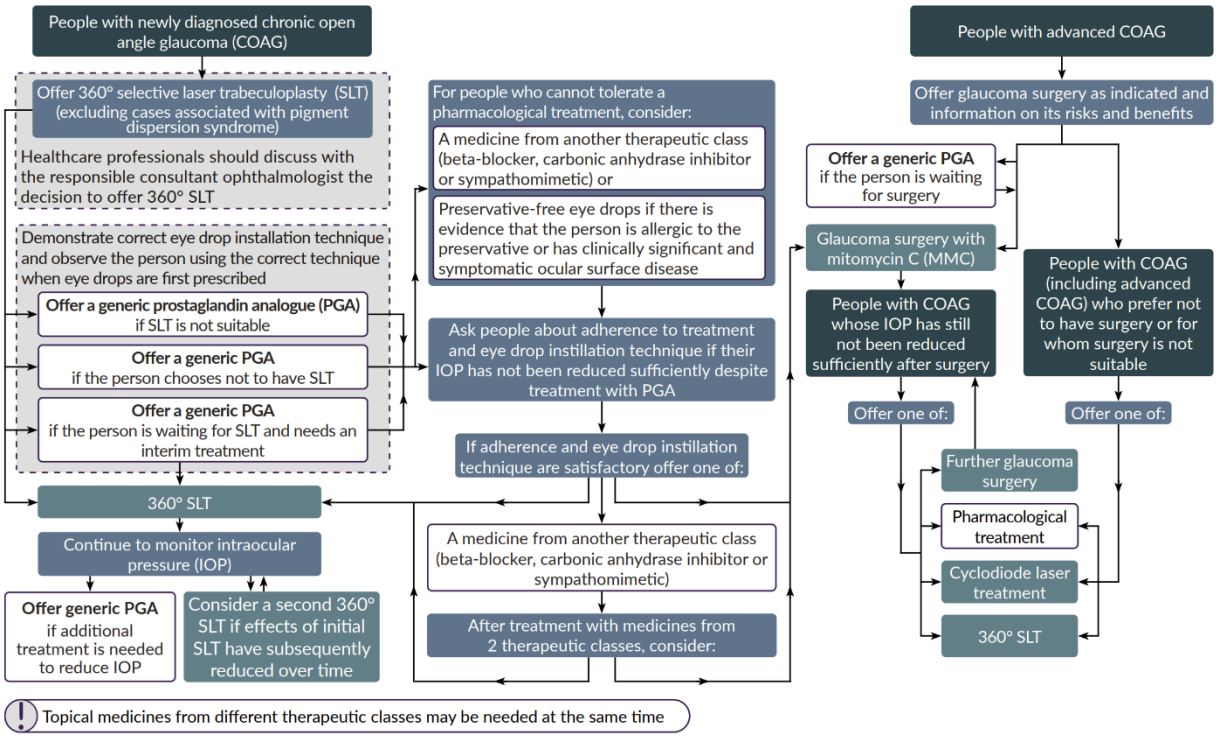

Figure 2. *Treatment algorithm for open angle glaucoma. Retrieved from the NICE 2022 Guidelines.*