

# MEDICATION COVERAGE POLICY

## PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE



<b>POLICY</b>	Glaucoma	<b>P&amp;T DATE:</b>	9/11/2018
<b>THERAPEUTIC CLASS</b>	Ophthalmic Disorders	<b>REVIEW HISTORY</b> (MONTH/YEAR)	2/17, 11/15, 9/12
<b>LOB AFFECTED</b>	Medi-Cal		

*This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.*

### OVERVIEW

Treatment of open-angle glaucoma includes 3 options, medical treatment, laser therapy, incisional glaucoma surgery, or in combination of treatments. Pharmacologic options are the most common initial intervention to reduce intraocular pressure and the choice of medication is typically determined by potential cost, side effects, dosing schedules, and degree of pressure needed to be reduced.<sup>1</sup>

Primary angle closure glaucoma usually requires surgery and acute management.<sup>2</sup> The purpose of this Glaucoma Coverage Policy is to review the coverage criteria of HPSJ's formulary glaucoma agents (*Table 1*).

**Tablet 1: Available Glaucoma Medications (Current as of 7/2018)**

Therapeutic Class	Generic (Brand)	Strengths	Formulary Limits	Avg Cost Per Rx	Notes
<b>BETA-ADRENERGIC BLOCKERS</b>	Betaxolol Hcl (Betoptic S)	Betoptic S Suspension;			
		0.25 %	-	\$334.56	
		Solution;			
	Carteolol Hcl	0.5 %	-	\$53.77	
		Solution;			
	Levobunolol Hcl (Betagan)	1 %	-	\$9.96	
		Solution;			
	Metipranolol	0.5 %	-	\$7.57	
		Solution;			
	Timolol hemihydrate (Betimol)	0.3 %	-	--	
		Solution;			
		0.25%		--	
	Timolol Maleate PF (Timoptic Ocudose)	0.5 %	-	\$125.87	
		Solution;			
	Timolol Maleate (Istalol, Timoptic, Timoptic-XE)	Preservative Free Dropperette:			
0.25 %		-	\$380.33		
0.5 %		-	---		
Istalol 0.5 % Solution		NF	\$152.22	Alternatives: Timolol maleate, Betaxolol, Carteolol, Levobunolol, Metipranol	
Solution;					
0.25 %		-	\$2.92		
<b>CARBONIC ANHYDRASE INHIBITORS</b>	Acetazolamide (Diamox)	0.5 %	-	\$4.10	
		Gel Forming Solution;			
		0.25 %	-	\$117.00	
	Methazolamide (Neptazane)	0.5 %	-	\$113.05	
		Solution;			
Oral;	Acetazolamide (Diamox)	125 mg tablet	-	\$95.46	
		250 mg tablet	-	\$120.95	
500 mg ER capsule		-	\$147.65		
Eye Drops;	Brinzolamide (Azopt)	25 mg tablet		\$55.16	
		50 mg tablet		\$299.60	
Suspension;	Dorzolamide Hcl (Trusopt)	1 %	-	\$293.12	
		Solution;			
	2 %	-	\$24.07		

<b>ALPHA-2 ADRENERGIC AGONISTS</b>	Solution;				
	Brimonidine Tartrate (Alphagan, Alphagan P, Lumify 0.025%-OTC)	0.1 %	-	\$146.67	
		0.15%	-	\$111.58	
		0.2%	-	\$13.18	
		0.025%	NF		Alternatives are Brimonidine 0.1%, 0.15%, 0.2%
	Apraclonidine Hcl (Iopidine)	0.5 %	--	\$64.34	
		1 %	--	--	
Phenylephrine (Altafrin, Mydrin)	2.5%	--	--		
	10%	--	--		
<b>PROSTAGLANDIN ANALOGUES</b>	Solution;				
	Bimatoprost (Lumigan)	Lumigan 0.01 %	--	\$192.63	
		Bimatoprost 0.03%	--	\$ 96.90	
	Latanoprost (Xalatan)	0.005 %	-	\$7.20	
	Latanoprostene Bunod {Vyzulta}	0.024%	NF		Alternatives are Lumigan, Latanoprost
	Tafluprost (Zioptan)	0.0015 %	NF	\$184.38	
	Travoprost (Travatan Z)	0.004 %	NF	\$255.13	
Travoprost benzalkonium	0.004 %	NF	--		
<b>CHOLINERGIC AGONISTS/ PARASYMPATHOMIMETIC</b>	Carbachol (Miostat)	Intraocular solution;			
		0.01 %	-	--	
	Echothiophate Iodide (Phospholine Iodide)	Solution;			
		0.125 %	-	\$90.44	
	Pilocarpine Hcl (Isopto, Carpine)	Solution;			
		1 %	-	\$66.53	
2 %		-	\$63.11		
	4 %	-	\$76.09		
<b>COMBINATION AGENTS</b>	Brinzolamide/ Brimonidine (Simbrinza)	Suspension;			
		1/0.2%		\$150.98	
	Dorzolamide Hcl/ Timolol Maleate (Cosopt, Cosopt PF)	Preservative Free Drops;			
		2/0.5 %	NF	\$158.81	Alternative: Dorzolamide/Timolol maleate or use as separate agents
Dorzolamide Hcl/Timolol Maleate (Cosopt)	Solution;				
	2/0.5 %	-	\$44.08		
Brimonidine Tartrate/Timolol (Combigan)	Solution;				
	0.2 /0.5 %	-	\$168.06		
<b>RHO KINASE INHIBITOR</b>	Netarsudil (Rhopressa)	Solution;			
		0.02%	NF	\$233.58	
<b>Miscellaneous Agents</b>	Unoprostone (Rescula)	Solution;			
		0.15%	NF	--	<b>Discontinued</b>

## ⊕ EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed & approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

### Beta-Adrenergic Blockers

*Betaxolol Hcl (Betoptic S), Carteolol Hcl, Levobunolol Hcl, (Betagan), Metipranolol, Timolol hemihydrate (Betimol), Timolol Maleate/PF (Timoptic Ocudose PF), Timolol Maleate (Istalol, Timoptic, Timoptic-XE)*

### **Betaxolol Hcl (Betoptic S), Carteolol Hcl, Levobunolol Hcl, Metipranolol, Timolol hemihydrate (Betimol), Timolol Maleate/PF (Timoptic Ocudose PF), Timolol Maleate (Timoptic, Timoptic-XE)**

- Coverage Criteria: NONE
- Limits: NONE
- Required Information for Approval: N/A
- Other Notes: NONE
- Non-Formulary: Istalol

### Carbonic Anhydrase Inhibitors

*Acetazolamide (Diamox), Brinzolamide (Azopt), Dorzolamide Hcl(Trusopt),, Methazolamide (Neptazane)*

### **Acetazolamide (Diamox), Brinzolamide (Azopt), Dorzolamide Hcl(Trusopt),, Methazolamide (Neptazane)**

- Coverage Criteria: NONE
- Limits: NONE
- Required Information for Approval: N/A
- Other Notes: NONE

### Alpha-2 Adrenergic Agonists

*Brimonidine Tartrate (Alphagan ,Alphagan P, Lumify 0.025%-OTC ), Apraclonidine Hcl (Iopidine), Phenylephrine (Altafrin)*

### **Brimonidine Tartrate (Alphagan ,Alphagan P, Lumify 0.025%-OTC ), Apraclonidine Hcl (Iopidine), Phenylephrine (Altafrin, Mydfrin)**

- Coverage Criteria: NONE
- Limits: NONE
- Required Information for Approval: N/A
- Other Notes: NONE
- Non-Formulary: Lumify 0.025%-OTC

### Prostaglandin Analogues

*Bimatoprost (Lumigan), Latanoprost (Xalatan), Latanoprostene Bunod (Vyzulta), Tafluprost (Zioptan), Travoprost (Travatan Z), Travoprost benzalkonium*

### **Bimatoprost (Lumigan), Latanoprost (Xalatan)**

- Coverage Criteria: NONE
- Limits: NONE
- Required Information for Approval: N/A
- Other Notes: NONE
- Non-Formulary: Tafluprost (Zioptan), Travoprost (Travatan Z), Latanoprostene Bunod [Vyzulta), Travoprost benzalkonium

### Cholinergic Agonists/Parasympathomimetic Drugs

*Carbachol (Miostat), Echothiophate Iodide (Phospholine Iodide), Pilocarpine Hcl*

### **Carbachol (Miostat), Echothiophate Iodide (Phospholine Iodide), Pilocarpine Hcl**

- Coverage Criteria: NONE
- Limits: NONE
- Required Information for Approval: N/A
- Other Notes: NONE

### Combination Agents

*Brinzolamide/Brimonidine (Simbrinza), Dorzolamide Hcl/Timolol Maleate (Cosopt , Cosopt PF), Brimonidine Tartrate/Timolol (Combigan)*

**Dorzolamide Hcl/Timolol Maleate (Cosopt), Brimonidine Tartrate/Timolol (Combigan), Brinzolamide/Brimonidine (Simbrinza)**

- Coverage Criteria: NONE
- Limits: NONE
- Required Information for Approval: N/A
- Other Notes: NONE
- Non-Formulary: Cosopt PF

**Rho Kinase Inhibitor**

*Netarsudil (Rhopressa)*

- Non-Formulary: Netarsudil (Rhopressa)

**Miscellaneous Agents;**

*Unoprostone (Rescula)*

- Non-Formulary: Unoprostone (Rescula)

⊕ **CLINICAL JUSTIFICATION**

Prostaglandin analog and beta-blocker eye drops are most commonly used as initial treatment for open-angle glaucoma. Prostaglandin analogs, with advantages of being most effective, well-tolerated and once daily dosing, are the most frequently prescribed eye drops for lower Intra ocular pressure (IOP). Adequate treatment of glaucoma requires adherence to therapy. The American Academy of Ophthalmology recommends weighing effectiveness, side effects, and frequency of dosing when considering pharmacologic therapy because side effects and dosing frequency may affect adherence. Systemic side effects of these agent should be taken into consideration which may greatly affect medication adherence. If one drug fails, the ophthalmologist can replace the drug or may use combination therapy depending on whether the patient has responded to the first medication (the first medication should not be continued if there is no response in IOP lowering).<sup>2</sup> Refractory glaucoma can be treated with laser therapy, surgery, or stents.<sup>2</sup>

Primary angle-closure is appositional or synechial closure of the anterior chamber angle, and is classified as: Primary angle-closure suspect ( $\geq 180$  degrees iridotrabeular contact (ITC), normal intraocular pressure [IOP], and no optic nerve damage), Primary angle closure ( $\geq 180$  degrees ITC with peripheral anterior synechiae [PAS] or elevated IOP, but no optic neuropathy), Primary angle-closure glaucoma ( $\geq 180$  degrees ITC with PAS, elevated IOP, and optic neuropathy), Acute angle-closure crisis (AACC; occluded angle with symptomatic high IOP), and Plateau iris configuration (any ITC persisting after a patent laser peripheral iridotomy [LPI]) or syndrome (any ITC persisting after a patent LPI with pressure elevation after dilation).

Primary angle-closure glaucoma is treated with iridotomy, using either a thermal or neodymium yttrium-aluminum-garnet (Nd:YAg) laser.<sup>1</sup> Acute attacks are treated to relieve acute symptoms and potential harmful high IOP. Patients are treated acutely with medications first to reduce pain and clear corneal edema followed by iridotomy as soon as possible. Medications include, topical beta-blockers; topical alpha2-agonists; topical, oral, or intravenous carbonic anhydrase inhibitors; topical miotics; or oral or intravenous hyperosmotic agents.

**Table 2: Primary Open-Angle Glaucoma 2015<sup>1</sup>**

Drug Classification	Methods of Action	IOP Reduction*	Potential Side Effects	Potential Contraindications	FDA Pregnancy Safety Category†
Prostaglandin analogs	Increase uveoscleral and/or trabecular outflow	25%–33%	<ul style="list-style-type: none"> <li>• Increased and misdirected eyelash growth</li> <li>• Periocular hyperpigmentation</li> <li>• Conjunctival injection</li> <li>• Allergic conjunctivitis/contact dermatitis</li> <li>• Keratitis</li> <li>• Possible herpes virus activation</li> <li>• Increased iris pigmentation</li> <li>• Uveitis</li> <li>• Cystoid macular edema</li> <li>• Periorbitopathy</li> <li>• Migraine-like headache</li> <li>• Flu-like symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• Macular edema</li> <li>• History of herpetic keratitis</li> <li>• Active uveitis</li> </ul>	C
Beta-adrenergic antagonists (beta-blockers)	Decrease aqueous production	20%–25%	<ul style="list-style-type: none"> <li>• Allergic conjunctivitis/contact dermatitis</li> <li>• Keratitis</li> <li>• Bronchospasm (seen with nonselective)</li> <li>• Bradycardia</li> <li>• Hypotension</li> <li>• CHF (classic teaching, although cardiologists use beta-blockers as first line treatment in CHF)</li> <li>• Reduced exercise tolerance</li> <li>• Depression</li> <li>• Impotence</li> </ul>	<ul style="list-style-type: none"> <li>• Chronic obstructive pulmonary disease (nonselective)</li> <li>• Asthma (nonselective)</li> <li>• CHF</li> <li>• Bradycardia</li> <li>• Hypotension</li> <li>• Greater than first-degree heart block</li> </ul>	C
Alpha-adrenergic agonists	<p>Nonselective: improve aqueous outflow</p> <p>Selective: decrease aqueous production; decrease episcleral venous pressure or increase uveoscleral outflow</p>	20%–25%	<ul style="list-style-type: none"> <li>• Allergic conjunctivitis/contact dermatitis</li> <li>• Follicular conjunctivitis</li> <li>• Dry mouth and nose</li> <li>• Hypotension</li> <li>• Headache</li> <li>• Fatigue</li> <li>• Somnolence</li> </ul>	<ul style="list-style-type: none"> <li>• Monoamine oxidase inhibitor therapy</li> <li>• Infants and children younger than 2 years</li> </ul>	B
Parasympathomimetic agents	Increase trabecular outflow	20%–25%	<ul style="list-style-type: none"> <li>• Increased myopia</li> <li>• Decreased vision</li> <li>• Cataract</li> <li>• Periocular contact dermatitis</li> <li>• Allergic conjunctivitis/contact dermatitis</li> <li>• Conjunctival scarring</li> <li>• Conjunctival shrinkage</li> <li>• Keratitis</li> <li>• Paradoxical angle closure</li> <li>• Retinal tears/detachment</li> <li>• Eye or brow ache/pain</li> <li>• Increased salivation</li> <li>• Abdominal cramps</li> </ul>	<ul style="list-style-type: none"> <li>• The need to regularly assess the fundus</li> <li>• Neovascular, uveitic, or malignant glaucoma</li> </ul>	C

Topical carbonic anhydrase inhibitors (mainly with systemic use)	Decrease aqueous production	15%–20%	<ul style="list-style-type: none"> <li>Allergic dermatitis/conjunctivitis</li> <li>Corneal edema</li> <li>Keratitis</li> <li>Metallic taste</li> </ul>	<ul style="list-style-type: none"> <li>Sulfonamide allergy</li> <li>Kidney stones</li> <li>Aplastic anemia</li> <li>Thrombocytopenia</li> <li>Sickle cell disease</li> </ul>	C
Oral carbonic anhydrase inhibitors	Decrease aqueous production	20%–30%	<ul style="list-style-type: none"> <li>Stevens-Johnson syndrome</li> <li>Malaise, anorexia, depression</li> <li>Serum electrolyte imbalance</li> <li>Renal calculi</li> <li>Blood dyscrasias (aplastic anemia, thrombocytopenia)</li> <li>Metallic taste</li> <li>Enuresis</li> <li>Parasthesia</li> <li>Diarrhea</li> <li>Abdominal cramps</li> </ul>	<ul style="list-style-type: none"> <li>Sulfonamide allergy</li> <li>Kidney stones</li> <li>Aplastic anemia</li> <li>Thrombocytopenia</li> <li>Sickle cell disease</li> </ul>	C
Hyperosmotic agents	Dehydration of vitreous	No data	<ul style="list-style-type: none"> <li>Headache</li> <li>CHF</li> <li>Nausea, vomiting</li> <li>Diarrhea</li> <li>Renal failure</li> <li>Diabetic complications</li> <li>Mental confusion</li> </ul>	<ul style="list-style-type: none"> <li>Renal failure</li> <li>CHF</li> </ul>	C

CHF = congestive heart failure; IOP = intraocular pressure

\* Data from the Heijl A, Traverso CE, eds. Terminology and Guidelines for Glaucoma. European Glaucoma Society. 4th ed. Savona, Italy: PubliComm; 2014:146-51. Available at: [www.eugs.org/eng/EGS\\_guidelines4.asp](http://www.eugs.org/eng/EGS_guidelines4.asp). Accessed May 29, 2015.

† FDA Pregnancy Category B = Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies on pregnant women. FDA Pregnancy Category C = Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

## REFERENCES

1. American Academy of Ophthalmology Glaucoma Panel. Preferred Practice Pattern® Guidelines. Primary Angle Closure. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practice-pattern/primary-angle-closure-ppp-2015>.
2. American Academy of Ophthalmology Glaucoma Panel. Preferred Practice Pattern® Guidelines. Primary Open-Angle Glaucoma. San Francisco, CA: American Academy of Ophthalmology; 2015 Available at: <https://www.aao.org/preferred-practice-pattern/primary-open-angle-glaucoma-ppp-2015>.
3. Vyzulta package insert.
4. Drugs@FDA: FDA Approved Drug Products. FDA Approval label <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=208254>

## REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Formulary Realignment 9-18-12.xlsx	9/2012	Jonathan Szkotak, PharmD
Update to Policy	HPSJ Coverage Policy – Ophthalmic Disorders – Glaucoma 2015-11.docx	11/2015	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Ophthalmic Disorders – Glaucoma 2017-02.docx	2/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Ophthalmic Disorders – Glaucoma 2018-09.docx	9/2018	Johnathan Yeh, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy