Molina Clinical Policy
Durysta (bimatoprost implant): Policy No. 370

Last Approval: 6/8/2022
Next Review Due By: June 2023

Ohio Medicaid: To exclude requirement of trying all(3) other anti-glaucoma medications and to only require trial and failure of at least 2 anti-glaucoma treatments. All requests will be reviewed on individual basis for medical necessity and no hard limits to be applied.

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Open-angle glaucoma (OAG) is a chronic, progressive, and irreversible multifactorial optic neuropathy that is characterized by open angle of the anterior chamber, typical optic nerve head changes, progressive loss of peripheral vision (typical visual field changes) followed by central visual field loss (blindness) for which intraocular pressure (IOP) is an important risk factor. Lowering IOP is the primary goal of therapy and has been shown to reduce the progression of visual field loss. The target IOP and subsequent monitoring intervals depends on several factors, including the extent of optic nerve damage, whether there is recent progression of damage, the stability of IOP, and the level of patient adherence. A target IOP ≥ 25 to 30% below initial IOP is cited a reasonable initial target. Lowering of IOP has been shown as the major modifiable risk factor for both glaucoma and OHT.

Ocular hypertension (OHT) is distinguished from glaucoma in that there are no detectable changes in vision, no evidence of visual field loss, and no damage to the optic nerve. OHT is generally defined as consistently elevated IOP, greater than 21mmHg, in one or both eyes in the absence of clinical evidence of optic nerve damage, visual field defect or other pathology (the defined normal range in the general population pressure is between 10 mm Hg and 21 mm Hg). Among patients with OHT, treatment to lower IOP may delay or prevent the onset of OAG. A clinical management strategy that targets a 20% reduction in IOP in people with OHT has been shown to delay or prevent the onset of glaucoma (Kass et al.; OHTS). Patients diagnosed with OHT are typically asymptomatic and managed either by treating the condition or by regular observation.

Pharmacologic therapy, laser therapy (trabeculoplasty), and/or surgery (trabeculectomy) have been shown to lower IOP. Pharmacologic or laser therapy is usually the first-line treatment. Surgical therapy a first-line approach only for patients with severe visual field loss at baseline, and a second-line approach for patients with advanced open-angle glaucoma who do not respond to medications or laser therapy. Topical IOP-lowering medication remains the mainstay of glaucoma therapy with topical prostaglandins generally recommended as first-line pharmacologic therapy. Meta-analyses have found prostaglandins are more effective at lowering IOP than beta blockers, carbonic anhydrase inhibitors, and alpha-adrenergic agonists for the treatment of open-angle glaucoma. (Li T, et al. 2016; van der VR, et al. 2005; Fung AT et al. 2007). When monotherapies do not reach the target IOP, combination therapy from different classes (i.e., beta blocker plus prostaglandin or beta blocker plus carbonic anhydrase inhibitor) generally result in a greater reduction in the IOP.

Durysta (bimatoprost implant), an intracameral, biodegradable, sustained-release implant, was FDA-approved to reduce IOP in those with OAG or OHT on March 4, 2020. Bimatoprost, is a synthetic structural analog of prostaglandin with ocular hypotensive activity and is believed to lower IOP by increasing outflow of aqueous humor through both the trabecular meshwork and uveoscleral routes. The implant delivers 10 µg of bimatoprost, a prostaglandin analog, and comes in a preloaded, single-use applicator to facilitate the administration directly into the anterior chamber of the eye. Insertion is performed under magnification in an office or ambulatory surgery center. Durysta is a biodegradable implant intended for a single administration and should not be re-administered to an eye

that received a prior Durysta.

COVERAGE POLICY

Durysta (bimatoprost implant) for the treatment of adults with open-angle glaucoma or ocular hypertension **may be considered medically necessary** when **ALL** of the following clinical criteria are met:

1. Diagnosis of **OAG** (i.e., primary OAG, pseudoexfoliation glaucoma, pigmentary glaucoma) OR **OHT** requiring intraocular pressure-lowering treatment

AND

2. Inadequate response, intolerance, contraindication, or clinical rationale supporting the inappropriateness to **ALL** of the following anti-glaucoma medications (at least ONE drug from each class). Documentation of ALL therapy with dates of failed therapy or clinical events.

    a. Ophthalmic prostaglandins (e.g., latanoprost, bimatoprost, travoprost); **AND**
    Informational Note: The topical prostaglandins are increasingly chosen as initial monotherapy in OAG and have been consistently shown to be effective at lowering IOP and well tolerated. Prostaglandins have the advantage of once-daily dosing and do not have the risk of systemic side effects seen with topical beta blockers (2021).

    b. Beta-adrenergic blocker or combination product (e.g., carteolol, levobunolol, metipranolol, timolol, betaxolol, dorzolamide plus timolol); **AND**

    c. Alpha-2-agonists (brimonidine).

    MOLINA REVIEWER: Review profile for anti-glaucoma drug claims and enter an authorization if applicable. Notify Prescriber if an authorization is entered.

AND

3. Member has an inability to manage regular glaucoma eye drop use (e.g., due to age, dexterity, or comorbidities including visual impairment). Documentation required.

AND

4. Documentation/attestation required:
    a. Member has not received prior Durysta administration to the affected eye(s). NOTE: Durysta should not be re-administered to an eye that received a prior Durysta.
    AND
    b. Member does not have ANY of the following conditions (exclusions):
        i. Previous eye surgery (including cataract surgery) and/or any eye laser surgery within the past 6 months in the affected eye; OR
        ii. History of glaucoma surgery; OR
        iii. Anticipated need for laser eye surgery within one year

CONTINUATION OF THERAPY

Retreatment will not be authorized due to insufficient evidence of therapeutic value since clinical benefit beyond one implant for the same eye has not been established.

LIMITATIONS AND EXCLUSIONS

The following are considered **contraindications/exclusions** based on insufficient evidence:

1. Hypersensitivity to bimatoprost or any of the other components of the therapy.
2. Active or suspected ocular or periocular infection.
3. Diagnosis of corneal endothelial cell dystrophy (e.g., Fuchs endothelial dystrophy).
4. Prior corneal transplantation or endothelial cell transplants (e.g., Descemet stripping automated endothelial

keratoplasty [DSAEK]).
5. Absence or rupture of posterior lens capsule owing to the risk of implant migration into the posterior segment.
   NOTE: Laser posterior capsulotomy in pseudophakia (not contraindicated if the intraocular lens fully covers the posterior capsule opening)
6. Previous eye surgery (including cataract surgery) and/or any eye laser surgery within the past 6 months in the affected eye.
7. History of glaucoma surgery.
8. Anticipated need for laser eye surgery within one year.

The following are considered **experimental, investigational and unproven** based on insufficient evidence:
1. Any indications other than those listed above
2. Repeat administration in the same eye

DURATION OF APPROVAL: ONE time authorization for one implant per eye

PRESCRIBER REQUIREMENTS: Prescribed by, or in consultation with, a board-certified specialist in glaucoma and/or neuro-ophthalmology, or ophthalmologist experienced in the administration of intracameral biodegradable implant. Submit consultation notes if applicable.

AGE RESTRICTIONS: 18 years of age or older

DOSING CONSIDERATIONS
Insert 1 implant (10 mcg) intracamerally in anterior chamber of affected eye. Limit to a single implant per eye; do not re-administer to an eye that has received a prior implant

Warnings and Precautions: The presence of Durysta implants has been associated with corneal adverse reactions and increased risk of corneal endothelial cell loss. Administration should be limited to a single implant per eye without retreatment due to possible corneal endothelial cell loss. Durysta has been associated with corneal adverse reactions and risks are increased with multiple implants. Use caution in patients with limited corneal endothelial cell reserve.

QUANTITY LIMITATIONS
ONE implant (10 mcg) per eye (lifetime total)

ADMINISTRATION:
1. May be authorized in an ophthalmologist's office or at a surgery center. Routine administration in a hospital or hospital outpatient setting (other than physician office or ambulatory surgical center) will not be authorized.

AND

2. If member meets all criteria and approval for therapy is granted, medication will be dispensed by a specialty pharmacy vendor at the discretion of Molina Healthcare.

AND

3. Refer to MHI Policy & Procedure (P&P): Specialty Medication Administration Site of Care Policy: MHI Pharm 11

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DRUG INFORMATION

ROUTE OF ADMINISTRATION: Intracameral implant

DRUG CLASS: Antiglaucoma, Prostaglandin analog

FDA-APPROVED USES: Elevated IOP: Reduction of elevated IOP in patients with OAG or OHT

COMPENDIAL APPROVED OFF-LABELED USES: None

SUMMARY OF MEDICAL EVIDENCE

FDA approval of Durysta is based on results from two Phase 3 multicenter, randomized, parallel-group, controlled 20-month (including 8-month extended follow-up) studies of Durysta compared to twice daily topical timolol 0.5% drops, in patients with OAG or OHT. The ARTEMIS trials evaluated 1,122 subjects with OAG or OHT on the efficacy and safety of Durysta versus topical timolol drops, an FDA accepted comparator for registrational clinical trials.

Durysta implant reduced IOP by approximately 30% from a baseline mean of 24.5 mmHg (lowering IOP by 5 to 8 mmHg) over a 12-week period in the two ARTEMIS trials, meeting the specified criteria for non-inferiority to the study comparator. Durysta lowered mean IOP more than timolol at all time points (hours 0 and 2, weeks 2, 6, and 12) and was found to be non-inferior to timolol at all timepoints.

Conjunctival hyperemia is the most frequently reported adverse effect (27%); other adverse effects (5%–10%) include foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, increased intraocular pressure, corneal endothelial cell loss, blurred vision, iritis, and headache.

ARTEMIS 1

The IOP-lowering efficacy and safety of 10- and 15-g bimatoprost implants in patients with OAG and OHT after initial and recurrent administrations were evaluated in this phase 3 trial. Participants were assigned to one of three treatment groups: 10-mcg bimatoprost implant (n=198), 15-mcg bimatoprost implant (n=198) or BID timolol drops (n=198). The mean age of the participants in the study was 62.5 years. Primary OAG was detected in the majority of the studied eyes (78.1%). The mean IOP in the study eyes was comparable across treatment groups. 90.4 percent (10 mcg), 79.3 percent (15 mcg), and 86.9% completed the study (timolol groups). There were 3 administration cycles, week 1, week 16 and week 32. The primary endpoints were IOP and the change in IOP from baseline to week 12. After the last bimatoprost implant or sham administration, participants were to be followed for at least 12 months, or until month 20.Corneal endothelial cell loss and corneal edema were the most common treatment-emergent adverse events (TEAE) leading to early withdrawal from the bimatoprost implant treatment groups. TEAEs, primarily corneal endothelial cell loss and edema, led to the removal of implants in 7 participants (3.6%) in the 10 mcg bimatoprost implant group and 16 subjects (8.3%) in the 15 mcg bimatoprost implant group.

Bimatoprost implants (10- and 15-µg) were shown to be noninferior to timolol in decreasing IOP through week 12. IOP was controlled in most participants after 3 administrations and no further treatment was required after a year. The risk-benefit analysis indicated that the 10mcg implant was preferable to the 15mcg implant. Durysta is an effective treatment for glaucoma, however it is not superior to standard of care. Durysta was implanted every four months for a year in the studies reviewed.

ARTEMIS 2

Phase 3, Randomized, 20-Month Study of the Efficacy and Safety of Bimatoprost Implant in Patients with Open-Angle Glaucoma and Ocular Hypertension (ARTEMIS 2) [ClinicalTrials.gov Identifier: NCT02250651]

This phase 3 study included 528 participants with OAG or OHT and an open iridocorneal angle inferiorly. Participants received 10 or 15 µg bimatoprost implanted or twice-daily topical timolol maleate 0.5% in the study eye. The primary endpoints were IOP and the change in IOP from baseline to week 12. TEAEs and corneal endothelial cell density were used as safety measures. Results supported the prior phase 3 bimatoprost implant research. The bimatoprost implant met the primary goal of lowering IOP. After the third dosage, most patients required no more treatment for 12 months. Benefit-risk assessment favored the 10g implant over the 15g implant. Other administration regimens with lower risk of corneal events are being studied.

Efficacy and Safety Study of Bimatoprost Sustained-Release (SR) in Participants with Open-angle Glaucoma or Ocular Hypertension (ClinicalTrials.gov Identifier: NCT02247804).This study was designed to evaluate the efficacy and safety of bimatoprost SR in participants with open-angle glaucoma or ocular hypertension. The study includes

a 12-month treatment period with an 8-month extended follow-up. Noninferiority is deduced with relative safety. No publication associated with this study reported (as of May 2022).

National and Specialty Organizations

American Academy of Ophthalmology (AAO)

The preferred practice guidelines (2015) for the treatment of primary open-angle glaucoma note that there are many considerations when choosing a target IOP, including the stage of the overall glaucoma damage as determined by the degree of structural optic nerve damage and/or functional visual field loss, baseline IOP at which damage occurred, age of patient, and additional risk factors. The initial treatment choice may be influenced by potential cost, adverse effect profile, and dosing schedule. The guidelines note prostaglandins as the most frequently used initial eye drops for lowering IOP in patients with glaucoma. The AAO does not prefer one prostaglandin over another. (Prum, 2015). Lowering the pretreatment IOP by ≥ 25% has been shown to slow progression of primary open-angle glaucoma. If the target IOP is not achieved by one medication, switching, or adding medications should be considered, depending on whether the patient had responded to the first medication. The guideline recommends switching eye-drop agents or adding on for combination therapy when target IOP is not achieved with one drug alone. A more aggressive target (i.e., a lower target IOP) can be justified if there is more severe nerve damage or the damage is progressing rapidly; a less aggressive target IOP may be reasonable if the risks of treatment outweigh the benefits. **The practice guidance has not been updated to include the use of Durysta in its recommendations at the time of this review.**

SUPPLEMENTAL INFORMATION

Glaucoma: A group of eye diseases traditionally characterized by elevated intraocular pressure (IOP) and more accurately defined as an optic neuropathy than a disease of high pressure. After cataracts, glaucoma is the second leading cause of blindness in the world.

IOP: A measurement of the fluid pressure inside the eye. When eye pressure increases and damages the optic nerve, glaucoma results. This damage reduces vision and if not treated can lead to total blindness.

CODING & BILLING INFORMATION

CPT	Description
66030	Injection, anterior chamber of eye (separate procedure); medication

HCPCS	Description
J7351	Injection, bimatoprost, intracameral implant, 1 microgram *Effective for dates of service on or after October 1, 2020, bill as 10 units

AVAILABLE DOSAGE FORMS: 10 mcg intracameral implant; single-use applicator

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

6/8/2022 MCPC Policy reviewed and updated. No changes in coverage criteria Updated references.
6/9/2021 MCPC Policy reviewed and revised. Updated references. IRO Peer Review. 5/12/2021. Practicing Physician. Board certified in Ophthalmology. Content update includes:

- In initial coverage criteria section 'Step/Conservative Therapy/Other Condition Requirements' added *'or combination*

	product' to beta-adrenergic blocker [updated criterion: beta-adrenergic blocker or combination product (e.g., carteolol, levobunolol, metipranolol, timolol, betaxolol, dorzolamide plus timolol)] • Reviewed and updated ongoing clinical trials
Q3 2020 P&T	New policy. IRO Peer Review. 6/11/2020. Practicing Physician. Board certified in Ophthalmology.

REFERENCES

Government Agencies

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database: National coverage determination (NCD) (search: Durysta, bimatoprost). Available from CMS; CMS NCD. There are no CMS NCDs for Durysta available as of May 2022.
2. ClinicalTrials.gov. The efficacy and safety of Bimatoprost SR in patients with open-angle glaucoma or ocular hypertension. ClinicalTrials.gov Identifier: NCT02250651 Available from ClinicalTrials.gov. Accessed April 2022.
3. Food and Drug Administration (FDA). FDA approves first treatment for thyroid eye disease. Available here. Accessed April 2022.

Prescribing Information and Drug Compendia

1. Durysta (bimatoprost) implant [prescribing information]. Madison, NJ: Allergan; November 2020.
2. Clinical Pharmacology, Elsevier. Available from ClinicalKey. Published 2022. Accessed April 2022. Registration and login required.
3. Drug Facts and Comparisons. Facts and comparisons eAnswers. Available from Wolters Kluwer Health, Inc. Accessed April 2022. Registration and login required.
4. DynaMed. Medications for primary open-angle glaucoma (record no. T914120). Updated Nov. 30, 2018. Available from DynaMed. Registration and login required.

Peer Reviewed Publications

1. Bacharach J, Tatham A, Ferguson G, et al. ARTEMIS 2 study group: Phase 3, randomized, 20-month study of the efficacy and safety of Bimatoprost implant in patients with open-angle glaucoma and ocular hypertension (ARTEMIS 2). Drugs. 2021 Nov;81(17):2017-2033. doi: 10.1007/s40265-021-01624-9.
2. Craven ER, Walters T, Christie WC, et al. Bimatoprost SR study group: 24-month phase I/II clinical trial of Bimatoprost sustained-release implant (Bimatoprost SR) in glaucoma patients. Drugs. 2020 Feb;80(2):167-179. doi: 10.1007/s40265-019-01248-0.
3. Fung AT, Reid SE, Jones MP, et al. Meta-analysis of randomized controlled trials comparing latanoprost with brimonidine in the treatment of open-angle glaucoma, ocular hypertension or normal-tension glaucoma. Br J Ophthalmol 2007; 91:62.
4. Garway-Heath DF, Crabb DP, Bunce C, et al. Latanoprost for open-angle glaucoma (UKGTS): A randomized, multicenter, placebo-controlled trial. Lancet 2015; 385:1295.
5. Kass MA, Heuer DK, Higginbotham EJ, et al. The ocular hypertension treatment study: A randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002 Jun. 120(6):701-13; discussion 829-30. Available from Medline.
6. Lewis RA, Christie WC, Day DG, et al. Bimatoprost sustained-release implants for glaucoma therapy: 6-month results from a phase I/II clinical trial. Am J Ophthalmol 2017; 175:137–147.
7. Medeiros FA, Walters TR, Kolko M, et al. Phase 3, randomized, 20-Month study of Bimatoprost implant in open-angle glaucoma and ocular hypertension (ARTEMIS 1). Ophthalmology. 2020 Jun 13:S0161-6420(20)30555-8. doi: 10.1016/j.ophtha.2020.06.018.
8. Li T, Lindsley K, Rouse B, et al. Comparative effectiveness of first-line medications for primary open-angle glaucoma: A systematic review and network meta-analysis. Ophthalmology 2016; 123:129.
9. Singh K, Lee BL, Wilson MR, et al. Glaucoma modified RAND-like methodology group: A panel assessment of glaucoma management - modification of existing RAND-like methodology for consensus in ophthalmology. Part II: Results and interpretation. Am J Ophthalmol 2008; 145:575.
10. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: A review. Available from JAMA. 2014 May 14; 311(18): 1901–1911.

National and Specialty Organizations

1. National Institute for Health and Clinical Excellence (NICE). Diagnosis and management of chronic open angle glaucoma and ocular hypertension. 2009. Available from NICE. Accessed April 2022
2. American Academy of Ophthalmology (AAO).
   - Preferred practice pattern guidelines: Primary open-angle glaucoma suspect. Ophthalmology. 2016 Jan;123(1):P112-51. doi doi: 10.1016/j.ophtha.2015.10.055. Erratum in: Ophthalmology. 2018 Jun;125(6):949. Accessed April 2022.
   - Primary open-angle glaucoma PPP 2020. AAO PPP Glaucoma Committee, Hoskins Center for Quality Eye Care. Nov 2020. Available from AAO. Accessed April 20, 2022.

Other Peer Reviewed and National Organization Publications (used in the development of this policy)

1. Jacobs DS. Open-angle glaucoma: Epidemiology, clinical presentation, and diagnosis. Available from UpToDate. Updated August 4, 2020. Accessed April 2022. Registration and login required.
2. Jacobs DS. Open-angle glaucoma: Treatment. Available from UpToDate. Updated August 18, 2021. Accessed April 2022. Registration and login required.

APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language,*

Medicaid criteria and other mandated criteria.

Ohio Medicaid: To exclude requirement of trying all(3) other anti-glaucoma medications and to only require trial and failure of at least 2 anti-glaucoma treatments. All requests will be reviewed on individual basis for medical necessity and no hard limits to be applied.