Original Effective Date: 12/13/2017
Current Effective Date: 06/13/2024
Last P&T Approval/Version: 04/24/2024
Next Review Due By: 10/2024
Policy Number: C11728-A

Iluvien (fluocinolone acetonide intravitreal implant)

PRODUCTS AFFECTED

Iluvien (fluocinolone acetonide intravitreal implant)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

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.

DIAGNOSIS:
Diabetic Macular Edema (DME)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. DIABETIC MACULAR EDEMA (DME):
1. Documented diagnosis of Diabetic Macular Edema (DME)
   AND

2. Documentation of baseline visual status with notation of eye being treated [DOCUMENTATION REQUIRED]
   AND
3. Documentation of an inadequate response (defined as 1-2 injections with minimal to no improvement), clinically significant adverse effects, or contraindication to bevacizumab
   AND
3. Documentation of an inadequate response to an appropriate trial of intravitreal glucocorticoids (i.e., triamcinolone)
   AND
4. Member was previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure
   AND
5. Prescriber attests or clinical reviewer has found that Iluvien (fluocinolone acetonide intravitreal implant) will NOT be administered simultaneously (bilateral implantation) and is NOT intended for administration with other intravitreal implants [i.e., Ozurdex (dexamethasone intravitreal implant), Retisert (fluocinolone acetonide intravitreal Implant)]
   MOLINA REVIEWER NOTE: Simultaneous bilateral implantation should not be performed to limit the potential for bilateral post-operative infection (due to the risk of, and resistance to infections reduced by corticosteroids)
   AND
6. Prescriber attests the member has been informed about the potential adverse effects of a corticosteroid intravitreal implant, including cataracts, intraocular pressure, or hypotony, endophthalmitis, and risk of need for additional surgical procedures

CONTINUATION OF THERAPY:

A. DIABETIC MACULAR EDEMA (DME):

1. Reauthorization request is for the same eye as initial authorization AND at least 36 months have passed since last Iluvien administration.
   NOTE: The continuation of therapy criteria is only for the same previously treated eye. If member has developed condition in an untreated eye, a new request should be submitted and meet all initial coverage criteria.
   AND
2. Documentation or improvement of stabilization of disease state (e.g., macular edema, etc.) and visual status [DOCUMENTATION REQUIRED]
   AND
3. Prescriber attests member is likely to benefit from re-treatment without being exposed to significant risk according to Prescriber's clinical judgement
   AND
4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., cataracts, increased intraocular pressure, hypotony, endophthalmitis)

DURATION OF APPROVAL:

Initial authorization: 36 months, Continuation of therapy: 36 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified ophthalmologist or retinal specialist experienced in the administration of intravitreal implants. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

ONE implant per eye per 36 months

PLACE OF ADMINISTRATION:
The recommendation is that intravitreal injection medications in this policy will be for pharmacy or medical benefit coverage and the implant administered in a place of service that is a non-hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Ophthalmic intravitreal injection

DRUG CLASS:
Anti-inflammatory Agent, Corticosteroid, Ophthalmic

FDA-APPROVED USES:
Treatment of diabetic macular edema in patients who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in IOP

COMPENDIAL APPROVED OFF-LABELED USES:

APPENDIX

APPENDIX:

Diabetic Macular Edema (DME): Leakage of fluid from retinal blood vessels which cause the macula to swell

Diabetic Retinopathy (DR): The progressive damage to the blood vessels in the back of the eye

Intravitreal: refers to that which is injected into the eye's vitreous humor between the lens and the retina. Intravitreal implants deliver a continuous concentration of drug over a prolonged period of time. Intravitreal corticosteroid implants are being studied for a variety of eye conditions leading to macular edema, including uveitis, diabetic retinopathy, and retinal venous occlusions. The goal of therapy is to reduce the inflammatory process in the eye while minimizing the adverse effects of the therapeutic regimen.

Phakic: An eye containing the natural lens

Pseudophakic: An eye in which a natural lens is replaced with an artificial lens implant

Retinopathy: Damage to the retina

Vascular Endothelial Growth Factor (VEGF): A chemical signal produced by the body's cells that stimulates growth of new blood vessels.

Uveitis: An inflammation of part or all of the uvea, the middle (vascular) tunic of the eye and commonly involving the other tunics (the sclera and cornea and the retina)

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Ehlers et al. (2022) wrote a report by the American Academy of Ophthalmology reviewing the safety and efficacy evidence for diabetic macular edema (DME) treatments. The review revealed that the current intravitreal pharmacotherapies, such as anti-VEGF injections and corticosteroid implants, are safe and effective. Corticosteroid implants carry a higher risk of increased intraocular pressure (IOP) related

adverse effects compared to anti- VEGF therapeutics. As there is a lack of robust comparative analysis evidence between anti- VEGF, corticosteroid implants, and combination therapies the authors emphasize that the choice of therapy is up to physician discretion and that access to all therapeutic options is imperative for appropriate care of individual patients.

Brambati et al (2022) conducted a retrospective cohort study on ten eyes from ten subjects with type 2 non-proliferative diabetic retinopathy and DME at baseline treated with Iluvien. A minimum of two 6 × 6-mm optical coherence tomography angiography (OCTA) scans were required to ensure that all cases had a baseline OCTA and an OCTA performed at 4 months of follow-up. Mean parafoveal perfusion density (PD) at baseline was 64.1 ± 1.8% at baseline, increasing to 66.1 ± 2.9% ($p = 0.013$) at the 4-month follow-up visit. In the qualitative assessment, 60 regions (10 areas for each subject) were graded to assess changes in retinal perfusion between the baseline and follow-up visits. This assessment revealed that 24 regions (40.0%) were characterized by a qualitative increase in perfusion after treatment, while 22 (36.7%) and 14 (23.3%) regions were featured by a stability and reduction in retinal perfusion, respectively.

Mansour et al. (2021) conducted a 24-month prospective observational study of participants treated with Iluvien to confirm safety and efficacy of the fluocinolone acetonide (FAc) intravitreal implant. Ninety-five participants (115 study eyes) were included in the study. The participants were previously steroid-challenged patients for up to 36 months pre-FAc and followed 24 months post-FAc implant. Mean IOP for the overall population remained stable post-FAc compared with pre-FAc implant. IOP- lowering therapies necessary were as follows, two trabeculoplasties and four IOP-lowering surgeries post-FAc. Mean visual acuity was stable post-FAc (mean improvement of 1-3 letters) and fewer DME treatments were required per year following FAc implant. Mean central subfield thickness was significantly reduced at 24 months post-FAc implant ($p<0.001$) and the percentage of patients with central subfield thickness ≤300 μm was significantly increased ($p=0.041$). Positive efficacy outcomes were noted after treatment, with stabilization of vision and reduction in inflammation. The FAc implant is a favorable treatment option for DME, especially when administered after a prior steroid challenge (Clinicaltrials.gov).

Adan et al. (2020) reviewed current literature and clinical practice to compile a clinical decision criterion to identify recurrent diabetic macular edema patients suitable for Iluvien, complete with follow up recommendations. The authors analyzed the data and concluded there is progressive and continuous improvement of the macula and visual outcomes with FAc. In response to clinical trial and real world evidence, the recommendations conclude that FAc implants should be positioned earlier in the DME treatment algorithm for those who have received one or two previous dexamethasone injections and continue to show presence of DME 3-4 post injection, as this indicates the patient has reoccurring DME and will require continued injections for a long period of time; moving to the FAc implant treatment will prevent patients from being subjected to a high number of unnecessary injections of suboptimal treatment. The recommendations conclude the main patient profile that could benefit from the FAc implant is for patients with a complete anatomical response after one injection of dexamethasone implant for those patients whom the retina layers are preserved; however, the FAc implant has shown efficacy even in those patients that had insufficient response to previous therapies.

Rittiphairoj et al. (2020), in a Cochrane review, compared intravitreal steroid therapy to other treatments for DME. The systematic review included 10 RCTs (4348 participants, 4505 eyes) that compared any type of intravitreal steroids as monotherapy to any other intervention (e.g., observation, laser photocoagulation, anti-VEGF for DME. These trials compared intravitreal steroid therapies to other treatments such as

intravitreal anti-VEGF therapy, laser photocoagulation, and sham injection. One study (560 eyes) compared intravitreal fluocinolone implant 0.19mg to sham. At 12 months, there was moderate certainty that fluocinolone improved visual acuity slightly more. Fluocinolone was more likely than placebo to increase visual acuity by three or more lines at 12 months, according to evidence of moderate certainty. Fluocinolone also increased the risk of cataract progression (participants = 335; moderate-certainty evidence), which occurred in approximately 8 out of 10 participants, and the use of IOP-lowering medications (participants = 558; moderate-certainty evidence), which was required in 2 to 3 out of 10 participants. The authors concluded that intravitreal steroids may improve vision in patients with DME compared to placebo or control. In most comparisons, the effects were negligible, approximately one line of vision or less. More evidence is available when comparing dexamethasone or fluocinolone implants to placebo, however evidence comparing dexamethasone with anti-VEGF therapy is limited and inconsistent. Any benefits should be evaluated against IOP rise, usage of IOP-lowering medication, and cataract advancement in phakic patients. Glaucoma surgery is also increasing but remains rare. Chakravarthy et al. (2019) conducted a multicenter open-label observational study collecting real-world data on the safety and effectiveness of five hundred and sixty-three patients (593 eyes) treated with the fluocinolone acetonide (FAc) intravitreal implant. Mean IOP for the overall population remained within the normal range throughout follow-up and 76.7% of patients did not require IOP-lowering therapy following treatment of the FAc implant. Sixty-nine per cent of eyes did not require additional DME treatments. Mean visual acuity in the overall population increased from 51.9 letters at baseline to 55.6 letters at month 12, with a significant increase of 2.9 letters at last observation. Patients with short-term DME experienced greater visual acuity gains than those with long-term DME. This data reinforces the safety and efficacy of the FAc treatment, and the benefit of early FAc treatment.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Iluvien (fluocinolone acetonide intravitreal implant) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Iluvien (fluocinolone acetonide intravitreal implant) include: Ocular or periocular infections, Glaucoma, and Hypersensitivity.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J7313	Injection, fluocinolone acetonide intravitreal implant (Iluvien), 0.01 mg

AVAILABLE DOSAGE FORMS:
Iluvien IMPL 0.19MG

REFERENCES

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12. United States Food and Drug Administration (FDA). Drugs@FDA: FDA-Approved Drugs. Iluvien. FDA.gov. Accessed August 28, 2023.

SUMMARY OF REVIEW/REVISIONS	DATE
MCP Conversion	Q2 2024
Policy reviewed and updated, no changes in coverage criteria, updated references	10/12/2023
Policy reviewed. References updated. Revision of criteria #3a broadened to 'a previous course of corticosteroid.' Previously 3a. Triamcinolone acetonide, intravitreal injection; Revised to: Triamcinolone acetonide, intravitreal injection previous course of corticosteroid. Reference: Fraser et al. (2020)	10/12/2022
MCPC Policy reviewed and updated, no changes in coverage criteria, updated references. IRO Peer Review 9/1/2021 by a practicing board certified in Ophthalmology physician	10/13/2021
Policy reviewed and updated, no changes in coverage criteria, updated references	Q4 2020

P&T Policy reviewed and updated, no changes in coverage criteria, updated references	Q4 2019
MCPC Policy reviewed and updated, no changes in coverage criteria, updated references	12/19/2018
MCPC New policy. IRO Peer Review 10/4/2017 by a practicing board certified in Ophthalmology, and Vitreoretinal Surgery physician.	12/13/2017