LOUISIANA BLUE

Select Loteprednol Ophthalmic Products

Policy # 00669
Original Effective Date: 04/24/2019
Current Effective Date: 01/01/2027

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Patient Selection Criteria

Based on review of available data, the Company may consider Inveltys™‡ (loteprednol 1% ophthalmic suspension) and Eysuvis™‡ (loteprednol 0.25% ophthalmic suspension) to be **eligible for coverage**** when the patient selection criteria are met for the requested drug.

Patient Selection Criteria

Coverage eligibility for Inveltys (loteprednol 1% ophthalmic suspension) and Eysuvis (loteprednol 0.25% ophthalmic suspension) will be considered when the criteria for the requested drug are met:

- For **Inveltys** requests:
  - Patient will use the requested drug for post-operative inflammation and pain following ocular surgery; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) a GENERIC ophthalmic corticosteroid (e.g., dexamethasone drops, fluorometholone drops, prednisolone drops, loteprednol gel/drops, difluprednate drops) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- For **Eysuvis** requests:
  - Patient has a diagnosis of dry eye disease; AND
  - Patient is 18 years of age or older; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) TWO of the following: GENERIC fluorometholone drops, GENERIC dexamethasone drops, GENERIC prednisolone drops, or GENERIC loteprednol gel/drops, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse rection to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Inveltys (loteprednol 1% ophthalmic suspension) OR Eysuvis (loteprednol 0.25% ophthalmic suspension) when the alternative products have not been tried and failed to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Inveltys (loteprednol 1% ophthalmic suspension) for any indication other than for post-operative inflammation and pain following ocular surgery to be **investigational.***

Based on review of available data, the Company considers the use of Eysuvis (loteprednol 0.25% ophthalmic suspension) for any indication other than dry eye disease OR in patients under 18 years of age to be **investigational.***

Background/Overview

Inveltys is an ophthalmic corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery. The American Academy of Ophthalmology's (AAO) preferred practice pattern (PPP) from 2016 for cataracts in the adult eye notes that clinically significant cystoid macular edema (CME) occurs infrequently after routine uncomplicated small-incision cataract surgery (1% to 3%). CME is generally associated with postsurgical inflammation and topical anti-inflammatories are used to prevent CME and to treat established CME. The report concludes that there is no firmly-established specific protocol for preventing cystoid macular edema (CME) following cataract surgery. All of the older ophthalmic corticosteroids (generics) are approved for steroid responsive inflammatory conditions of the eye. These include generic ophthalmic products such as dexamethasone, fluorometholone, prednisolone, and loteprednol. The generic products have been a mainstay for use in various conditions. Ophthalmic non-steroidal anti-inflammatory drugs are often co-administered with the ophthalmic steroids following ocular surgery (as they are approved for the treatment of post-operative pain). Brand name products approved for the same indication as Inveltys (pain and inflammation following ocular surgery) include Durezol®‡ (as well as its generic) and Lotemax ointment. Dosing among the brand name products varies. Inveltys is dosed twice daily, while Durezol (and its generic) is dosed 4 times daily for the first two weeks, then two times daily for a week. Lotemax is dosed four times daily. Besides the dosing interval component advantage, there have been no head-to-head studies versus the other available products for the condition that would suggest superiority of Inveltys.

Eysuvis is an ophthalmic corticosteroid indicated for the short-term treatment of the signs and symptoms of dry eye disease. Dry eye disease is typically managed with environmental modifications, dietary changes, artificial tears, and drugs such as Restasis®‡, Cequa™‡, and Xiidra®‡. Although other ophthalmic steroid products are not indicated for the treatment of dry eye disease, the American Academy of Ophthalmology recommends low dose topical corticosteroid therapy use intermittently for short periods of time to suppress ocular surface inflammation. These products include fluorometholone drops, dexamethasone drops, prednisolone drops, loteprednol drops/gel, Lotemax ointment, and Lotemax SM.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Inveltys is an ophthalmic corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery. Eysuvis is an ophthalmic corticosteroid indicated for the short-term treatment of the signs and symptoms of dry eye disease.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The clinical efficacy of Inveltys was evaluated in 2 multi-centered, randomized, double-masked, placebo-controlled trials in which patients with an anterior cell grade greater than or equal to "2" (a cell count of 6 or higher using a slit-lamp biomicroscope) after cataract surgery were assigned to Inveltys or placebo (vehicle) following surgery. One to two drops of Inveltys or vehicle was self-administered twice a day for 14 days, beginning the day after surgery. Complete resolution of inflammation (a cell count of 0 maintained through day 15 without rescue medication) and complete resolution of pain (a patient-reported pain grade of 0 maintained through day 15 without rescue medication) was assessed 4, 8, and 15 days post-surgery. In the intent-to-treat analysis of both studies, a significant benefit was seen in the Inveltys-treated group for complete resolution of ocular inflammation at days 8 and 15, and complete resolution of pain at days 4, 8, and 15, when compared with placebo. In terms of complete resolution of inflammation at day 8, 24% of Inveltys subjects reached this endpoint vs. 13% in the vehicle group. At day 15, 50% of Inveltys subjects had a complete resolution of inflammation vs. 27% in the vehicle group. In terms of those who were pain free, 43%, 56%, and 69% of Inveltys subjects were pain free at days 4, 8, and 15, respectively. In the vehicle group, 25%, 36%, and 48% of subjects were pain free at days 4, 8, and 15, respectively. The safety and efficacy of Eysuvis for the treatment of dry eye disease was assessed in approximately 2,900 patients with dry eye disease. Patients received either Eysuvis or vehicle (1:1 ratio) four times a day for 2 weeks in 4 multi-centered, randomized, double-masked, placebo-controlled trials. The use of artificial tears was not allowed during the trials. In Study 1, the reductions in ocular discomfort severity scores and bulbar conjunctival hyperemia scores at day 15 for Eysuvis and vehicle were -9.02 vs. -3.80 [-5.27, 95% CI (-10.52, -0.03)] and -0.66 vs. -0.34 [-0.26, 95% CI (-0.45, -0.07)], respectively. In Study 2, the reductions in ocular discomfort severity scores and bulbar conjunctival hyperemia scores for Eysuvis and vehicle at day 15 were -14.53 vs. -9.16 ($P < 0.0001$) and -0.40 vs. -0.16 ($P < 0.0001$), respectively. In Study 3, the reductions in ocular discomfort severity scores and bulbar conjunctival hyperemia scores for Eysuvis and vehicle at day 15 were -11.14 vs. -9.24 ($P = 0.1298$) and -0.38 vs. -0.24 ($P < 0.0001$), respectively. In Study 4, the reduction in ocular discomfort severity scores and bulbar conjunctival hyperemia scores for Eysuvis and vehicle at day 15 were -13.58 vs. -8.91 ($P = 0.0002$) and -0.35 vs. -0.18 ($P < 0.0001$), respectively.

The intent of this policy is to maintain usage to Inveltys and Eysuvis' FDA approved indications as well as ensuring use of the preferred products in this class.

References

1. Inveltys [package insert]. Kala Pharmaceuticals, Inc. Waltham, Massachusetts. Updated 8/2018.
2. Ophthalmic Corticosteroids Therapy Class Summary. Express Scripts. Updated September 2018.
3. Eysuvis [package insert]. Kala Pharmaceuticals, Inc. Waltham, Massachusetts. Updated October 2020.
4. Eysuvis Drug Evaluation. Express Scripts. Updated November 2020.
5. American Academy of Ophthalmology cornea/external disease panel. Preferred Practice Pattern Guidelines. Dry eye syndrome. San Francisco, CA: American Academy of Ophthalmology; 2018. Available at: www.aao.org/ppp.

Policy History

Original Effective Date: 04/24/2019
Current Effective Date: 01/01/2027

04/04/2019	Medical Policy Committee review
04/24/2019	Medical Policy Implementation Committee approval. New policy.
04/02/2020	Medical Policy Committee review
04/08/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/01/2021	Medical Policy Committee review
04/14/2021	Medical Policy Implementation Committee approval. Title changed from "Inveltys™ (loteprednol ophthalmic suspension)" to "Select Loteprednol Ophthalmic Products". Added a new drug, Eysuvis, to the policy along with criteria and relevant background information. Also added loteprednol as a generic option and Lotemax SM as a brand option for Inveltys.
04/07/2022	Medical Policy Committee review
04/13/2022	Medical Policy Implementation Committee approval. Added a new generic, difluprednate drops, as an option to try and fail prior to Inveltys.
01/05/2023	Medical Policy Committee review
01/11/2023	Medical Policy Implementation Committee approval. Removed Durezol as a try and fail option prior to Inveltys because it has been moved to non-formulary since flipping to a multi-source brand.
01/04/2024	Medical Policy Committee review
01/10/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/02/2025	Medical Policy Committee review
01/08/2025	Medical Policy Implementation Committee approval. Removed brand Alrex as a try and fail option prior to Eysuvis due to availability of generic.
01/05/2026	Medical Policy Committee review
01/07/2026	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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07/21/2026 Pre Pharmacy & Therapeutics Committee review
07/22/2026 Pharmacy & Therapeutics Committee review approval. Coverage criteria were updated to reflect preferred products. Criteria for Inveltys were updated to remove criterion requiring trial and failure of Lotemax ointment or Lotemax SM. Criteria for Eysuvis were updated to remove Lotemax ointment and Lotemax SM as try and fail options.
Next Scheduled Review Date: 07/2027

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.