Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 11/1/23**
(See policy history boxes for previous effective dates)

Title: Autologous Serum Eye Drops

Description/Background

Tears have antimicrobial, nourishing, mechanical and optical properties. They contain components such as growth factors, fibronectin and vitamins to support proliferation, migration and differentiation of the corneal and conjunctival epithelium. A lack of these epitheliotropic factors, for example in dry eye disease, can result in severe ocular surface disorders.

Autologous serum eye drops are proposed as a form of treatment of severe ocular surface disorders such as Sjögren's syndrome tear deficiency, non-Sjögren's syndrome tear deficiency associated with graft versus host disease, neurotrophic keratitis and persistent epithelial defects. The rationale for the topical ophthalmic use of serum is based on the premise that vitamins and growth (epitheliotropic) factors present in tears are also present in serum and that the biomechanical and biochemical properties of serum are similar to normal tears.

Serum eye drops are produced using the patient's blood serum, which eliminates the potential for allergic reactions. The serum is diluted to a 20 to 50 percent solution with sterile non-preserved saline. Preparation requires the services of a hospital pharmacy, working under refrigeration within strict protocols to avoid contamination.

Regulatory Status

Autologous serum eye drops are a blood product and are not regulated by the United States Food and Drug Administration.

Medical Policy Statement

Autologous serum eye drops are considered experimental/investigational. The safety and effectiveness of these eye drops have not been proven.

Inclusionary and Exclusionary Guidelines

N/A

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

92499 J3590

Rationale

In vitro cell culture experiments showed that corneal epithelial cell morphology and function are better maintained by serum than by pharmaceutical tear substitutes. Clinical cohort studies have reported the successful use of serum for severe dry eyes and persistent epithelial defects. Studies generally show improvement in the short-term; however improvement in symptoms over longer periods of follow-up has not been demonstrated. Protocols to prepare autologous serum eye drops and the concentrations used vary considerably between studies.

Pan et al (2017),[1] in a Cochrane Systematic Review, evaluated the efficacy and safety of autologous serum eye drops given alone or in combination with artificial tears as compared with artificial tears alone, saline, placebo or no treatment for adults with dry eye. Five eligible RCTs were found, for a total of 92 participants, that compared autologous serum versus artificial tears or saline in individuals with dry eye of various origins. The certainty of evidence was assessed as being low or very low because of lack of reporting of quantitative data for most outcomes and unclear or high risk of bias among trials. Overall, investigators reported inconsistency in possible benefits of autologous serum for improving participant-reported symptoms and other objective clinical measures. The investigations felt there might be some benefit in symptoms with autologous serum compared with artificial tears in the short-term, but found no evidence of an effect after 2 weeks of treatment. Well-planned, large, high-quality RCTs were recommended.

Shtein et al (2020)[2] prepared an analysis on behalf of the American Academy of Ophthalmology. A literature search was performed and 10 studies of the use of autologous

serum-based eye drops for severe dry eye disease and 4 studies of persistent epithelial defect were reviewed. Several studies showed good effectiveness, with some improvement in symptoms, signs, or both. Eight studies reported improved symptoms for severe dry eye disease, and all noted improvement in at least 1 clinical sign. For persistent epithelial defects, all of the studies showed improvement, with 3 of the 4 demonstrating an improvement rate of more than 90%. Adverse events were rare. The reviewers concluded that although autologous serum-based tears may be effective in the treatment of severe dry eye and persistent epithelial defect, conclusions are limited owing to the absence of controlled trials.

Large, high-quality randomized controlled studies are needed to determine the role of serum eye drops in the treatment of dry eyes.

Government Regulations National/Local:

There is no national or local coverage determination on this topic.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Amniotic Membrane Transplantation for Ocular Conditions (Retired)
- Eyelid Thermal Pulsation and Interferometric Color Assessment of the Tear Film for the Diagnosis and Treatment of Dry Eye Syndrome
- Measurement of Tear Osmolarity in the Assessment of Dry Eye Using a Point of Care Device (Retired)

References

1. Pan Q et al. Autologous serum eye drops for dry eye. Cochrane Database Syst Rev,. 2017, 2:CD009327. Doi:10.1002/14651858.CD009327.pub3.
2. Shtein RN, Shen JF, Kuo AN, et al. Autologous serum-based eye drops for treatment of ocular surface disease: a report by the American Academy of Ophthalmology. Ophthalmology. Jan 2020;127(1):128-133

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 5/30/23, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
3/1/09	1/9/09	12/9/08	Joint policy established
1/1/11	10/12/10	10/27/10	Routine maintenance
11/1/12	8/21/12	8/21/12	Routine maintenance
3/1/14	12/10/13	1/6/14	Routine maintenance
1/1/16	10/13/15	10/27/15	Routine maintenance
1/1/17	10/11/16	10/11/16	Routine maintenance
11/1/17	8/15/17	8/15/17	Routine maintenance
11/1/18	8/21/18	8/21/18	Routine maintenance
11/1/19	8/20/19		Routine maintenance
11/1/20	8/18/20		Routine maintenance
11/1/21	8/17/21		Routine maintenance. Ref 3 added.
11/1/22	8/16/22		Routine maintenance (ls)
11/1/23	8/15/23		Routine maintenance (jf) Vendor Managed: NA Removal of reference 1 as duplicate

Next Review Date: 3rd Qtr, 2024

BLUE CARE NETWORK BENEFIT COVERAGE POLICY: AUTOLOGOUS SERUM EYE DROPS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered
BCNA (Medicare Advantage)	See Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.