Medical Coverage Policy | Autologous Serum Eye Drops

EFFECTIVE DATE: 10|01|2024
POLICY LAST REVIEWED: 10|01|2025

OVERVIEW
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.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
Medicare Advantage Plans
Autologous serum eye drops are not covered as the evidence is insufficient to determine the effects of the technology on health outcomes.

Commercial Products
Autologous serum eye drops are considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

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

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.
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 nonpreserved saline. Preparation requires the services of a hospital pharmacy, working under refrigeration within strict protocols to avoid contamination.

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 3 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.

COVERAGE

Benefits may vary between groups/contracts. Please refer to the Evidence of Coverage or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage.

CODING

Medicare Advantage Plans and Commercial Products

There is no specific code for these devices. Therefore, the following CPT/ HCPCS code should be filed:
92499 - Unlisted ophthalmological service or procedure
J3590 - Unclassified biologics

RELATED POLICIES

Unlisted Procedures

PUBLISHED

Provider Update, December 2025
Provider Update, August 2024

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

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