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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Manufacturing process for “Serum autolog KSGR, Augentropfen”

International non-proprietary name:	autologous human serum
Pharmaceutical form:	eye drops, solution
Dosage strength(s):	100%
Route(s) of administration:	ocular
Marketing authorisation holder:	Stiftung Kantonsspital Graubünden
Marketing authorisation no.:	68584
Decision and decision date:	approved on 23 February 2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, definitions, abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AS	Autologous serum
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
DED	Dry eye disease
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

Autologous human serum eye drops were used as magistral formula medicinal products for several years in the past. Following a change in the law in 2020, the manufacturing process for non-standardisable medicinal products, such as human serum eye drops, became subject to the authorisation requirement set out in Articles 33 and 34 TPO. The aim of subjecting the manufacturing process for such products to approval is to ensure patient-specific preparations of sufficient quality, safety and efficacy.

2.1 Applicant's request(s) and information regarding procedure

Authorisation of a manufacturing process for non-standardisable medicinal products in accordance with Articles 33 and 34 TPO
The applicant requested the authorisation of a manufacturing process for the non-standardisable medicinal product "Serum autolog KSGR, Augentropfen" in accordance with Articles 33 and 34 TPO.

2.2 Indication and dosage

2.2.1 Requested indication

For lubricating, cleaning and nourishing the ocular surface in various forms of dry eye (sicca syndrome, keratoconjunctivitis, epithelial defects, corneal ulcer in chronic polyarthritis, Sjögren's syndrome, neurotrophic keratopathy, graft-versus-host diseases, chemical burns, etc.), as well as for special indications, e.g. severe corneal diseases, graft-versus-host diseases of the eyes after stem cell transplants and poorly healing injuries to the eyes.

2.2.2 Approved indication

Serum autolog KSGR, eye drops are indicated for the treatment of dry eye disease (keratoconjunctivitis sicca) in patients aged 18 years and older who do not achieve adequate symptom control with other approved therapies.

2.2.3 Requested dosage

Summary of the requested standard dosage:
The frequency of application depends on the severity of the eye surface problem and is determined by an ophthalmologist. As a rule, one drop is applied to the lower conjunctival sac of the affected eye one to several times a day. The dosage can be increased or decreased by the ophthalmologist depending on the extent of the ophthalmological findings.

2.2.4 Approved dosage

(See appendix)

2.3 Regulatory history (milestones)

Application	1 July 2021
Submission of additional information	30 March 2022
Formal control completed	17 June 2022
List of Questions (LoQ)	18 January 2023
Response to LoQ	16 November 2023

LoQ 2	2 May 2024
Response to LoQ 2	27 November 2024
Preliminary decision	24 February 2025
Response to preliminary decision	24 June 2025
Preliminary decision 2	11 September 2025
Response to preliminary decision 2	27 November 2025
Labelling corrections and/or other aspects	2 February 2026
Response to labelling corrections and/or other aspects	9 February 2026
Final decision	23 February 2026
Decision	approval

3 Medical context

Dry eye disease (DED) is a complex multifactorial condition that is characterised by homeostatic disturbances of the ocular surface and tear film. Any disease or environmental factor that disrupts the function of the lacrimal functional unit by altering the volume or composition of the tear film will lead to a loss of ocular surface homeostasis.
A combination of tear film instability, hyperosmolarity and inflammation is triggered, which can result in progressive damage to the ocular surface and lead to neurosensory abnormalities with a significant impact on visual tasks.
Overall, DED has a significant impact on quality of life and functionality.
The prevalence of DED is high, with a variable reported range. European estimates in adult populations range from 10% to 30%[1].
The most widely used classification of dry eye is that proposed by TFOS DEWS II in 2017[2]. It includes a clinical decision algorithm based on the pathophysiology of dry eye. In this report, the management of dry eye is based on a progressive approach divided into four stages depending on the severity of the pathology.
Autologous serum (AS) eye drops are recommended from stage 3 onwards when standard treatments have failed.
The AS mainly found in the literature is 20% AS, although higher concentrations (between 50% and 100%) are also used and described in the literature.

4 Quality aspects

4.1 Drug substance

The production of autologous serum eye drops started in 2014, and the medicinal process has been approved on the basis of long-standing use and the literature.
The drug substance of “Serum autolog KSGR, Augentropfen” consists of a human blood preparation obtained through autologous blood donation. According to the literature autologous serum eye drops contain proteins, growth factors, vitamins, antioxidants, and electrolytes that closely mimic the biochemical properties of natural basal tears. The detailed composition of the product “Serum autolog KSGR, Augentropfen” has not been determined, as the composition varies with each blood donation.
The manufacturing process includes blood collection, coagulation and centrifugation of the collected blood to obtain serum. Specifications include donor screening and visual inspection for haemolysis and lipemia.
No drug substance shelf life has been established since the drug substance is immediately introduced into the drug product manufacturing process.

4.2 Drug product

The finished drug product is 100% serum. The product is intended for administration to the eye.
The manufacturing process involves aseptic dispensing into low-density polyethylene multidose container with a dropper device.
The specifications include sterility testing, container closure integrity and visual control for particles.
A shelf-life of 6 months at ≤ -15°C has been accepted based on literature data. The drug product is stored at ≤ -15°C in original, unopened containers.
The proposed in-use shelf-life after thawing of 10 days at 2-8°C has been accepted.

[1] Stapleton F, Alves M, Bunya VY, et al. TFOS DEWS II Epidemiology report. Ocul Surf. 2017;15:334–365.
[2] Jones L, Downie LE, Korb D, Benitez-Del-Castillo JM, Dana R, Deng SX, et al. TFOS DEWS II Management and Therapy Report. Ocul Surf. juill 2017;15(3):575-628.

4.3 Quality conclusions

The assessment of quality aspects focused on the primary safety concern, the risk of microbiological contamination, which necessitates aseptic manufacturing and sterility testing.

5 Nonclinical aspects

The proof-of-concept, pharmacokinetics and toxicology of the autologous serum product were not evaluated in conventional nonclinical studies. This was considered acceptable owing to a weight-of-evidence assessment that took account of clinical experience in the treatment of dry eye disease with autologous serum, the absence of reported serious adverse events in the clinical setting, the minimal expected systemic exposure after administration, as well as the autologous nature of the product, which limits the selection of relevant animal species. Additional animal studies are not expected to provide information beyond what is already known from clinical experience with autologous serum drug product.

6 Clinical aspects

6.1 Clinical pharmacology

N/A

6.2 Dose finding and dose recommendation

N/A

6.3 Efficacy

Multiple systematic reviews, meta-analyses and a Cochrane review[3] have been published on the efficacy and safety of AS for the treatment of DED using products similar to “Serum autolog KSGR, Augentropfen”.
The main evidence for the efficacy of AS in DED was based on a Cochrane review of five randomised clinical trials (92 participants) comparing AS with artificial tears or saline in individuals with DED of various origins (Sjögren's syndrome-related dry eye, non-Sjögren's syndrome dry eye, and postoperative dry eye induced by laser-assisted in situ keratomileusis (LASIK)). All five trials evaluated 20% AS.
This Cochrane review suggested that autologous serum had a short-term (two-week) beneficial effect on symptoms compared with artificial tears. However, this review found no evidence of any effect beyond two weeks of treatment.
An updated systematic literature review was by Swissmedic and provided by the applicant (not published). The updated literature search identified two additional randomised controlled trials not included in the Cochrane review. No new evidence of clinical efficacy has been obtained from these studies. The overall conclusions of this literature review are consistent with the benefits suggested by the Cochrane review.
Other studies and meta-analyses have explored the long-term use of serum eye drops and suggest long-term efficacy, but it is uncertain whether these effects are transferrable to patient-relevant long-term benefits, since there is no robust evidence for long-term use and effect on quality of life. Moreover, there is no established definition of “long-term”, and there is no scientific consensus in the guidelines on the optimal duration of use of AS.
Nonetheless, the evidence is limited with incomplete outcome reporting and heterogeneity among outcomes and follow-up periods. In addition, the data from clinical studies are highly heterogeneous, as procedural aspects of AS preparation, posology and patient populations differed significantly. Although there appears to be no consensus on an optimal concentration, most studies use 20%. Other published studies explore higher concentrations (50%, 80%, and undiluted) and suggest non-inferiority compared to the 20% concentration.

6.4 Safety

The primary safety consideration for AS is the risk of microbial growth during storage, because serum-based solutions are essentially growth media. Microbial contamination of AS containers has been reported with prolonged use (over one week at +4°C). The literature describes one case of an eye infection during treatment with AS caused by a contaminated AS container.
Four of the five studies in the Cochrane review did not report outcomes for adverse events or complications. One study reported conjunctivitis in two participants, with cultures showing no growth followed by resolution of the symptoms.

[3] Pan Q, Angelina A, Marrone M, Stark WJ, Akpek EK. Autologous serum eye drops for dry eye. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD009327.

Among the other numerous published clinical studies and case reports on AS, the following complications have been reported (rarely): conjunctivitis, eyelid eczema, immunoglobulin deposits in the cornea, corneal peripheral infiltrates, scleral vasculitis and scleral melt in patients with rheumatoid arthritis.
A Swiss study also specifically investigated the risk of infection using over 100,000 serum drop bottles over an observation period of 5 years and found three cases of infectious keratitis that could potentially have been associated with AS[4].
These data suggest that AS may be safe for the treatment of DED.

6.5 Final clinical benefit risk assessment

Conclusive evidence on the safety and efficacy of AS in DED is limited by the relative lack of controlled studies with a sufficient level of evidence and long-term data.
A major difficulty faced by the review in endeavouring to obtain conclusive safety and efficacy results with a high level of evidence was heterogeneity among participant populations, interventions, and comparisons**,** as well as variations in the procedures used to prepare AS.
This review suggested AS was beneficial to symptom resolution compared with artificial tears in the short term (two weeks). However, it also found no evidence of an effect beyond two weeks of treatment.
Other studies, meta-analyses and a systematic review of the literature conducted by the applicant have explored the long-term use of serum eye drops and suggest long-term efficacy, but patient-relevant long-term benefits have not been clearly demonstrated. There is no solid evidence of efficacy in long-term use, and the effects on quality of life have not been investigated.
The generalisability of the results to the “Serum autolog KSGR, Augentropfen” product could not be directly demonstrated.
AS seems to offer a hypothetical, unproven benefit over standard recommended therapies under the assumption that AS not only serves as a lacrimal substitute to provide lubrication but contains other biochemical components that enable it to mimic natural tears. This therapy represents an additional burden for patients compared to conventional therapies, as it requires blood draws.
The major risk associated with the AS procedure is the risk of microbial growth during production, manipulation or storage. The possibility of eye infection (rarely reported in the literature) cannot be ruled out, particularly on a wounded surface in the process of healing, which can support microbial infestation. To minimise this risk, AS must be prepared under sterile conditions, and patients must strictly adhere to the instructions for use and storage.
The Information for healthcare professionals, Patient information and risk management plan adequately mitigate this risk.
Other complications have been reported (rarely): conjunctivitis, eyelid eczema, immunoglobulin deposits in the cornea, corneal peripheral infiltrates, scleral vasculitis and scleral melt in patients with rheumatoid arthritis.
At present, the benefit/risk profile for AS in DED patients recalcitrant to conventional therapy is considered positive. Authorisation was granted on the basis of medical need, the manageable toxicity profile, the benefit suggested (but not fully demonstrated) compared to standard of care, and the major postmarketing conditions imposed on the MAH, which involve providing additional supporting data on identified uncertainties:
- Long term registry of DED patients recalcitrant to conventional therapy treated with AS
- Annual updates on any new information concerning the safety and efficacy of AS.

[4] Sanak F et al. Five-Year Risk and Safety Profile of Autologous Serum Eye Drop Therapy. Klin Monbl Augenheilkd. 2024 Apr;241(4):388-391

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for “Serum autolog KSGR, Augentropfen” was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

Serum autolog KSGR, eye drops

Composition

Active substances

Human blood serum, autologous

Excipients

None

Pharmaceutical form and active substance quantity per unit

Eye drops, solution.
One 11 ml multi-dose eye drop bottle contains 5 ± 0.5 ml of Serum autolog KSGR, eye drops.
Standard drops have a volume of 0.04 ml each.

Indications/Uses

Serum autolog KSGR, eye drops are indicated for the treatment of dry eye disease (keratoconjunctivitis sicca) in patients aged 18 years and older who do not achieve adequate symptom control with other approved therapies.

Dosage/Administration

Serum autolog KSGR, eye drops may only be prescribed by a qualified ophthalmologist.

Adults

The frequency of administration depends on the severity of the ocular surface disorder and is determined by the ophthalmologist. Generally, one drop is applied once or several times daily to the lower conjunctival sac of the affected eye. The dosage may be reduced or increased by the ophthalmologist depending on the extent of the ophthalmologic findings.
Treatment duration depends on the prescription of the ophthalmologist. Serum autolog KSGR, eye drops are often administered over a longer period of time and their use requires regular ophthalmological monitoring.
Hands must be washed and dried thoroughly before use. Before applying the eye drops, the label on the bottle must be checked for accuracy of the personal information (surname, first name, date of birth). If the information is incorrect, the eye drops must not be used.

The unopened bottle of eye drops contains sterile autologous serum. It does not contain any preservatives. Contact between the dopper tip of the eye drop bottle and any surface must be avoided, as this can contaminate the eye drops. Contact of the dropper tip with the eye can cause injury to the ocular surface.
After use, the eye drop bottle must be closed by screwing on the protective cap and stored at 2-8°C (in the refrigerator) until the next use.

Paediatric population

Serum autolog KSGR, eye drops are not authorised for use in the paediatric population.

Contraindications

Serum autolog KSGR, eye drops are contraindicated in patients in the following cases:

- Severe or untreated anaemia
- Syphilis, hepatitis B, hepatitis C, and/or HIV infection
- Infectious conjunctivitis and infectious keratitis
- Patients with a known contact hypersensitivity to silver should not use this product, as the dispensed drops may contain traces of silver from the container
- Hypersensitivity to the active ingredient

Warnings and precautions

Serum autolog KSGR, eye drops may only be applied to the patient whose blood was used for the preparation of the eye drops. They must not be used on any other person.
If the application of Serum autolog KSGR, eye drops to the patient is performed by a third party, it is essential for that person to wear medical gloves for their own protection.
The accuracy of the personal information (name, first name, date of birth of the patient) on the label of the eye drop bottle must be checked before each use.
If adverse events occur at the administration site, such as eye irritation, eye pain, eye redness or changes in vision, or if the patient condition worsens, ophthalmological consultation is required and discontinuation of treatment should be considered.

Interactions

No clinically relevant interactions are currently known. However, since no clinical interaction studies have yet been conducted, it is recommended to maintain an interval of at least 15 minutes between the administration of two products when using one or more other ophthalmic treatments.

Note for contact lens wearers

There is no reliable data on the use of Serum autolog KSGR, eye drops in contact lens wearers. The application of Serum autolog KSGR, eye drops is not recommended while wearing contact lenses.

Pregnancy, lactation

There are no adequate and well-controlled studies in pregnant or breastfeeding women. Therefore, Serum autolog KSGR, eye drops should not be used during pregnancy and lactation.

Effects on ability to drive and use machines

No corresponding studies have been performed.
Serum autolog KSGR, eye drops have a negligible influence on the ability to drive and use machines. Blurred vision may occur temporarily after applying Serum autolog KSGR, eye drops until distribution. This should be taken into account when operating machines or driving. The impairment usually disappears a few minutes after applying Serum autolog KSGR, eye drops. The activities mentioned above must be avoided until vision has returned to normal after application.

Undesirable effects

The undesirable effects are arranged according to the system organ classes of the MedDRA classification in declining frequency categories:
"Very common" (≥1/10)
"common" (≥1/100, <1/10),
"uncommon" (≥1/1000, <1/100)
"rare" (≥1/10,000, <1/1000)
"very rare" (<1/10,000)
“not known“ (frequency cannot be estimated from the available data).

Eye conditions:
Common: Immediately after administration, an unpleasant sensation of irritation and burning, a feeling of the eyelids sticking together, and blurred vision may occur. These effects are temporary and have no long-term consequences.
Rare: The following side effects have been reported in clinical trials: eczema of the eyelids, scleral vasculitis and lysis in rheumatoid arthritis, immunoglobulin deposits in the cornea, peripheral corneal infiltrates, eye infection during treatment with eye drops due to a contaminated eye drop container.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

No cases of overdose have been reported.

Properties/Effects

ATC code

No ATC code assigned.

Mechanism of action

According to literature, the therapeutic effect of autologous serum eye drops in severe ocular surface disorders is based on the epitheliotrophic effect of various substances naturally present in blood serum. The same components are also present in the tear film of a healthy eye in varying concentrations. In cases of surface disorders, the concentration is often insufficient. Mentioned substances include regenerative growth factors (such as EGF, NGF, PDGF), proteins (such as fibronectin, albumin, lysozyme), and vitamin A.
In addition to their tear-like biochemical characteristics, autologous serum eye drops also provide nutrient components. Therefore, they are used not only to hydrate the ocular surface but also to provide i) nutritive and growth factors to maintain cellular integrity during epithelial repair, and ii) bactericidal components that can reduce the risk of contamination or infection. Autologous serum eye drops are also a suitable tear substitute because their physicochemical properties, especially viscosity, are adapted to the corresponding parameters of the tear film.

Pharmacodynamics

See «Mechanism of Action».

Clinical efficacy

No clinical studies have been conducted with Serum autolog KSGR, eye drops.
Several systematic literature reviews, meta-analyses and one Cochrane review have been published on the efficacy and safety of autologous serum eye drops for the treatment of dry eye (dry eye syndrome, sicca syndrome).
The main evidence for the efficacy of serum eye drops in dry eye is based on a Cochrane review (Pan et al. 2017) of 5 randomized clinical trials (92 participants); autologous serum eye drops 20% were compared with artificial tears or saline solution in patients with sicca syndrome of various causes (including in association with Sjögren's syndrome, after laser surgery).
The Cochrane review indicated temporary, short-term symptom relief for approximately two weeks with serum eye drops compared to artificial tears. However, this study found no evidence of efficacy following the two weeks of treatment.
Other published studies with lower levels of evidence have investigated the long-term use of serum eye drops and suggest efficacy with long-term use. Patient relevant long-term benefits have not been clearly demonstrated.
There is no solid evidence regarding its effectiveness with long-term use, and the impact on quality of life has not been studied.

The Stiftung Kantonsspital Graubünden does not use the concentration of 20% autologous serum eye drops evaluated in the Cochrane review.
Although there is no apparent consensus among experts regarding the selection of the optimal concentration (TFOS DEWS III Management and Therapy Report), most studies use 20% autologous serum eye drops. Other published studies investigate higher concentrations (50% and undiluted). These data are only exploratory and do not provide clear evidence of equivalence or superiority of higher-concentration serum eye drops compared to a concentration of 20% autologous serum eye drops.

Pharmacokinetics

Absorption

Not investigated

Distribution

Not investigated

Metabolism

Not investigated

Elimination

Not investigated

Kinetics in specific patient groups

Not investigated

Preclinical data

No preclinical safety studies were conducted in animals

Other information

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Shelf life

Do not use this medicine after the expiry date marked as "EXP" on the pack.

Shelf life after opening (thawing):

After thawing, the bottle must be stored in the refrigerator (2°-8°C) in its original packaging and used within 10 days.
After 10 days, any remaining contents must be disposed of.

Special precautions for storage

Store in the freezer (below -15°C).
After thawing, store in the refrigerator (2°-8°C).
Store in the original packaging.
Keep the container tightly closed.
Keep out of the reach of children.

Instructions for handling

The bottle containing the eye drops must be thawed slowly at 2°-8°C before use (overnight in the refrigerator).
To maintain sterility, do not touch the dropper tip with your hands or eyes.
Unused medicine or waste material must be disposed of in accordance with national requirements.

Authorisation number

68584, (Swissmedic)

Packs

Serum autolog KSGR 100%, eye drops: 5 ml eye drop bottle [B]
Package size depends on the volume of blood collected.

Marketing authorisation holder

Stiftung Kantonsspital Graubünden, Chur

Date of revision of the text

Februar 2026