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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Manufacturing process for “Serum autolog Insel, Augentropfen”

International non-proprietary name:	autologous human serum
Pharmaceutical form:	eye drops, solution
Dosage strength(s):	20%, 100%
Route(s) of administration:	ocular
Marketing authorisation holder:	Insel Gruppe AG
Marketing authorisation no.:	68558
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.

Table of contents

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 processes 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 Insel, Augentropfen" in accordance with Articles 33 and 34 TPO.

2.2 Indication and dosage

2.2.1 Requested indication

Keratoconjunctivitis sicca without improvement with artificial tears.

2.2.2 Approved indication

Serum autolog Insel, eye drops are used for the treatment of dry eye (keratoconjunctivitis sicca) in patients aged 18 years and older who have failed to respond to other approved therapies.

2.2.3 Requested dosage

Summary of the requested standard dosage:
The dosage should be determined individually and depends on the severity of the keratoconjunctivitis sicca. Unless otherwise indicated, 4-6 drops should be instilled into the conjunctival sac of the affected eye.
Children and adolescents: The use and safety of autologous serum drops in children and adolescents has not been well studied.

2.2.4 Approved dosage

(See appendix)

2.3 Regulatory history (milestones)

Application	21 June 2021
Submission of additional information	25 March 2022
Formal control completed	30 June 2022
List of Questions (LoQ)	18 January 2023
Response to LoQ	20 November 2023
LoQ 2	2 May 2024
Response to LoQ 2	5 December 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	6 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 was started in 2019 at the pharmacy of Inselspital (having taken place at Inselspital's eye bank between 2004 and 2018) and the medicinal process has been approved on the basis of long-standing use and the literature.
The drug substance of "Serum autolog Insel, Augentropfen" is a preparation of human blood received 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 tears. The detailed composition of the product "Serum autolog Insel, Augentropfen" has not been determined, as the composition varies for 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 or 20% serum diluted with balanced salt solution. 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 7 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 Insel, 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 in the. However, this review found no evidence of an effect beyond two weeks of treatment.
An updated systematic literature review was requested 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 the 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.
The 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 any 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 Insel, 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 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 Insel, 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 medicine is subject to additional monitoring. This allows rapid identification of new safety information. Healthcare professionals are required to report any suspected new or serious side effects. See the section on ‘Side effects’ for information on how to report side effects.

Serum autolog Insel, eye drops

Composition

Active substances

Human blood serum, autologous

Excipients

Serum autolog Insel 20%, eye drops contain balanced salt solution, 80% v/v (BSS) as an excipient.
Composition of BSS:
Sodium chloride, potassium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate, sodium acetate trihydrate, sodium citrate dihydrate, sodium hydroxide and/or hydrochloric acid for pH adjustment, water for injections q.s.

Pharmaceutical form and active substance quantity per unit

Eye drops, solution
One 11 ml multi-dose bottle of eye drops contains 5.0 ± 0.5 ml of Serum autolog Insel 100%, eye drops, or Serum autolog Insel 20%, eye drops.
Standard drops have a volume of 0.04 ml each.

Indications/Uses

Serum autolog Insel eye drops are used for the treatment of dry eye (keratoconjunctivitis sicca) in patients aged 18 years and older who have failed to respond to other approved therapies.

Dosage/Administration

Serum autolog Insel eye drops should only be prescribed by a qualified ophthalmologist.
The dosage is to be determined individually and depends on the severity of keratoconjunctivitis sicca. Unless otherwise indicated, instill one drop into the conjunctival sac of the affected eye 4-6 times a day.

Duration of treatment

The duration of treatment depends on the type and severity of the disease and is determined by the ophthalmologist. Treatment can last from a few weeks to several years and should be regularly reevaluated by an ophthalmologist.

Children and adolescents

Serum autolog Insel eye drops are not approved for use in the pediatric population.

Method of administration

Before use, patients should be informed that:

- The eye drop bottle must be thawed slowly at 2°-8 °C (overnight in the refrigerator).
- Hands must be thoroughly washed and carefully dried.
- The personal identification (surname, first name, date of birth) on the label on the eye drop bottle must be checked to ensure that they are correct. If the information is incorrect, Serum autolog Insel eye drops must not be used.

During use, patients should be advised that:

- Avoid any contact between the tip of the dropper bottle and the eye or surrounding structures to prevent microbial contamination.
- The tip of the dropper bottle must not come into contact with any part of the body or any objects to prevent contamination.
- Incorrect handling of Serum autolog Insel eye drops may result in bacterial contamination, which can lead to eye infections. The use of contaminated eye drops can lead to serious eye infections.

Patients should also be informed that:

- The eye drop bottle should be tightly closed immediately after use and stored in the refrigerator at 2°-8°C.
- The eye drop bottle should not be used for longer than 7 days after thawing.

Contraindications

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

- Severe or untreated anemia.
- Syphilis, hepatitis B, hepatitis C, or HIV infection.
- Infectious conjunctivitis and infectious keratitis.
- Patients with a known history of hypersensitivity to silver should not use this product, as the drops dispensed may contain traces of silver from the container.
- Hypersensitivity to the active substance or any of the excipients in the eye drops.

Warnings and precautions

Serum autolog Insel eye drops may only be used for/by the person from whom the blood was collected and from which it was manufactured. Therefore, before each use, the label on the eye drop bottle should be checked to ensure that the personal details (surname, first name, date of birth of the patient) are correct. The product must not be used on another person.
Use by a third party could lead to the transmission of infectious diseases.

If the Serum autolog Insel eye drops are administered by a third party, it is essential that this person wears gloves for their own protection and that of the patient.
If adverse events occur at the site of administration, such as eye irritation, pain, redness, or changes in vision, or if the patient's condition worsens, discontinuation of treatment should be considered.

Interactions

No interactions are known. When applying another ophthalmic therapeutic agent, an interval of at least 15 minutes should be observed.

Contact lens wearers

Although Serum autolog Insel, eye drops do not contain any preservatives, there is no reliable data on their use in contact lens wearers. The administration of Serum autolog Insel, eye drops is therefore not recommended when wearing contact lenses.

Pregnancy, lactation

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

Effects on ability to drive and use machines

No relevant studies have been conducted.
Serum autolog Insel eye drops have a negligible effect on the ability to drive or operate machinery. Since the administration of autologous serum eye drops can cause temporary blurred vision, which normally disappears after a few minutes, you should wait until you can see clearly again before driving or operating machinery.

Undesirable effects

The undesirable effects are classified according to the organ system classes of the MedDRA classification and according to frequency according to the following convention:
"very common" (≥1/10),
"common" (≥1/100 to <1/10),
"occasional" (≥1/1000 to <1/100),
"rare" (≥1/10,000 to <1/1,000),
"very rare" (<1/10,000),
"not known" (cannot be estimated from the available data).

Eye disorders:
Common: Immediately after administration, an unpleasant feeling of irritation and burning, a feeling of sticking of the eyelids, 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 side effects after approval is very important. It allows for continuous monitoring of the benefit-risk ratio of the drug. Healthcare professionals are required to report any suspected new or serious side effects via the ElViS (Electronic Vigilance System) online portal. Information on this can be found at www.swissmedic.ch.

Overdose

No cases of overdose have been reported.

Properties/Effects

ATC code

No ATC code has been assigned.

Mechanism of action

According to the literature, the therapeutic effect of autologous serum eye drops in severe damage to the ocular surface is based on the epitheliotrophic effect of various substances, which occur in varying concentrations in the serum and tear film of a healthy eye. Among other things, these substances promote the proliferation, differentiation, and migration of epithelia, in particular growth factors (epidermal growth factor (EGF), transforming growth factor-α (TGF-α), keratinocyte growth factor (KGF), hepatocyte growth factor (HGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF), nerve growth factor (NGF), proteins (such as fibronectin, albumin, lysozyme) and vitamin A.
In addition to biochemical properties similar to those of physiological tear fluid, autologous serum eye drops also contain components that promote wound healing. Fibronectin, which is present in serum in quantities 10 to 15 times higher than in tear fluid, plays an essential role in the attachment of the epithelial layers to the cornea and is involved in wound healing.

Pharmacodynamics

See “Mechanism of Action.”

Clinical efficacy

No clinical studies have been conducted with *Serum autolog Insel eye drops*.
Several systematic literature reviews, meta-analyses, and a 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 and after laser surgery).
This Cochrane review suggested temporary relief of symptoms for approximately two weeks with autologous serums compared to artificial tears. However, this study found no evidence of any effect following 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, but patient-relevant long-term benefits have not been clearly established.
There is no strong evidence of efficacy in long-term use, and the effects on quality of life have not been studied.
Insel Gruppe AG also uses a different concentration than the 20% autologous serum eye drops evaluated in the Cochrane review.
Although there appears to be no 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 conclusively prove the equivalence or superiority of higher serum eye drop concentrations over a concentration of 20% autologous serum eye drops.

Pharmacokinetics

Absorption

No data

Distribution

No data

Metabolism

No data

Elimination

No data

Kinetics in specific patient groups

No data

Preclinical data

No preclinical safety studies have been conducted in animals.

Other information

Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

Effects on diagnostic methods

Not studied.

Shelf life

The medicine may only be used until the date marked "EXP" on the package.

Shelf life after opening (thawing)

After thawing, the medicine can be stored in the refrigerator (2-8°C) for 7 days.

Special precautions for storage

Store frozen (below -15°C).
Store in a refrigerator (2-8°C) after thawing.
Store in the original packaging.
Keep the container tightly closed.
Keep out of reach of children.

Instructions for handling

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

Authorisation number

68558 (Swissmedic)

Packs

Serum autolog Insel 100%, eye drops: 5 ml eye drop bottle [B]
Serum autolog Insel 20%, eye drops: 5 ml eye drop bottle [B]
The package size depends on the volume of blood collected.

Marketing authorisation holder

Insel Gruppe AG, Bern

Date of revision of the text

February 2026