# Summary of safety and clinical performance HYASE™-10X

*This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.*

*The SSCP is not intended to replace the Instructions for Use (IFU) as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.*

*The following information is intended for users/healthcare professionals.*

## 1 Device identification and general information

| | | |
|---|---|---|
| 1.1 | Device trade name | HYASE™-10X |
| 1.2 | Manufacturer's name and address | Vitrolife Sweden AB, Gustaf Werners gata 2, SE-421 32 Västra Frölunda, Sweden |
| 1.3 | Manufacturer's single registration number (SRN) | SE-MF-000002389 |
| 1.4 | Basic UDI-DI | 735002591AAME2 |
| 1.5 | Global Medical Device Nomenclature (GMDN) code | 44046 |
| 1.6 | Class of device | Class III |
| 1.7 | Year when the first certificate (CE) was issued covering the device | 1994 |
| 1.8 | Authorized representative if applicable; name and SRN | Not applicable |
| 1.9 | NB's name (the NB that will validate the SSCP) and the NB's single identification number | DNV Product Assurance AS,<br>Veritasveien 1, NO-1363 Høvik<br>Single Identification Number: 2460 |

## 2 Intended use of the device

### 2.1 Intended purpose

HYASE-10X is a medical device intended for use in Assisted Reproductive Technology (ART) as a medium for removal of cumulus cells.

### 2.2 Indication and target population

HYASE-10X: Medium for removal of cumulus cells.

The target patient population is an adult or reproductive-age population that undergoes *in vitro* fertilization (IVF) treatment or fertility preservation.

### 2.3 Contraindications and/or limitations

HYASE™-10X contains gentamicin. Do not use in patients with known hypersensitivity/allergy to the component. The contraindication and precautions are listed in section 4.2.

## 3 Device description

### 3.1 Description of the device

HYASE-10X is a physiological salt buffer containing hyaluronidase, HSA and gentamicin. For use after dilution 1:10 with either of the following two alternatives:

1. G-MOPS™ PLUS or G-MOPS™ supplemented with HSA-solution™ and equilibration at +37°C and ambient atmosphere.
2. G-GAMETE™ and equilibration at +37°C and 6% $CO_2$ atmosphere.

The concentration of hyaluronidase in HYASE-10X is 800 IU/mL before dilution.

The composition of HYASE-10X has been developed to support removal of cumulus cells. Based on its Indication for Use, HYASE-10X does not have patient contact.

HYASE-10X is available as 5 × 0.1 mL vials (Figure 1). The media is sterile filtered using aseptic technique. Media bottles should not be stored after opening. Discard excess media after completion of the procedure. Based on regulatory guidelines, the medicinal components present in HYASE-10X are HSA and gentamicin.


Figure 1. HYASE-10X

### 3.2 A reference to previous generation(s) or variants if such exists, and a description of the differences

HYASE-10X REF 10017.

The previous version of HYASE-10X contained penicillin G. Vitrolife changed the antibacterial agent used in several of its media devices from penicillin G to gentamicin due to its greater longevity.

Based on its Indication for Use, HYASE-10X does not have patient contact. The antibacterial agent is not intended to affect the patient; its presence is only as an ancillary substance to support medium function. Further, according to its Instruction for Use (IFU), HYASE-10X is for use after dilution 1:10 with or G-MOPS PLUS, G-GAMETE or G-MOPS, all of which contain gentamicin. Changing the antibacterial agent in HYASE-10X from penicillin G to gentamicin, reduced the number of antibacterial agents used.

### 3.3 Description of any accessories which are intended to be used in combination with the device

Not applicable.

### 3.4 Description of any other devices and products which are intended to be used in combination with the device

General equipment and sterile non-toxic disposables for the IVF lab. In addition, G-MOPS PLUS, G-MOPS supplemented with HSA-solution or G-GAMETE.

## 4 Risks and warnings

### 4.1 Residual risks and undesirable effects

After mitigation, there are two unacceptable residual risks due to the presence of HSA, with the hazardous situations “Patient exposed to contaminated human serum albumin (HSA)” and “User exposed to contaminated human serum albumin (HSA)”. The end user (IVF professional) is expected to follow Good IVF-laboratory practice and use the device according to its IFU. The benefit-risk analysis of these risks concluded that the benefits of including HSA in HYASE-10X outweigh the risks associated with blood-borne contamination. No case reports of allergic/hypersensitivity reactions or infections associated with HSA during ART procedures have been reported.

No adverse events or undesirable side-effects have been reported for the device during its time on the market. To control risks, raw materials for HYASE-10X are quality tested and each LOT of the final product is tested for pH, osmolality, sterility, bacterial endotoxins, and cumulus cell removal assay. Additionally, the user is informed about the device components, contraindication, and precautions by providing information on labels and Instruction for Use.

All the clinical risks that could occur during the use of HYASE-10X are presented in below.

| Effect | Hazardous situation |
| --- | --- |
| Patient | Patient exposed to contaminated human serum albumin (HSA)* |
| End user | Allergic user exposed to gentamicin |
| | User exposed to gentamicin |
| | User exposed to human serum albumin (HSA) or recombinant human albumin (rHA) |
| | User exposed to contaminated human serum albumin (HSA)* |

*Unacceptable residual risks. All other clinical risks are acceptable after risk control measures.

### 4.2 Warnings and precautions

Warnings or precautions related to the use of HYASE-10X are listed (SPC-4019-v.3.0).

- Discard product if bottle integrity is compromised. Do not use HYASE-10X if it appears cloudy.
- HYASE-10X contains hyaluronidase and human serum albumin.
- Caution: All blood products should be treated as potentially infectious. Source material from which this product was derived was found negative when tested for antibodies to HIV, HBc, HCV, and HTLV I/II and non-reactive for HbsAg, HCV RNA and HIV-1 RNA and syphilis. No known test methods can offer assurance that products derived from human blood will not transmit infectious agents.
- Re-use may result in microbiological contamination and/or property changes in the product.
- To avoid contamination Vitrolife strongly recommends that media should be opened and used only with aseptic technique.
- The risks of reproductive toxicity and developmental toxicity for IVF media, including Vitrolife's IVF media, have not been determined and are uncertain.
- Any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the Member State in which the user and/or patient is established.
- Not for injection.
- Discard the product according to standard clinical practice for medical hazardous waste when the procedure is finished.

### 4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

No field safety corrective actions (FSCAs) have been taken for HYASE-10X during its lifetime.

## 5 Summary of clinical evaluation and post-market clinical follow-up

### 5.1 Summary of clinical data related to equivalent device, if applicable

Not applicable.

### 5.2 Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

Not applicable.

## 5.3 Summary of clinical data from other sources, if applicable

A systematic literature search was conducted to identify clinical data on the safety and performance of HYASE-10X. The ICSI fertilization rates reported after use of HYASE-10X align with the ESHRE competency values (Kadoura et al. 2022; Ombelet et al. 2022; Torra-Massana et al. 2022; Bulgurcuoglu-Kuran et al. 2023; Emirdar and Acet 2023; Esmaeilian et al. 2023; Fraire-Zamora et al. 2023; Jiang et al. 2023; Le et al. 2023; Nobrega et al. 2023; Prasetiawati et al. 2023; Salehpour et al. 2023; Wang et al. 2023; Zhang et al. 2023; Ersahin et al. 2024; Escudé-Logares et al. 2024). Additionally, some studies including the use of the device have reported fertilization data in terms of mean numbers of oocytes fertilized (Jannatifar et al. 2022; Lara-Cerrillo et al. 2023) and the results were not compared to the competency percentage reference value. However, the data add support to the safe use of HYASE-10X as a medium for removal of cumulus cells.

The clinical pregnancy rates reported after use of HYASE-10X (Jannatifar et al. 2022; Kadoura et al. 2022; Ombelet et al. 2022; Singh et al. 2022; Torra-Massana et al. 2022; Zafardoust et al. 2022; Broussard et al. 2023; Bulgurcuoglu-Kuran et al. 2023; Emirdar and Acet 2023; Erdoğan et al. 2023a; Erdoğan et al. 2023b; Jiang et al. 2023; Lara-Cerrillo et al. 2023; Le et al. 2023; Prasetiawati et al. 2023; Salehpour et al. 2023; Tepla et al. 2023; Wang et al. 2023; Wei et al. 2023; Zhang et al. 2023; Dastjerdi et al. 2024; Li et al. 2024) align with the yearly European results published by ESHRE (Wyns et al. 2022).

Several references reported data on live births after the use of HYASE-10X (Jannatifar et al. 2022; Singh et al. 2022; Torra-Massana et al. 2022; Zafardoust et al. 2022; Bulgurcuoglu-Kuran et al. 2023; Emirdar and Acet 2023; Fraire-Zamora et al. 2023; Jiang et al. 2023; Lara-Cerrillo et al. 2023; Wei et al. 2023; Zhang et al. 2023; Escudé-Logares et al. 2024; Li et al. 2024).

According to the results from the literature search, no deviation was found in the safety or performance of the device. No post-market clinical follow-up (PMCF) studies have been conducted for HYASE-10X. There were no non-serious incidents or undesirable side-effects identified after use HYASE-10X with a frequency or severity that negatively impact its benefit-risk profile.

These studies may have used the previous version of the device (HYASE-10X REF 10017). As mentioned in section 3.2, the previous version of HYASE-10X contained penicillin G. Based on its Indication for Use, HYASE-10X does not have patient contact. The antibacterial agent is not intended to affect the patient; its presence is only as an ancillary substance to support medium function. Furthermore, according to its IFU, HYASE-10X is for use after dilution 1:10 with G-MOPS PLUS, G-MOPS or G-Gamete, all of which contain gentamicin. Hence, changing the antibacterial agent in HYASE-10X from penicillin G to gentamicin, has reduced the number of antibacterial agents used. Therefore, the clinical data on HYASE-10X REF 10017 are still relevant to confirm safety and/or clinical performance of the current version.

## 5.4 An overall summary of the clinical performance and safety

According to the Indication for Use, HYASE-10X is used to remove cumulus cells to facilitate ART. The ICSI fertilization rates reported after use of HYASE-10X  align with the ESHRE competency values (ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine 2017). The clinical pregnancy rate reported after use of HYASE-10X align with the yearly European results published by ESHRE (Wyns et al. 2022). Data from PMS and risk management also support the safety and performance of HYASE-10X. There are no indications of any negative effects from use of HYASE-10X. As identified in the risk management documents, the residual risks due to the presence of HSA are unacceptable. However, after benefit-risk evaluation, the benefits of using HSA in the device outweigh the risks associated with blood-borne contamination. All other risks are acceptable after risk control measures. According to the results of the literature search, the risk of an allergic/hypersensitivity reaction (or infection) associated with HSA or gentamicin when used for ART procedures is very low. No new

risks have been identified or are expected when the device is used according to its Indications for Use. Therefore, the benefit-risk profile is acceptable according to current knowledge/state of the art.

### 5.5 Ongoing or planned post-market clinical follow-up

There are no ongoing or planned post-market clinical follow-up studies (PMCF) for HYASE-10X. However, general PMCF procedures, such as screening of scientific literature and searching adverse event databases and performing a PMCF end user survey will be performed.

## 6 Possible diagnostic or therapeutic alternatives

ART is a treatment option for patients failing to conceive naturally as well as patients who have tried other treatments such as medications and surgical procedures without success. Hence, there are no therapeutic alternatives for patients at this stage.

Fertility preservation is a possibility/option for patients needing or having a desire to postpone reproduction. It serves as a proactive approach to safeguard reproductive potential, especially when medical conditions or treatments may impact fertility (Lee and Zhang 2022).

Devices with similar intended uses as HYASE-10X are available in the European Union or other international markets.

## 7 Suggested profile and training for users

The end user (IVF professional) is expected to follow Good IVF-laboratory Practice and use the device according to the IFU. As no special design feature or safety concerns were identified for HYASE-10X, no specific training is required for end-users.

## 8 Reference to any harmonized standards and common specifications applied

- Medical Devices Regulation (MDR) (EU) 2017/745
- EN ISO 14971:2019. Medical devices — Application of risk management to medical devices
- EN ISO 15223-1:2016. Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements
- EN ISO 20417:2021. Medical devices — Information to be supplied by the manufacturer MEDDEV 2.7/4
- ISO/TR 20416:2020. Medical devices — Post-market surveillance for manufacturers
- MDCG 2020-6 Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. A guide for manufacturers and notified bodies. April 2020
- MDCG 2019-9 Rev.1. Summary of safety and clinical performance. A guide for manufacturers and notified bodies. March 2022

The conformity assessment will be performed according to the procedure outlined in Annex IX of the MDR (EU) 2017/745.

# 9 Revision history

| SSCP revision number | Date issued | Change description | Revision validated by the Notified Body |
|---|---|---|---|
| 1 | 2022/01/24 | Initial version of SSCP for HYASE-10X™ (REP-4400-v.1.0) | |
| 2 | 2022/09/07 | Address DNV clinical NCs (REP-4400-v.2.0) | |
| 3 | 2022/10/04 | Address DNV clinical NCs (REP-4400-v.3.0) | |
| 4 | 2022/11/16 | Annual update of SSCP for HYASE-10X (REP-4400-v.4.0) | |
| 5 | 2022/12/19 | Address DNV clinical NCs (REP-4400-v.5.0) | |
| 6 | 2023/08/29 | Annual update of SSCP for HYASE-10X (REP-4400-v.6.0) | |
| 7 | 2023/12/23 | To address case CC-34220 ACT-34553 (REP-4400-v.7.0) | |
| 8 | 2024/08/14 | Annual update of SSCP for HYASE-10X (REP-4400-v.8.0) | |
| 9 | 2025/01/29 | Correction on Section 9, of SSCP for HYASE-10X (REP-4400-v.9.0) | |
| 10 | See publish date | To edit Section 6 of SSCP for HYASE-10X (REP-4400-v.10.0) | ☑ Yes<br>Validation language: English |

# 10 References


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