Annual Safety Report

Administrative information

Annual Safety Report number	1
EU CT number	2024-516208-41-00
Clinical trial title	The Intensive Care Platform Trial (INCEPT)
Platform sponsor	Rigshospitalet (prof. Anders Perner)
Platform sponsor address	Blegdamsvej 9, 2100 Copenhagen, Denmark
Designated reporter	Rikke Faebo Larsen
Date of initial authorization	2026-02-18

Period of reporting: 2025-02-18 to 2026-02-18

Reference documents at the time of reporting:

- *The Intensive Care Platform Trial (INCEPT) Core protocol*, version 1.4 and date 2025-08-20
- *INCEPT-Albumin Domain-specific appendix*, version 1.4 and date 2025-08-20
- *INCEPT-Thromboprophylaxis Domain-specific appendix*, version 1.1 and date 2025-08-20

Summary of product characteristics (SmPC) for the investigational medicinal products: human albumin (5 percent and 20 percent), Tinzaparin, Dalteparin, Enoxaparin and Nadroparin as approved by the reporting member state for each domain approval.

Countries actively enrolling during period of reporting:

Denmark

Statement:

This annual safety report contains confidential information.

Executive summary

This is ASR number 1 for the INCEPT trial (EU CT no. 2024-516208-41-00), covering the period 2025-02-18 to 2026-02-18. The INCEPT trial has 2 active domains (INCEPT-Albumin and INCEPT-Thromboprophylaxis) at the time of reporting. Safety information for each domain is reported in this ASR with separate table of contents referring to the Clinical Trials Coordinating Group (CTCG) simplified template.

The investigational medicinal products are:

- Human albumin 5 percent and 20 percent (ATC code B05AA01), infusion fluids, for intravenous administration on specific clinical circumstances as specified in the domain-specific appendix.
- Enoxaparin (ATC code B01AB05), tinzaparin (ATC code B01AB10), dalteparin (ATC code B01AB04) and nadroparin (ATC code B01AB06) solutions for injection, for subcutaneous injection once daily.

From trial authorisation to data lock for the current ASR report, a total of 56 subjects have been exposed to study drug in the INCEPT-Albumin, and 59 subjects in the INCEPT-Thromboprophylaxis domain.

Datasets for the reporting periods:

- The INCEPT-Albumin and INCEPT-Thromboprophylaxis ASR datasets include all participants randomised to the respective domain with complete 90-day follow-up including a 15-day data lag at time of reporting period closure (i.e., 2026-02-18).

The predefined domain-specific SARs and reported SAEs and SUSARs are summarised in the body for each domain in this report. For both domains, no new important identified or potential risks have been identified during this reporting period and the benefit-risk balance is considered unchanged.
For both domains, the IDMSCs will receive an additional report of safety events during the analyses of the respective feasibility analyses during summer 2026.

Abbreviations

ASR: *annual safety report*

ATC code: *anatomical therapeutic chemical code*

IDMSC: *independent data monitoring and safety committee*

INCEPT: *the Intensive Care Platform Trial*

IQR: *interquartile range*

IMP: *investigational medicinal product*

SAE: *serious adverse event*

SAR: *serious adverse reaction*

SmPC: *summary of product characteristics*

SUSAR: *suspected unexpected serious adverse reaction*

Safety information for the *INCEPT-Albumin* domain

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1. Introduction

ASR number: 1

Reporting period: 2025-02-18 to 2026-02-18

The dataset for the INCEPT-Albumin domain in this ASR report includes all participants with complete 90-day follow-up including a 15-day data lag at time of reporting period closure (i.e., 2026-02-18).

The INCEPT-Albumin domain investigates two approaches to fluid use in adult ICU patients with shock: the use of albumin for resuscitation and substitution (human albumin 5 percent or 20 percent administered intravenously according to protocolised criteria in doses at clinicians' discretion) or no use of albumin (intravenous human albumin only allowed in a few specific circumstances). Neither the platform sponsor nor domain sponsor-investigator have access to manufacturing, non-clinical, or post-marketing data from the marketing authorisation holders.

The *INCEPT-Albumin* domain has been approved as a risk level 1 low-risk (low intervention) domain, based on use of investigational medicinal products with marketing authorization in Europe, widespread use as part of standard care in intensive care units, and well-known safety profiles that are not subject to stricter monitoring per the European Medicines Agency's "*List of medicines under additional monitoring*", and where the risk of new safety signals arising is considered minimal.

In accordance with the above risk classification and a risk-adapted safety reporting approach, detailed, systematic reporting of serious adverse events (SAEs) and serious adverse reactions (SARs) is not required for the domain. Clinically relevant SARs are defined in the domain-specific appendix and systematically registered. These numbers are presented in this report along with the numbers of reported SAEs and suspected unexpected adverse reactions (SUSARs).

In addition to the aggregated safety data, relevant clinical outcomes and predefined process data are presented in the open and closed reports for the yearly independent data monitoring and safety (IDMSC) meetings. These reports provide supplementary information supporting the overall safety monitoring of the domain. The minutes and open report, including the recommendations, from the latest IDMSC safety meeting are included as *Appendix 1* and *Appendix 2*. The closed IDMSC meeting reports may be shared with the authorities if requested.

2. Worldwide marketing approval status

Not applicable. The domain IMPs hold marketing authorisations in Denmark and other EU/EEA member states. Neither the platform sponsor nor the domain sponsor is marketing authorisation holder.

3. Actions taken in the reporting period for safety reasons

No actions for safety reasons were taken during this reporting period, and no requests placing limitations on the study have been received. At the time of the first yearly IDMSC review, completed follow-up data were available for only 99 patients. Given the high inclusion rate and risk of undetected safety signals accumulating before the next scheduled yearly review, the IDMSC has requested an additional interim safety report. This request will be accommodated by providing an additional report of safety events during the planned feasibility analysis (covering the first 200 enrolled participants). The IDMSC also suggested that the INCEPT management committee considers cross-domain safety monitoring of adverse events (interaction analysis across domain interventions). The INCEPT management committee will evaluate this request at a coming meeting, including the overall value of procedures for any cross-domain monitoring.

4. Changes to reference safety information

The uploaded SmPCs for human albumin [Human Albumin ”CSL Behring”, 5 % version date: 2023-12-20 and Human Albumin ”CSL Behring”, 20 % version date: 2022-01-27], as approved in Denmark at the start of the reporting period, serves as reference safety information (RSI). No changes to the RSI were made during this reporting period.

5. Inventory of clinical trials

EU CT number	Domain-name	Country/ Countries	Study design (including randomisation ratio)	Study population	Start date	Planned enrolment	Subject exposure *
2024-516208-41-00	INCEPT-Albumin	Denmark	Investigator-initiated, open-label domain with an integrated feasibility phase on the pragmatic, parallel-group, randomised, embedded, multifactorial, international, adaptive Intensive Care Platform Trial (INCEPT). Restricted response-adaptive randomisation (min. 40% in each group).	Acutely admitted adult ICU patients with shock.	First domain enrolment: 2025-06-30	Maximum sample size is 10,000 participants. Expected (mean) sample sizes range from 1,137 to 3,547 participants.	56

*From trial authorisation to data lock point of this ASR.

6. Estimated cumulative subject exposure

6.1. Cumulative subject exposure*

Treatment	**Number of subjects exposed to treatment – n/N** **Volume (mL) of IMP received among exposed - Median (IQR)**
Human Albumin 5 percent	35/99 750 (375 to 1000)
Human Albumin 20 percent	40/99 400 (250 to 550)

*From trial authorisation to data lock point of this ASR. The dataset includes all participants with complete 90-day follow-up including 15 days data lag.

Abbreviations, IQR: interquartile range, mL: milliliters, n: number of participants exposed; N: the total number of participants in the domain included in this report. There were no missing values for exposure status or volume of IMP received among exposed.

6.2. Patient exposure from marketing experience

Patient exposure from marketing experience: Not applicable. Neither the platform sponsor nor the domain sponsor is marketing authorisation holder.

7. Data in line listings and summary tabulations

7.1 Reference information

MedDRA version 29.0. was used for coding of adverse events. Please refer to section 4 for information on the RSI.

7.2 Line listing of reported SUSARS in the INCEPT-Albumin domain during the reporting period (2025-02-18 to 2026-02-18)

There were no reported SUSARs during the period of reporting and therefore the line listing in 7.2 is empty.

ID.nr	Country	Age	Sex	Drug	Dose and route	Date	Severity grade	Allocation group	Onset date	Causality	Outcome	Event (diagnosis)
Participant identification number	Only EU	Years	Male/Female	Drug	Daily dose and route of administration	Last dose of trial medication given	A: Death B: Life-threatening C: Persistent/significant disability/incapacity D: Prolongation of hospitalisation E: Important medical event F: Other	Allocation group	Date of onset of the adverse reaction	1: yes (possible, probable, definite) 2: no (none, unlikely)	1: ongoing 2: resolved 2: resolved with sequelae 3: fatal 4: unknown	

The dataset for the reporting period includes all participants with complete 90-day follow-up including 15 days data lag.

7.3 Line listing of reported SAEs in the INCEPT-Albumin domain during the reporting period (2025-02-18 to 2026-02-18)[a]

There were no reported SAEs during the period of reporting and therefore the line listing in 7.3 is empty.

ID.nr	Country	Age	Sex	Drug	Dose and route	Date	Severity grade	Allocation group	Onset date	Event (diagnosis)
Participant identification number	Only EU	Years	Male/Female	Drug	Daily dose and route of administration	Last dose of trial medication given	A: Death B: Life-threatening C: Persistent/significant disability/incapacity D: Prolongation of hospitalisation E: Important medical event F: Other	Allocation group	Date of onset of the adverse reaction	
				NA	*NA*	*NA*				
				NA	*NA*	*NA*				
				NA	*NA*	*NA*				
				NA	*NA*	*NA*				

The dataset for the reporting period includes all participants with complete 90-day follow-up including 15 days data lag.
Abbreviations: NA: not applicable
[a]All SAEs are unrelated to the trial medication and are therefore reported without data regarding trial medication.

8. Significant findings from clinical trials during the reporting period

8.1 Completed clinical trials

Not applicable.

8.2 Ongoing clinical trials

This ASR contains safety information from this investigator-initiated clinical trial only and it is ongoing.

8.3 Long-term follow-up

Not applicable.

8.4 Other therapeutic use of investigational drug

Not applicable.

8.5 New safety data related to combination therapies

Not applicable.

9. Safety findings from non-interventional trials

Not applicable.

10. Other clinical trial/study safety information

During the period of reporting, the domain sponsor and principial investigator are aware of results from two other relevant clinical trials using the same investigational medicinal product: doi:10.1001/jamanetworkopen.2025.59297 and doi:10.1001/jamasurg.2025.1683. The first was a multicenter randomised clinical trial of 440 adults with septic shock allocated to albumin therapy aiming at a target serum albumin concentration versus standard fluid therapy (doi:10.1001/jamanetworkopen.2025.59297). Ninety-day mortality was not statistically significantly different between the albumin group (43.3%) and the controls (45.9%). The occurrence of adverse events in the albumin group was 54.5% and in the control group it was 48.1%; statistically, this was also not significantly different between the groups. The investigators concluded that albumin administration was safe but did not improve 90 days survival, and that the results remain inconclusive due to premature termination of the trial.

The second was a multicenter randomised clinical trial of 611 adults undergoing major cardiac surgery and at high risk of kidney injury, who were allocated to postoperative albumin infusions or usual care. The primary outcome, acute kidney injury, occurred in more patients in the albumin group (48.9%) than in the usual care group (43.4%). There were also more blood transfusions in the albumin group than in the usual care group (37.8% versus 29.9%, respectively). Mortality at 28 days censored at hospital discharge was 2.0% in the albumin group versus 0.7% in the usual care group. The investigators concluded that their findings do not support the routine use of albumin infusions in patients undergoing high-risk cardiac surgery. The latter trial population is surgical and markedly different to that of INCEPT-albumin, including that patients who needed longer postoperative ICU care were excluded. However, the potential concern of kidney injury with use of albumin is assessed in part through the primary and guiding outcome in INCEPT-Albumin, days alive without life support at day 30, which includes renal replacement therapy. The findings of the two trials have not led to changes in the safety profile or general conduct of the INCEPT-Albumin domain.

11. Safety findings from marketing experience

Neither the platform sponsor nor the domain sponsor is marketing authorisation holder and have no access to post-marketing safety data.

12.Non-clinical data

Not applicable. Neither the platform sponsor nor the domain sponsor is marketing authorisation holder and have no access to non-clinical data.

13. Literature

A systematic literature search was conducted for human albumin covering the reporting period 2025-02-18 to 2026-02-18. Relevant safety findings from two completed trials were identified and described in section 10. No other relevant safety findings were identified in published or unpublished literature.

14.Other DSURs

Not applicable. The domain and platform sponsors conduct only this domain with these IMPs.

15.Lack of efficacy

Please refer to section 10. The domain sponsor/investigator are not aware of other data regarding the efficacy of human albumin in shock during the reporting period.

16. Region-specific information

16.1 Cumulative summary tabulation of serious adverse reactions during the reporting period (2025-02-18 to 2026-02-18)

System Organ Class	All participants (N = 99) n/N (%)
Immune system disorders	
Severe anaphylactic reaction to albumin at 30 days	0/99 (0.0%)
Severe anaphylactic reaction to albumin at 90 days	0/99 (0.0%)
Vascular disorders	
Major bleeding during hospital stay at 30 days	17/97 (17.5%)
Major bleeding during hospital stay at 90 days	18/97 (18.6%)
Any serious adverse reaction (SAR)	
Any SAR at 30 days	17/97 (17.5%)
Any SAR at 90 days	18/97 (18.6%)

The dataset for the reporting period includes all participants with complete 90-day follow-up including 15 days data lag.
Abbreviations, n: number of participants with the outcome; N: the total number of participants in the domain included in this report; SAR: serious adverse reaction.
* Two participants had missing data for major bleeding at 30 and 90 days, and therefore also missing for any SAR at 30 and 90 days.

16.2 Subjects who died during the reporting period

As INCEPT-Albumin is approved as a low intervention trial, SAEs are not systematically registered. Mortality at 30, 90, and 180 days is assessed as secondary outcomes without any assessment of causality to the IMP of individual events.

Case ID	Assigned treatment	Causality to IMP	Cause of death	Comments
NA	*NA*	*NA*	*NA*	*NA*

16.3 Subjects who discontinued due to an adverse event during the reporting period

There were no discontinuations due to an adverse event during the period of reporting and therefore the line listing in 16.3 is empty.

Case ID	Assigned treatment	Causality to IMP	AE leading to discontinuation	Comments

The dataset for the reporting period includes all participants with complete 90-day follow-up including 15 days data lag.
Discontinuation of the treatment assignment under the term 'adverse events' is due to SAR/SUSARs, only.

For INCEPT in general, discontinuation of the intervention under the term adverse events will always be due to either a SAR (any SAE assessed to be related to the intervention) or SUSAR (any suspected adverse reaction which is both serious and unexpected). These are per se adjudicated to be related to the IMP, and therefore causality assessment in table 16.3 is always 'yes'.
Additionally, the pre-specified SARs registered for all interventions in a domain are a priori expected to being causally related to the intervention. This is done to ensure complete and unbiased reporting, especially for open-label domains.

17.Late-breaking information

No late-breaking safety information has emerged after the data lock point of this ASR.

18. Overall safety assessment

Based on the information described in this ASR we do not have any new safety concerns.

18.1 Evaluation of the risks

No new safety concerns and no new information relative to previously identified safety concerns, have been identified during the reporting period.

18.2 Benefit-risk considerations

Not applicable.

19 Summary of important risks

No new important identified or potential risks have been identified during this reporting period.

20 Conclusions

Number of independent data monitoring and safety committee (IDMSC) meeting(s) for the *INCEPT-Albumin* domain: 1 meeting during the current period of reporting, 1 meeting in total (minutes from the most recent meeting is included as *Appendix 2*).

Conclusions based on the observed safety data and the recommendations from IDMSC:

The safety data are as expected for this population. Neither the platform and domain sponsors nor the IDMSC have concerns about the unchanged continuation of the domain.

Benefit-risk evaluation:

Based on the above and updated knowledge about the investigational products, the risks and benefits for the participants are considered unchanged.

Implications for the clinical trial population:

Change in / amendment to domain-specific appendix	☐ **yes**	☒ **no**
Change in trial procedures	☐ **yes**	☒ **no**
Change in participant information	☐ **yes**	☒ **no**
Change in informed consent form	☐ **yes**	☒ **no**

Date: 2026-04-15

Signature:

Appendix 1. Open report for the most recent *INCEPT-Albumin* IDMSC safety meeting

Open report for yearly safety meetings: *INCEPT-Albumin*

Date of data export for the report: 2026-03-13
Date of last enrolment for participants included in the report: 2025-11-05
Domain or arms stopped: no

Table 1. Albumin-domain safety data

	Aggregated (N = 99) n/N (%) or median (IQR)	**Missing** n (%)
Days alive without life support at 30 days	19.0 (0.0 to 27.0)	2 (2.0%)
Mortality at 30 days	37/98 (37.8%)	1 (1.0%)
Mortality at 90 days	42/98 (42.9%)	1 (1.0%)
One or more domain-specific safety outcomes at 30 days[1]	17/97 (17.5%)	2 (2.0%)
One or more domain-specific safety outcomes at 90 days[1]	18/97 (18.6%)	2 (2.0%)
Major bleeding at 30 days	17/97 (17.5%)	2 (2.0%)
Major bleeding at 90 days	18/97 (18.6%)	2 (2.0%)
Severe anaphylactic reaction to albumin at 30 days	0/99 (0.0%)	0 (0.0%)
Severe anaphylactic reaction to albumin at 90 days	0/99 (0.0%)	0 (0.0%)
Any SUSAR at 30 days	0/99 (0.0%)	0 (0.0%)
Any SUSAR at 90 days	0/99 (0.0%)	0 (0.0%)
Any reported SAE at 30 days	0/99 (0.0%)	0 (0.0%)
Any reported SAE at 90 days	0/99 (0.0%)	0 (0.0%)

Abbreviations: n: denotes number of participants with the outcome; N: denotes the total number of participants; SAE: serious adverse event; SAR: serious adverse reaction; SUSAR: suspected unexpected serious adverse reaction.

[1]One or more domain-specific safety outcomes including any domain-specific SARs (major bleeding and severe anaphylactic reaction to albumin) and any SUSARs; reported SAEs are not included in this outcome.

Table 2. Albumin-domain process data

	Aggregated (N = 99)	By intervention group (percentages only)		Missing	Separation between arms
		Albumin	No albumin		Absolute difference in albumin volumes
	n/N (%,) median (IQR) or mean (SD)	%, median (IQR) or mean (SD)	%, median (IQR) or mean (SD)		
Proportion recruited	99/124 (79.8%)	-	-	-	-
Proportion of participants without consent to continued data collection	1/99 (1.0%)	0.0%	2.0%	0 (0.0%)	-
Proportion of participants with protocol violations	8/99 (8.1%)	10.0%	6.1%	0 (0.0%)	-
Proportion of participants in the albumin arm receiving ≥100 ml albumin	-	90.0%	-	0 (0.0%)	-
Proportion of participants in the no albumin arm receiving ≥100 ml albumin	-	-	22.4%	0 (0.0%)	-
Proportion of participants with primary outcome data within maximum of 15 days of follow-up	63/99 (63.6%)	62.0%	65.3%	0 (0.0%)	-
Percentage of intervention days with protocol violations	Median (IQR): 0.0% (0.0 to 0.0%)	Median (IQR) :0.0% (0.0 to 16.4%)	Median (IQR): 0.0% (0.0 to 0.0%)	0 (0.0%)	-
	Mean (SD): 5.1% (11.3%)	Mean (SD): 8.7% (13.1%)	Mean (SD): 1.5% (7.5%)	0 (0.0%)	-
Albumin volumes, mL	-	Median (IQR): 600 (300 to 1288)	Median (IQR): 0 (0 to 0)	0 (0.0%)	Difference in medians: 600
	-	Mean (SD): 909 (834)	Mean (SD): 110 (297)	0 (0.0%)	Difference in means: 798

Abbreviations: n: denotes number of participants with the outcome; N: denotes the total number of participants.

Appendix 2. Minutes including recommendations from the most recent *INCEPT-Albumin* IDMSC safety meeting

IDMSC Recommendation — INCEPT-Albumin Domain

Date: April 7, 2026

From: INCEPT-Albumin Independent Data Monitoring and Safety Committee (IDMSC)

To: INCEPT-Albumin Domain Management Committee and INCEPT Platform Management Committee

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Meeting

The INCEPT-Albumin domain IDMSC convened for the mandated annual safety meeting on 7 April 2026. The committee reviewed the open and closed reports based on data exported on 13 March 2026, covering 99 participants enrolled between 30 June and 5 November 2025. No adaptive analyses have been conducted or triggered.

Recommendation

The IDMSC recommends that the INCEPT-Albumin domain **continues without modification**.

Additional requests

The IDMSC makes the following additional requests to the domain management committee:

1. **Interim safety report:** The IDMSC requests additional report of safety events during the feasibility analysis to be done with the first 200 patients.

2. **Feasibility monitoring:** The IDMSC notes that certain feasibility criteria may warrant attention ahead of the formal feasibility analysis planned for this summer. The IDMSC encourages the domain management committee to review adherence to all pre-specified feasibility criteria and to consider whether corrective actions at sites are needed.
3. **Cross-domain safety monitoring:** The IDMSC suggests that the steering committee considers sharing adverse events among domains in the platform.

Conclusion

The IDMSC has no concerns that require pausing or stopping the domain at this time. The committee looks forward to reviewing updated safety data at the feasibility report.

On behalf of the INCEPT-Albumin IDMSC

Fernando G Zampieri, IDMSC Chair

On behalf of other IDMSC members

Yassen Arabi

Erin Gabriel

Safety information for the *INCEPT-Thromboprophylaxis* domain

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1. Introduction

ASR number: 1

Reporting period: 2025-02-18 to 2026-02-18.

The dataset for the *INCEPT-Thromboprophylaxis* domain in this ASR report includes all participants with complete 90-day follow-up including a 15-day data lag at time of reporting period closure (i.e., 2026-02-18)

The *INCEPT-Thromboprophylaxis* domain investigates low molecular weight heparin (LMWH) for thromboprophylaxis, administered once daily in either a fixed low, fixed intermediate, or weight-adjusted dose. Four LMWH types are used: enoxaparin, tinzaparin, dalteparin, or nadroparin. Each participating site selects one preferred LMWH type prior to patient enrollment. Neither the platform sponsor or domain sponsor-investigator have access to manufacturing, non-clinical, or post-marketing data from the marketing authorisation holders.

The *INCEPT-Thromboprophylaxis* domain has been approved as a risk level 1 low-risk domain, based on use of investigational medicinal products with marketing authorization in Europe, widespread use as part of standard care in intensive care units, and well-known safety profiles. None of the included investigational products (enoxaparin, tinzaparin, dalteparin, and nadroparin) are subject to stricter monitoring per the European Medicines Agency's "*List of medicines under additional monitoring*", and thus the risk of new safety signals arising is considered minimal.

In accordance with the above risk classification and a risk-adapted safety reporting approach, detailed, systematic reporting of serious adverse events (SAEs) and serious adverse reactions (SARs) is not required for the domain. Clinically relevant SARs are defined in the domain-specific appendix and systematically registered. These numbers are presented in this report along with the numbers of reported SAEs and suspected unexpected adverse reactions (SUSARs).

In addition to the aggregated safety data, relevant clinical outcomes and predefined process data are presented in the open and closed reports for the yearly independent data monitoring and safety (IDMSC) meetings. These reports provide supplementary information supporting the overall safety monitoring of the domain. The minutes and open report, including the recommendations, from the latest IDMSC safety meeting are included as *Appendix 1* and *Appendix 2*. The closed IDMSC meeting reports may be shared with the authorities if requested.

2. Worldwide marketing approval status

Not applicable. The domain IMPs hold marketing authorisations in Denmark and other EU/EEA member states. Neither the platform sponsor nor the domain sponsor is marketing authorisation holder.

3. Actions taken in the reporting period for safety reasons

No actions for safety reasons were taken during this reporting period, and no requests placing limitations on the study have been received.

At the time of the first yearly IDMSC review, completed follow-up data were available for only 60 patients. Given the high inclusion rate and risk of undetected safety signals accumulating before the next scheduled yearly review, the IDMSC has requested an additional interim safety report. This request will be accommodated by providing an additional report of safety events during the planned feasibility analysis (covering the first 300 enrolled participants).

4. Changes to reference safety information

The uploaded SmPCs for LMWH [Innohep, 2024-11-07; Fragmin, 2022-11-18; enoxaparin, 2025-04-01; fraxiparine, 2024-01-15] as approved in Denmark at the start of the reporting period, serves as reference safety information (RSI). No changes to the RSI were made during this reporting period.

5. Inventory of clinical trials

EU CT number	Domain-name	Country/ Countries	Study design (including randomisation ratio)	Study population	Start date	Planned enrolment	Subject exposure *
2024-516208-41-00	INCEPT-Thromboprophylaxis	Denmark	Investigator-initiated, open-label domain with an integrated feasibility phase on the pragmatic, parallel-group, randomised, embedded, multifactorial, international,	Acutely admitted adult ICU patients with decision to start/continue LMWH thromboprophylaxis.	First domain enrolment: 2025-09-18	Maximum sample size is 10,000 participants. Expected (mean) sample sizes range from 2,265 to 4,892 participants.	59

			adaptive Intensive Care Platform Trial (INCEPT). The domain employs adaptive stopping and arm dropping for superiority/inferiority, stopping for practical equivalence, and restricted response-adaptive (min. 25% in each arm).				

*From trial authorisation to data lock point of this ASR.

One of the 60 participants in the *INCEPT-Thromboprophylaxis* domain included in this report was not exposed to the treatment, because participation ended before the treatment intervention commenced (due to informed consent deemed to be unobtainable).

6. Estimated cumulative subject exposure

6.1. Cumulative subject exposure*

Treatment	**Number of subjects exposed to treatment (N = 59)** *n/N (%)*
Tinzaparin	53/60 (88.3%)
Dalteparin	6/60 (10.0%)
Nadroparin	0/60 (0.0%)
Enoxaparin	0/60 (0.0%)

*From trial authorisation to data lock point of this ASR. The dataset includes all participants with complete 90-day follow-up including 15 days data lag.

Abbreviations, IQR: interquartile range, mL: milliliters, n: number of participants exposed; N: the total number of participants in the domain included in this report. One of the 60 participants in the *INCEPT-Thromboprophylaxis* domain included in this report was not exposed to the treatment, because participation ended before the treatment intervention commenced (due to informed consent deemed to be unobtainable).

6.2. Patient exposure from marketing experience

Patient exposure from marketing experience: Not applicable. Neither the platform sponsor nor the domain sponsor is marketing authorisation holder.

7. Data in line listings and summary tabulations

7.1 Reference information

MedDRA version 29.0. was used for coding of adverse events. Please refer to section 4 for information on the RSI.

7.2 Line listing of reported SUSARs in the INCEPT-Thromboprophylaxis domain during the reporting period (2025-02-18 to 2026-02-18)

There were no reported SUSARs during the period of reporting and therefore the line listing in 7.2 is empty.

ID.nr	Country	Age	Sex	Drug	Dose and route	Date	Severity grade	Allocation group	Onset date	Causality	Outcome	Event (diagnosis)
Participant identification number	Only EU	Years	Male/Female	Drug	Daily dose and route of administration	Last dose of trial medication given	A: Death B: Life-threatening C: Persistent/significant disability/incapacity D: Prolongation of hospitalisation E: Important medical event F: Other	Allocation group	Date of onset of the adverse reaction	1: yes (possible, probable, definite) 2: no (none, unlikely)	1: ongoing 2: resolved 2: resolved with sequelae 3: fatal 4: unknown	

The dataset for the reporting period includes all participants with complete 90-day follow-up including 15 days data lag.

7.3 Line listing of reported SAEs in the INCEPT- Thromboprophylaxis domain during the reporting period (2025-02-18 to 2026-02-18)[a]

There were no reported SAEs during the period of reporting and therefore the line listing in 7.3 is empty.

ID. nr	Country	Age	Sex	Drug	Dose and route	Date	Severity grade	Allocation group	Onset date	Event (diagnosis)
Participant identification number	Only EU	Years	Male/Female	Drug	Daily dose and route of administration	Last dose of trial medication given	A: Death B: Life-threatening C: Persistent/significant disability/incapacity D: Prolongation of hospitalisation E: Important medical event F: Other	Allocation group	Date of onset of the adverse reaction	
				NA	*NA*	*NA*				
				NA	*NA*	*NA*				
				NA	*NA*	*NA*				
				NA	*NA*	*NA*				

The dataset for the reporting period includes all participants with complete 90-day follow-up including 15 days data lag.
Abbreviations: NA: not applicable
[a]All SAEs are unrelated to the trial medication and are therefore reported without data regarding trial medication.

8. Significant findings from clinical trials during the reporting period

8.1 Completed clinical trials

Not applicable.

8.2 Ongoing clinical trials

This ASR contains safety information from this investigator-initiated clinical trial only and it is ongoing.

8.3 Long-term follow-up

Not applicable.

8.4 Other therapeutic use of investigational drug

Not applicable.

8.5 New safety data related to combination therapies

Not applicable.

9. Safety findings from non-interventional trials

Not applicable.

10. Other clinical trial/study safety information

During the period of reporting, the domain sponsor and principial investigator are aware of results from another trial using the same investigational medicinal product in a relevant population (https://doi.org/10.1164/rccm.202409-1727OC). In this multicenter randomized clinical trial, 172 adult patients with sickle cell disease and acute chest syndrome (ACS) were randomized between prophylactic (4500 IU) versus therapeutic (175 IU/kg/24h) dose tinzaparin. The primary efficacy outcome, time to ACS resolution, was shorter with therapeutic anticoagulation than with prophylactic doses (hazard ratio, 0.71; 95% confidence interval, 0.51 to 0.99; P = 0.044). The primary safety outcome, major bleeding, did not occur in either group. The investigators concluded that in adult patients with sickle cell disease and ACS therapeutic dose tinzaparin reduces time to ACS resolution. The results have not led to changes in the safety profile or general conduct of the *INCEPT-Thromboprophylaxis* domain.

11. Safety findings from marketing experience

Neither the platform sponsor nor the domain sponsor is marketing authorisation holder and have no access to post-marketing safety data.

12. Non-clinical data

Not applicable. Neither the platform sponsor nor the domain sponsor is marketing authorisation holder and have no access to non-clinical data.

13. Literature

A systematic literature search was conducted for LMWH in ICU patients covering the reporting period 2025-02-18 to 2026-02-18. Findings from one completed trial were identified and described in section 10. No other relevant safety findings were identified in published or unpublished literature.

14. Other DSURs

Not applicable. The domain and platform sponsors conduct only this domain with these IMPs.

15. Lack of efficacy

Please refer to section 10. The domain sponsor/investigator are not aware of other data regarding the efficacy of LMWH in ICU patients during the reporting period.

16. Region-specific information

16.1 Cumulative summary tabulation of serious adverse reactions during the reporting period (2025-02-18 to 2026-02-18)

System Organ Class	**All participants (N = 60)** *n/N (%)*
Immune system disorders	
Severe anaphylactic reaction to LMWH at 30 days	0/60 (0.0%)
Severe anaphylactic reaction to LMWH at 90 days	0/60 (0.0%)
Blood and lymphatic system	
Heparin-induced thrombocytopenia at 30 days	0/60 (0.0%)
Heparin-induced thrombocytopenia at 90 days	0/60 (0.0%)
Any serious adverse reaction (SAR)	
Any SAR at 30 days	0/60 (0.0%)
Any SAR at 90 days	0/60 (0.0%)

The dataset for the reporting period includes all participants with complete 90-day follow-up including 15 days data lag.
Abbreviations, n: number of participants with the outcome; N: the total number of participants in the domain included in this

report; SAR: serious adverse reaction.
There were no missing values for SARs at 30 and 90 days.

16.2 Subjects who died during the reporting period

As *INCEPT-Thromboprophylaxis* is approved as a low intervention trial, SAEs are not systematically registered. Mortality at 30, 90, and 180 days is assessed as secondary outcomes without any assessment of causality to the IMP of individual events.

Case ID	Assigned treatment	Causality to IMP	Cause of death	Comments
NA	*NA*	*NA*	*NA*	*NA*

16.3 Subjects who discontinued due to an adverse event during the reporting period

There were no discontinuations due to an adverse event during the period of reporting and therefore the line listing in 16.3 is empty.

Case ID	Assigned treatment	Causality to IMP	AE leading to discontinuation	Comments

The dataset for the reporting period includes all participants with complete 90-day follow-up including 15 days data lag.
Discontinuation of the treatment assignment under the term 'adverse events' is due to SAR/SUSARs, only.

For INCEPT in general, discontinuation of the intervention under the term adverse events will always be due to either a SAR (any SAE assessed to be related to the intervention) or SUSAR (any suspected adverse reaction which is both serious and unexpected). These are per se adjudicated to be related to the IMP, and therefore causality assessment in table 16.3 is always 'yes'.
Additionally, the pre-specified SARs registered for all interventions in a domain are a priori expected to being causally related to the intervention. This is done to ensure complete and unbiased reporting, especially for open-label domains.

17. Late-breaking information

No late-breaking safety information has emerged after the data lock point of this ASR.

18. Overall safety assessment

Based on the information described in this ASR we do not have any new safety concerns.

18.1 Evaluation of the risks

No new safety concerns and no new information relative to previously identified safety concerns, have been identified during the reporting period.

18.2 Benefit-risk considerations

Not applicable.

19. Summary of important risks

No new important identified or potential risks have been identified during this reporting period.

20. Conclusions

Number of independent data monitoring and safety committee (IDMSC) meeting(s) for the *INCEPT-Thromboprophylaxis* domain: 1 meeting during the current period of reporting, 1 meeting in total (minutes from the most recent meeting is included as *Appendix 2*).

Conclusions from the observed safety data and the recommendations from IDMSC:

The safety data are as expected for this population. Neither the platform and domain sponsors nor the IDMSC have concerns about the unchanged continuation of the domain.

Benefit-risk evaluation:

Based on the above and updated knowledge about the investigational products, the risks and benefits for the participants are considered unchanged.

Implications for the clinical trial population:

Change in / amendment to domain-specific appendix	☐ **yes**	☒ **no**
Change in trial procedures	☐ **yes**	☒ **no**
Change in participant information	☐ **yes**	☒ **no**
Change in informed consent form	☐ **yes**	☒ **no**

Date: 2026-04-15

Signature: _____

Appendix 1. Open report for the most recent *INCEPT-Thromboprophylaxis* IDMSC safety meeting

Open reports for yearly safety meetings: *INCEPT-Thromboprophylaxis*

Date of data export for the report: 2026-03-13
Date of last enrolment for participants included in the report: 2026-11-06
Domain or arms stopped: no.

Table 1. Thromboprophylaxis-domain safety data

	Aggregated (N = 60) n/N (%) or median (IQR)	**Missing** n (%)
Days alive out of hospital at 30 days	1.0 (0.0 to 15.0)	1 (1.7%)
All-cause 30-day mortality	11/59 (18.6%)	1 (1.7%)
All-cause 90-day mortality	13/59 (22.0%)	1 (1.7%)
One or more domain-specific safety outcomes at 30 days[1]	0/60 (0.0%)	0 (0.0%)
One or more domain-specific safety outcomes at 90 days[1]	0/60 (0.0%)	0 (0.0%)
Heparin-induced thrombocytopenia at 30 days	0/60 (0.0%)	0 (0.0%)
Heparin-induced thrombocytopenia at 90 days	0/60 (0.0%)	0 (0.0%)
Severe anaphylactic reaction to LMWH at 30 days	0/60 (0.0%)	0 (0.0%)
Severe anaphylactic reaction to LMWH at 90 days	0/60 (0.0%)	0 (0.0%)
Any SUSAR at 30 days	0/60 (0.0%)	0 (0.0%)
Any SUSAR at 90 days	0/60 (0.0%)	0 (0.0%)
Any reported SAE at 30 days	0/60 (0.0%)	0 (0.0%)
Any reported SAE at 90 days	0/60 (0.0%)	0 (0.0%)
Venous thromboembolism during hospital stay at day 30	3/59 (5.1%)	1 (1.7%)
Venous thromboembolism during hospital stay at day 90	3/59 (5.1%)	1 (1.7%)
Major bleeding during hospital stay at day 30	7/59 (11.9%)	1 (1.7%)
Major bleeding during hospital stay at day 90	8/59 (13.6%)	1 (1.7%)

Abbreviations (in alphabetical order): n: denotes number of participants with the outcome; N: denotes the number of participants; LMWH: low-molecular-weight heparin; SAE: serious adverse event; SAR: serious adverse reaction; SUSAR: suspected unexpected serious adverse reaction.

Table 2. Thromboprophylaxis-domain process data

	Aggregated (N = 60)	By intervention group (percentages only)			Missing
		Low	Int	Weight-adj.	
	n/N (%)	%	%	%	n (%)
Proportion recruited	60/62 (96.8%)	-	-	-	-
Proportion of participants without consent to continued data collection	0/60 (0.0%)	0.0%	0.0%	0.0%	0 (0.0%)
Proportion of participants with protocol violations	9/60 (15.0%)	15.8%	9.5%	20.0%	0 (0.0%)
Proportion of participants with primary outcome data within maximum of 15 days of follow-up	59/60 (98.3%)	100.0%	95.2%	100.0%	0 (0.0%)
Proportion of participants in the weight-adjusted arm receiving a different dose than if they were allocated to the fixed low dose arm	-	-	-	100.0%	0 (0.0%)
Proportion of participants in the weight-adjusted arm receiving a different dose than if they were allocated to the fixed intermediate dose arm	-	-	-	60.0%	0 (0.0%)

Abbreviations (in alphabetical order): Int: intermediate dose low-molecular-weight heparin; Low: low dose low-molecular-weight heparin; n: denotes number of participants with the outcome; N: denotes the number of participants; Weight-adj.: weight-adjusted dose low-molecular-weight heparin.

Appendix 2. Minutes including recommendations from the most recent *INCEPT-Thromboprophylaxis* IDMSC safety meeting

Van: Danny McAuley <d.f.mcauley@qub.ac.uk>
Verstuurd: dinsdag, maart 31, 2026 1:22:52 a.m.
Aan: Eck, RJ (int) <r.j.eck@umcg.nl>; Anders Perner <Anders.Perner@regionh.dk>
CC: Christian Hassager <Christian.Hassager@regionh.dk>; erin.gabriel@sund.ku.dk <erin.gabriel@sund.ku.dk>
Onderwerp: IDSMC meeting, INCEPT-Thromboprophylaxis

Dear both

The IDSMC reviewed data from 60 participants who had completed follow-up. A total of approximately 400 participants have been recruited to date.

The IDSMC recommended that the trial continue unchanged.

The IDSMC would like

1. to have an additional formal report of safety within approximately 6 months.
2. where mortality data is missing the reason for this should be included in the report.
3. a secondary frequentist analysis for the safety outcomes to be included in the DSMB report until the first adaptive analysis is undertaken.

Please let me know if you have any questions or need anything else.

Best wishes
Danny on behalf of the INCEPT-Thromboprophylaxis IDSMC