Clinical Investigation Plan

CP346

PIP 1.0 - **P**ressure **I**njury **P**revention

Post-market Clinical Follow up study, Biatain Silicone Sacral

August 2022 – December 2022

Title:
A Prospective Single-arm Study Investigating the Safety of Biatain Silicone Sacral While Used as Prevention in Hospital-admitted Patients at Risk of Developing a Pressure Injury

NCT05619003

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SYNOPSIS OF THE CLINICAL INVESTIGATION

Title:

A prospective single-arm study investigating the safety of Biatain Silicone Sacral while used as prophylactic prevention amongst hospital admitted patients at risk of developing a pressure injury.

Test products:

Biatain Silicone Sacral is a CE-marked five-layer foam dressing, that has been sold in the US since April 2018. It comes in two sacral sizes, a small heart-shape and a larger diamond-shape.

(The test product is Biatain® Silicone sacral 15 cm x 19 cm / 6 in x 5.5 in. There is no comparator product in this investigation)

Intended use:

The Biatain Silicone Sacral products are sterile packed, single use polyurethane foam dressings with silicone adhesive intended for wound management and can be used as part of a prophylactic therapy to help prevent skin damage e.g., pressure injuries.

Aim and Objectives:

The aim of the clinical investigation is to evaluate safety of Biatain Silicone, when used as prophylactic prevention on hospital-admitted patients at risk of developing a pressure injury.

- **Primary objective**: Evaluate safety

- **Explorative objective**: Establish the proportion of subjects, that develop pressure injuries during hospitalization while wearing Biatain Silicone Sacral bandage

The proportion of hospital-acquired pressure injuries will be compared to relevant existing proportions in literature[3].

Design of the investigation:

During the study period, data will be collected to determine a *proportion of hospital acquired pressure injuries in hospital admitted patients with a limited level of mobility*. The study is designed as a non-comparative, single-arm, prospective multi-center observational study. The study will be conducted in Danish hospitals and the establish proportion of hospital-acquired pressure injuries will be compared to global, European, and Scandinavian proportions of hospital-acquired pressure injuries reported in literature.

(The investigation is a non-comparative, single-arm investigation with one test period. In total 67 hospital-admitted patients will be included. Each subject will have daily test-visits overseen by the Principal Investigator

or designee during an expected 7-day test period in total or until the subject is discharged. The subjects will test the CE marked test product Biatain Silicone Sacral 15 cm x 19 cm / 6 in x 5.5 in).

Expected duration of the clinical investigation:
The investigation will be conducted from August 2022 through December 2022.

Primary endpoint:
Number of Adverse Events

Secondary endpoint:
Number of Device Deficiencies

Exploratory endpoint:
Hospital-acquired sacral pressure injuries during investigation period (Yes/No)

Population/subjects:
The subjects to be included in the study will be a range of partially immobilized hospital-admitted patients (from e.g., medical, surgical, lung and orthopedic surgical units) with a Braden score of 6-18.

(Hospital-admitted patients with a limited level of mobility and a Braden score between 6-18).

Inclusion and Exclusion Criteria:

Inclusion criteria	**Exclusion criteria**
Hospital-admitted patients at risk of developing a pressure injury with an expected hospital-stay of more than 24 hours from time of screening	Suspected or actual spinal injury precluding the patient from being turned
≥18 years of age and has full legal capacity	Sacral erythema, sacral pressure marks, pre-existing sacral pressure injury
Has given written consent to participate by signing the **I**nformed **C**onsent signature **F**orm	Trauma to sacrum.
Has a Braden score of 6-18 at screening (within the last 24 hours or at time of screening) *(Appendix 2)*	Topical treatment with steroid cream in the sacral area. (treatment must have been terminated at least 14 days prior to enrollment)
Intact sacral skin (non-breached skin, without signs of non-blanchable erythema over bony prominence/pre-existing sacral pressure injury over bony prominence) *(Appendix 3)*	Pregnancy or breastfeeding

LIST OF ABBREBIATIONS

ABBREVIATION	WRITTEN OUT	EXPLANATION
ADE	Adverse Device Effect	See section 18.2
AE	Adverse Event	See section 18.1
ASADE	Anticipated Serious Adverse Device Effect	See section 18.4.2
CIP	Clinical Investigation Plan	
CIR	Clinical Investigation Report	See section 20
CRF	Case Report Form (paper or electronic)	
CM	Clinical Manager	
DQF	Data Query Forms	A DQF is a query specifically used in clinical research. The DQF is the primary data query tool from the sponsor to clarify discrepancies and ask the investigator for clarification. The DQF is part of the data validation process in a clinical investigation.
DD	Device deficiency	See section 18.3
EC	Ethics Committee	
IB	Investigator's Brochure	Compilation of the current clinical and non-clinical information on the investigational medical device(s,) relevant to the clinical investigation.
IFU	Instruction for Use	Appendix 1
ITT	Intention to Treat	See section 10.1
PI	Principal Investigator	Qualified person responsible for conducting the clinical investigation at an investigation site. If the clinical investigation is conducted by a team of individuals at an investigation site, the PI is the responsible leader of the team. Whether this is the responsibility of an individual or an institution can depend on national regulations.
SADE	Serious Adverse Device Effect	See section 18.4.1
SAE	Serious Adverse Event	See section 18.4
USADE	Unanticipated Serious Adverse Device Effect	See section 18.4.3

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1. List of personnel involved in the Investigation

1.1. Sponsor representatives

1.2. Investigators

2. Rational/justification for conducting the clinical investigation

The Biatain Silicone Sacral and Multishape dressings are multi-layer polyurethane foam dressings. They are CE-marked products and have been on the US market since April 2018. They are evaluated as safe to use and perform according to their intended purpose and indications.

This investigation is a Post-market Clinical Follow-up Study, which aims to support the clinical performance of Biatain Silicone Sacral regarding the use of the dressing as part of prophylactic therapy to help prevent skin damage, e.g. pressure injuries. A pressure injury (PI) or pres-sure ulcer (PU) is defined as localized damage to the skin and/or underlying tissue, as a result of pressure or pres-sure in combination with shear. PIs usually occur over a bony prominence but may also be related to a medical de-vice or other object.[1-2]

The need for follow-up clinical data regarding this indication has been suggested in the Clinical Evaluation for Bi-atain Silicone Sacral and Multishape, and an outline of investigation CP346 is described in the Post-market Clinical Follow-up section of the Clinical Evaluation Report (CER) VV-0247441 for Biatain Silicone Sacral and Multishape.

3. Objective(s) and hypotheses of the clinical investigation

3.1. Aim and Objective

The aim of the clinical investigation is to evaluate safety of Biatain Silicone, when used as prophylactic pre-vention on hospital-admitted patients at risk of developing a pressure injury.

- **Primary objective**: Evaluate safety

- **Exploratoryobjective**: Establish the proportion of subjects, that develop pressure injuries during hospitali-zation while wearing Biatain Silicone Sacral

The proportion of hospital-acquired pressure injuries will be compared to relevant existing proportions in liter-ature[3].

4. Investigational device and comparator(s)

The Biatain Silicone Sacral product is a sterile pouch-packed, single use polyurethane foam dressings with silicone adhesive intended for wound management and can be used as part of a prophylactic therapy to help prevent skin damage e.g., pressure injuries.

The Biatain Silicone Sacral and dressings are available in different shapes to fit the sacral area of the body. In this investigation it will primary be the heart-shaped product, which will be used. However, if needed the dia-mond shaped, can be chosen.

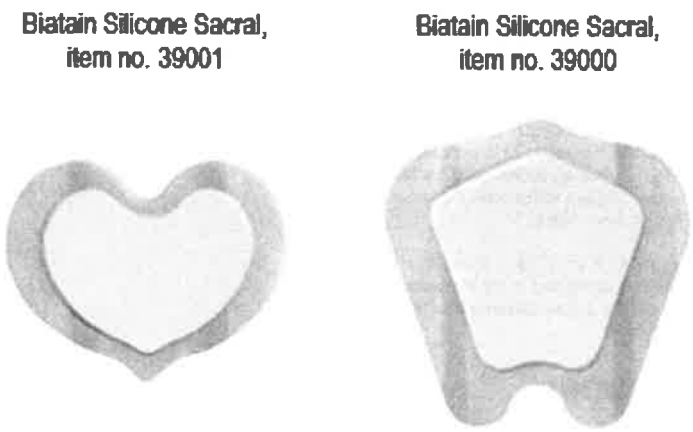


Figure 1: Biatain Silicone Sacral dressings.

The two Biatain Silicone Sacral dressings consist of the same five layers:

- Polyurethane (PU) top film – a permeable barrier film of PU that is printed with dots
- Tissue layer – a tissue layer of cellulose fibres
- Super absorber layer – a cellulose fibre matrix with super absorbing particles
- Biatain foam pad – a PU foam with a thickness of 2.3 mm
- Silicone adhesive bi-layer– a silicone adhesive gel

4.1.1. Manufacturing

Biatain Silicone Sacral dressings are single packed in pouches consisting of a top layer of paper and a bottom layer of film. The two layers of primary packaging material (paper/film) are heat welded together, thus creating the pouch, which is the sterile barrier of the product. The Biatain Silicone Sacral products are ethylene oxide sterilised.

The products are packed in a retail box, and the instruction for use (IFU) is a leaflet in the retail box.

4.2. Identification and traceability of the device

Coloplast A/S, Holtedam 1-3, 3050 Humlebæk, Denmark, is the manufacturer of the CE marked Investigational de-vice (Biatain Silicone).

Item No. 5 digit	Product Name	Actual size: - Total dressing - Absorbing pad	Product Description
39001	Biatain Silicone Sacral	15.0 cm x 19.0 cm 10.9 cm x 14.0 cm	Sacral dressing with dimensions, 15 cm x 19 cm / 6 in x 7.5 in Absorbing pad with dimensions, 11 cm x 14 cm / 4.3 in x 5.5 in
39000	Biatain Silicone Sacral	25.0 cm x 25.0 cm 17.0 cm x 17.2 cm	Sacral dressing with dimensions, 25 cm x 25 cm / 9.8 in x 9.8 in Absorbing pad with dimensions, 17 cm x 17 cm / 6.7 in x 6.7 in

Table 1: An overview of the item numbers and product variants for Biatain Silicone Sacral.

4.3. Intended use of the device in the clinical investigation

The Biatain Silicone Sacral product is a sterile pouch-packed, single use polyurethane foam dressing with silicone adhesive intended for wound management and can be used as part of a prophylactic therapy to help prevent skin damage e.g., pressure injuries amongst a population with Braden Score 6-18.

4.4. Handling of the investigational device

The handling of Biatain Silicone is described in detail in the Instruction for Use (IFU), which is included in the box following the device. Storage conditions are also stated in the IFU.

The PI (Principal Investigator) and PI delegate will receive training by sponsor and/PI in handling and correct use of the investigational device. The PI or delegate will inform the subjects in the investigational properties of the device.

(Biatain Silicone Sacral, Instruction for Use – Appendix 1)

4.5. Handling of the investigational device

The subjects will be included for up to 7 days.

Subjects that are included in the investigation and applied the investigational product, are expected to wear the product up to 7 days or until discharged. The same product will be applied for the entire test period, however if necessary, due to contamination or rolling edges, the product must be replaced with a new product.

Therefore, the subjects are expected to use approximately 1 product, however the site will be supplied with enough products in case of replacements of products for the duration of the investigation.

In total 67 subjects will be enrolled. To allow for unpredicted dressing changes, 1 patient requires 7 heart shaped/small products, which is per 67 patients: 67 x 7 = 469 small sacral products.

Around 30 patients may need the large sacral bandage: 30 x 7 = 210 large sacral products.

5. Design of the clinical investigation

5.1. General

The Clinical investigation is an open-labelled, non-comparative, single-arm, prospective, multi-center observational investigation.

Subjects will be applicated Biatain Silicone Sacral dressing in the sacral area at Baseline Visit / V1 in a test period up to 7 days or until discharged.

In total, 67 hospital-admitted patients will be enrolled. Each subject will have a screening visit (V0/Day 0), a Baseline visit (V1/Day1) and daily visits (V2/Day2 to V8/termination visit) performed. If the subject is discharged prior to visit 8, the termination visit will be performed at the day of the discharge.

All visits will be carried out by the Principal Investigator or delegate.

Before scheduling V0 the subject will be informed about the investigation, where the PI or delegate will give a detailed in-formation about the requirements, the content and what it involves participating in the investigation. See section 6.4 for recruitment.

Screening visit (V0/Day0) and Baseline visit (V1/Day1) can be performed the same day. If the subject wishes to re-consider his or her participation after Screening (Visit0/Day0), the subject has the right to wait minimum 24 hours before decision to participate. If the subject hereafter decides to participate in the clinical investigation, Baseline visit (V1/Day1) will be scheduled, and the inclusion procedures will be performed. Screening visit/V0 and baseline visit must be performed on following days unless performed the same day.

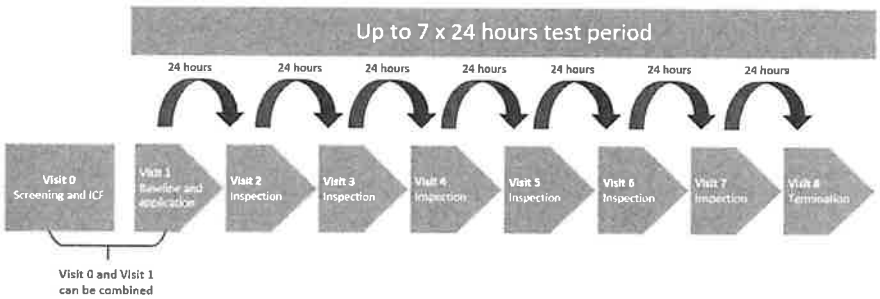


Figure 2: Study Design CP346

5.2. Primary endpoint

Number of Adverse Events

5.3. Secondary Endpoint

Number of Device Deficiencies

5.4. Exploratory endpoint

Hospital-acquired sacral pressure injuries during investigation period (Yes/No)

5.5. Rationale for selection and measurement of endpoints

The primary endpoint, number of adverse events and the secondary endpoint number of device deficiencies, has been chosen to examine the safety of Biatain Silicone Sacral.

The exploratory endpoint, hospital-acquired sacral pressure injuries during investigation period, has been chosen to examine the performance of Biatain Silicone Sacral, regarding its ability to help prevent pressure injuries.

5.6. Demography and potential compromising factors

The subjects should not be treated with topical steroid creams, skin lotions, barrier sprays or barrier wipes in the sacral area during the investigation.

- Gender/age/height/weight.
- Braden Scale Score
- Urine incontinence (y/n)
- Faecal incontinence (y/n)
- Date and primary reason for admission (e.g., diabetes mellitus, cardiovascular disease, renal disease, pulmonary disease, anemia, trauma, other)

5.7. Equipment/methods and timing for assessing the variables

Please go to Flowchart table 5 section 7.2 for information regarding timing of endpoint date capture and section 11 for information about data collection.

5.8. Randomisation Procedure

Subjects are not randomized as the control group comes from the Border Trial Study (3).

5.9. Total expected duration of clinical investigation

The dates below are approximate, and no subjects will be enrolled before all required approvals have been obtained. If changes are required, applicable EC and regulatory authorities will be notified.

First subject enrolled: August 15th 2022.

Last subject enrolled: December 1st 2022.

Last subject completed: December 8th 2022.

Final report: June 2023.

6. Clinical Investigation population

The clinical investigation will be conducted with 67 hospitalized subjects enrolled at 3 clinical investigation sites. Each site will enrol about 22-24 subjects at a competitive rate, until the investigation target of 67 subjects is reached.

According to the sample size calculations (see section 10.2) 50 subjects are required to complete the investigation with at least 24 hours of wear time to be counted as completers. Considering a drop-out rate of 30%, the required total number of subjects to be enrolled in the trial shall be 67.

6.1. Eligibility criteria

To be included in the investigation, the subjects must comply with the selection criteria described below.

6.2. Inclusion criteria and Exclusion criteria

Inclusion criteria	Justification for inclusion criteria
Hospital-admitted patients at risk of developing a pressure injury with an expected hospital-stay of more than 24 hours from visit 1	Intended patient population
≥18 years of age and has full legal capacity	To meet the Helsinki declaration
Has given written consent to participate by signing the Informed Consent signature Form	To meet the Helsinki declaration
Has a Braden score of 6-18 at screening (performed within the last 24 hours) *(Appendix 2)*	To meet primary endpoint
Intact sacral skin (non-breached skin, without signs of non-blanchable erythema over bony prominence/pre-existing sacral pressure injury over bony prominence) *(Appendix 3)*	Skin must be intact on admission to detect developing pressure injuries during investigation period

Table 2. Inclusion criteria

Exclusion criteria	Justification for exclusion criteria
Suspected or actual spinal injury precluding the patient from being turned	Turning of the patient (to mobilize them) at regular intervals are a part of standard procedure for pressure injury prevention
Sacral erythema, sacral pressure marks, pre-existing sacral pressure injury	Skin must be intact on admission to detect developing pressure injuries during investigation period
Trauma to sacrum	Skin must be intact on admission to detect developing pressure injuries during investigation period.
Topical treatment with steroid creme in the sacral area (treatment must have been terminated at least 14 days prior to enrollment)	Steroid creme may interfere with the skin condition and make it more fragile
Pregnancy or breastfeeding	Even though the ingredients and recipes have been approved for human beings, their effect on embryos, fetuses and infants are unknown

Table 3. Exclusion criteria

6.3. Pregnancy and breastfeeding

For female subjects with childbearing potential (they have had at least one period during the last 12 months), a urine pregnancy test will be performed at the inclusion visit, to ensure the subject is not pregnant. The urine pregnancy test will be performed by dipstick at the trial site. Furthermore, the female subjects should not be breastfeeding, when participating in the clinical investigation.

6.4. Recruitment and enrolment

Recruitment of potential subjects will begin once approval have been obtained from the Ethics Committee (EC).

Recruitment will occur through competitive enrolment at 3 different sites in Denmark. The recruitment period from first subject enrolled to last subject enrolled will be approximately 4 months.

Recruitment from hospitals will be via patient screening visits or subject records kept at the participating sites.

The Coloplast Clinical Manager will have close contact to each site during the recruitment and enrolment period.

Sites will be instructed to enrol 22-24 eligible hospitalized subjects at a competitive rate. Once the Coloplast Clinical Manager is aware, that 67 subjects have been enrolled, the recruitment will stop.

If, at this time, there are subjects, who have been informed about the investigation (V0) and are reflecting on participation, they will be given the opportunity to be included within the 24 hours post V0.

Recruitment method	Hospital
Potential subjects	Recruitment will go through the Hospital sites. Potential subjects are identified by screening in patient journals using the following searching criteria: • ≥ 18 years of age • *Hospital-admitted patients with a limited level of mobility and a Braden score between 6-18* • *Expected hospital stay of at least 72 hours*
First contact	The potential subjects will be contacted during a planned visit in the ward at the hospital. If a subject is eligible and interested in participating in the investigation upon a short introduction, then written information about the investigation (Informed Consent Form) will be distributed to the subject. The Principal Investigator or delegate will invite the subject to a Screening Visit (V0).
Screening Visit (V0)	At the scheduled Screening Visit (V0) the Principal Investigator or delegate will introduce the investigation and review the inclusion and exclusion criteria. If the subject wishes to reconsider his/her participation at V0, the subject has the right to wait minimum 24 hours before deciding on participation. If the subject hereafter decides to participate in the clinical investigation a Baseline Visit (V1) will be scheduled unless performed the same day as the Screening Visit. If the subject does not meet the inclusion criteria or meet the exclusion criteria, this will be registered at the Subject Pre-Screening Log.
Baseline Visit (V1)	If the subject decides to participate and it is certain, that it is understood, what the investigation entails, the subject will be asked to sign the ICF. When the ICF is signed the subject is considered included in the investigation.

Table 4: Overview of the recruitment process

6.5. Subject withdrawal criteria

The subject can withdraw from the investigation at any time for whatever reason, without any consequences for their future treatment outside the clinical investigation. The Investigator may withdraw a subject from the investigation at any time if they judge it to be the subject's interest.

If dropouts are more than 17 subjects, which entails less than 50 completers, subjects shall be replaced by new subjects.

The investigator must withdraw a subject from the investigation due to:

- Noncompliance with the CIP impacting the scientific integrity of the investigation.
- If subject's safety and wellbeing is compromised by further participation.

- Subjects lost to follow-up. At least three documented attempts will be made to verify subjects lost to follow-up.

Subjects who are prescribed steroid creme for the sacral area, while participating in the investigation, must be with-drawn.

Withdrawn subjects will not be replaced by new subjects. A subject who is withdrawn from the investigation, for any reason, will be encouraged to contact the investigator if problem arises, that the subject believes are related to the clinical investigation. Subject who has not experienced any adverse events, will not be followed up. For subjects who experience adverse events see section 18.1.

6.6. Point off enrolment

A subject is considered enrolled in the investigation when the written Informed Consent is obtained. The expected duration for each subject is described in 5.1.

6.7. Subject Identification and Confidentiality

Subjects will be identified on the electronic CRF (e-CRF) and any other document transmitted to the sponsor by the Principal Investigator or clinical site staff, by a unique identification/subject number only.

7. Procedures

7.1. Clinical investigation-related procedures

Screening Visit (V0), Day 0:

- Introduction to the investigation and review of Subject information Form
- Check of in- and exclusion criteria
- Informed Consent Form – ICF signed at Visit 0. If subject wishes to have time for consideration, it is possible and the ICF is signed at Visit 1 the following day
- Inclusion in investigation and allocation of subject number after ICF is signed

Baseline Visit (V1), Day 1:

- Introduction to the investigation and review of Subject information Form
- ICF signed (if not signed at Visit 0)
- Confirmation of inclusion and exclusion criteria if more than 24 hours has passed since Visit 0
- Collect baseline information:
  - Gender (male/female)
  - Age (at time of enrollment (years)
  - Height (cm)
  - Weight (kg)
  - Urinary incontinence (Y/N)
  - Faecal incontinence (Y/N)
  - Date and main reason for admission (e.g., diabetes mellitus, cardiovascular disease, renal disease, pulmonary disease, anaemia, trauma, other)
  - Skin inspection
  - Braden Scale Score
- Apply Biatain Silicone Bandage on the sacral area

Baseline 2-7, skin inspection, Day 2-7:

- **Partial lift of test product and skin inspection for signs of non-blanchable erythema over bony prominence/sacral pressure injury over bony prominence**

- Re-application of the test product
- Has there been a test product change (Y/N)?
  - if yes, please register what the cause of the change was (dressing soilage, weakened border, damp/saturated dressing, bulky foam, other)

Termination Visit 8, Day 8 or at the day of discharge/earlier termination date:

- Have signs of non-blanchable erythema over bony prominence/sacral pressure injury over bony prominence developed (Y/N)?
  - If yes, please specify stage of pressure injury *(Appendix 3)*
- Was there any non-compliance to the local pressure injury prevention guideline (Y/N)?
  - If yes, explain non-compliance
  - if yes, please include a summary in the comment page

7.2. Schedule of assessments

ASSESSMENT	PERFORMED BY	SCREENING / V0 DAY 0	BASELINE / V1 DAY 1	VISIT 2-7 DAY 2 TO 7	VISIT 8 / TERMINATION DAY 8
Review of Subject Information and Consent Form	**Investigator**	X			
Sign Informed Consent	Investigator	X			
Check of in- and exclusion criteria	Investigator	X	X		
Collect Screening Information	Investigator or delegate	X			
Collect Baseline Information	Investigator or delegate		X		
Partial lift of test product and skin inspection of sacral skin	Investigator or delegate			X	X
Application of Biatain® Silicone Sacral	Investigator or delegate		X		
Dressing inspection	Investigator or delegate			X	
Removal of Biatain® Silicone Sacral	Investigator or delegate				X
Review of AEs/ADEs/SAEs/SADEs	Investigator or delegate		X	X	X
Insurance of subjects' wellbeing and compliance with CIP	Investigator or delegate		X	X	X
Termination form at discharge or V8	Investiga-tor/Subject			(X)	X
eCRF reporting	Investigator	X	X	X	X

Table 5. Visit overview. (Screening V0 and Baseline V1 can be performed the same day).

7.3. Case Report Forms

All assessments and observations throughout the investigation for each subject must be carefully recorded in an electronic CRF (eCRF) or in a paper CRF.

CRFs will be completed by the investigator and/or delegated site personal, who have signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log.

An eCRF is provided for each subject. It is the responsibility of the Investigator that all data are entered promptly and correctly.

7.4. Concomitant treatment

Concomitant medication taken from the time of consent through the investigation until termination will be registered in the eCRF in the concomitant section.
Any changes in medicine during the test period must be reported in the concomitant section in the eCRF.

Topical treatment with steroid cream in the sacral area within the past 14 days or during the investigation is an exclusion criterion.

7.5. Supplementary materials and equipment (if applicable)

The investigation product is applied on the subject by the site personnel and will not be handed out to the subject. The investigational products will be stored at the site.

Sponsor will provide the PI, or delegate with supplementary materials for this investigation. Supplementary materials would be:

- Computer with access to eCRFs

8. Risk – benefit analysis and ethical considerations

8.1. Risk-benefit analysis of the investigational device

A risk analysis according to ISO 14971 Application of risk management to medical devices has been conducted. Risks have been proven minimized or eliminated through appropriate design control, confirmed by pre-clinical bench, laboratory and clinical testing.

All unacceptable risks related to the device have been mitigated as far as possible and have been deemed acceptable for the clinical investigation. The Biatain Silicone Sacral Bandage is already CE marked.

8.2. Risk-benefit for subjects participating in the clinical investigation

The investigation is conducted in accordance with current law and applicable standards, see section 15. Statement of Compliance. The rights, safety and well-being of human subjects shall prevail over the interest of science of society.

Risks in this investigation are considered to be equal to the use of Silicone Sacral bandage products already on the market. Risks associated with the use of sacral bandage products are skin irritation and mechanical trauma. Please also see Adverse events, adverse device effects and device deficiencies section 18.

There is no known interaction between the use of the investigational device and the medication participants can take. Disadvantages of testing (trial engagement) may be the time spent on visits and responding to questions regarding baseline questions.

Possible benefits for the subjects in this investigation, are that subjects might have a lower risk of developing a pressure ulcer during hospitalization, which maybe will be beneficial for the subjects.

8.3. Risk Analysis for the conduct of the clinical investigation

A risk assessment of the clinical investigation will be conducted initially prior to the first subject enrolment and periodically re-assessed based on any new risks identified through the process. This assessment will be completed throughout the duration of the investigation, as defined by the study team. A risk-based monitoring strategy may be implemented including on-site remote, and central monitoring. Details of the strategy are defined in the monitoring plan.

8.4. Delegation of responsibility

Before initiation of the clinical investigation, sponsor must be provided with key personnel signed and dated curriculum vitae (not more than 2 years old) to verify their qualifications. Key site personnel are those, who treat or evaluate subject data in the clinical investigation. Also, the sponsor will ensure that all site personnel are trained in the investigation procedures, how to complete the CRFs, procedure for reporting an adverse

event or serious adverse event (how, when, to whom), and who to contact in case of emergency related to the investigational device.

9. Monitoring Plan

The sponsor is responsible for ensuring appropriate monitoring of the clinical investigation activities as described below.

The monitor will be the primary contact for the PI and healthcare delegates.

Monitoring activities are mandatory as per good clinical practice, however the extend and depth of these activities depend on the criticality of the clinical investigation, speed of enrolment, the experience of the Clinical investigation personnel in carrying out clinical investigations and specific investigation designs.

For the purpose of this clinical investigation the below described monitoring procedures have been determined.

9.1.1. Site selection visit

Depending on the prospective clinical investigation sites experience with the specific investigational device, an on-site qualification or site selection visit shall be performed during which, the feasibility of the clinical investigation requirements will be discussed and common agreement between sponsor and Principal Investigator shall be reached. This visit may also be replaced by one or more phone calls if the Principal Investigator is known to the sponsor.

9.1.2. Initiation visit

An initiation visit with full training on all aspects of the clinical investigation will be provided.
The initiation visit will be held as a physical meeting or remotely using Microsoft Teams, Skype or Face Time and the visit will be held as close to investigation start as possible.

9.1.3. Monitoring visit(s)

The sponsor shall determine the extent and nature of monitoring appropriate for the clinical investigation based on the risk assessment. The sponsor shall ensure, through oversight of the clinical investigation and timely adverse event reporting, that unanticipated adverse device effects are identified and investigated rapidly so that, where necessary, additional risk control measures can be implemented.

The dedicated monitor is to ensure adherence to the clinical investigation plan, the safety of the subjects, accurate data recording on the eCRFs and to monitor recruitment rates and adherence to follow-up schedules. During the clinical investigation, monitors shall check that appropriate written informed consents have been obtained. The Principal Investigator shall permit and assist the monitor to carry out verification of completed e-CRFs against data in the source documents.

The Principal Investigator can delegate tasks to his collaborators, however the roles and responsibilities as time peri-od of involvement for each clinical investigation personnel must be documented on the Site Personnel signature and Delegation list as well as training received before getting involved with the clinical investigation must be document-ed in the Clinical Investigation Training Log.

The monitor shall inform the sponsor about any problems relating to facilities, technical equipment, or medical staff involved in the clinical investigation. The monitor shall also be responsible for notifying such deficiencies in writing to the Principal Investigator and convene with the clinical investigation personnel appropriate and timely corrective actions.

The sponsor, or delegate, will provide clinical monitoring, including review of eCRF with verification to the source documentation, as defined in the monitoring plan.

The monitor shall make written reports to the sponsor, including documentation of any deviations after each visit and provide written follow up action items if any, to the Principal Investigator and/or clinical investigation personnel.

Source data verification will be performed to the extent it is possible. The Source Data Specification Form must be completed at the initiation visit detailing the location of the source data for each data point. Where no source data (besides the eCRF) is available the contents of the eCRF will be monitored.

The informed Consent Form and AE/ADE/DD will be 100% monitored for timely completeness.

Only the sponsor representatives will have access to all the eCRF´s.

9.2. Source data verification

Source data is all information in original records, certified copies of original records of clinical findings, observations, or other activities in the clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation. This includes source data initially recorded in an electronic format.

All documents and data related to the clinical investigation handled by site personnel, shall be produced and maintained in a way that assures reliability, integrity, control and traceability, and shall be appropriately stored to provide a complete history.

The Principal Investigator shall assure the accuracy, attribution, completeness, legibility and timeliness of the data reported to the sponsor in the eCRFs and in all required reports. All printed copies of electronic source documents shall be certified, as indicated by a dated signature by the investigational site personnel at the time the document is printed. Special requirements should be applied to the capture, review and retention of electronic source data, to ensure reliability, quality, integrity and traceability.

The data reported in the eCRFs shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. The eCRF can serve as the source document and this must be documented on the Source Data Specification Form. The Source Data Specification Form must be completed at the initiation visit detailing the location of the source data for each data point agreed upon by the Principal Investigator.

10. Statistical considerations

10.1. Statistical design, method and analytical procedures

Definition of analysis populations

Safety populations and Intention to Treat (ITT) will be defined at a formal data review meeting before database lock. As a minimum, the data manager, the clinical manager and the statistician will be involved in the classification of subjects.

The safety population will be constituted by all subjects with valid informed consent. The ITT population (full analysis set) will be constituted by all subjects with valid informed consent, who have been exposed to the Test Product, with information on at least one endpoint.

The summary of the primary and secondary endpoints will be based upon the safety population, whereas the statistical analysis of the exploratory endpoint will be based on the ITT population. Invalid individual data points may be omitted from analysis even though the corresponding subject is part of the ITT population. Any exclusion of data points will be documented.

A formal per protocol (PP) population is not planned due to the explorative nature of the investigation. Considering the data obtained it might be considered to make additional explorative analyses based on a subset of the ITT population.

Analysis of the endpoints and baseline data.

The endpoints as well as baseline assessments will be listed and summarized by descriptive statistics. The summaries will be made for relevant visits (baseline or V1-V8), separately.

Summary statistics for continuous variables are presented with N, Mean, SD (standard deviation), Median, Min and Max, where N denotes the number of subjects contributing with non-missing data. For discrete variables, summary statistics are presented with N and percentage, where percentage is based on the total number of subjects/observations with non-missing data.

The incidence rate (proportion) of hospital-acquired pressure injuries in hospital-admitted patients will be estimated based on the exploratory endpoint (pressure injuries: Yes/No). The proportion of completed subjects answering "Yes" will be calculated. By use of an exact test in the Binomial distribution a 95% confidence interval will be estimated for the proportion.

All statistical analysis will be performed with SAS (version 9.4/Enterprise Guide version 7.1).

10.2. Sample size

A sample size of 67 subjects will be enrolled with a minimum of 50 completers. This number is assessed to be sufficient to evaluate safety of the product.

The exploratory purpose of the investigation is to estimate the proportion of hospital-acquired pressure injuries in hospital-admitted patients with a 95% confidence interval. The confidence interval is then to be compared with the confidence interval of the results found by Mölnlycke. In the Mölnlycke investigation, the incidence in the control group was estimated to 5.3% [2.3%; 10.1%][3]. 50 completing subjects will give a power of more than 80% to show an upper 95% confidence limit of 7.2% or less. This calculation assumes, that the true incidence rate for Biatain Silicone Sacral is 1.2% as we expect it to be as good as the intervention group in the Mölnlycke investigation[3]. It is further assumed that the confidence interval will be estimated as an exact confidence interval for binomial proportions. The precision of the estimated rate and the chosen sample size is evaluated to be sufficient to draw comparative conclusions between the rate of hospital-acquired sacral pressure injuries found in the suggested observational investigation and rates of hospital-acquired pressure injuries reported in literature.

To account for an estimated drop-out rate of 30%, 67 subjects must be enrolled to assure, that 50 subjects will complete the investigation.

10.3. Level of significance and power

A two-sided significance level of 5% will be applied. For a description of the power see section 10.2 above.

10.4. Pass/fail criteria

There will be no formal success criteria for safety in this PMCF investigation.

The estimate rate (proportion) of hospital-acquired pressure injuries in hospital-admitted patients with a 95% confidence interval must be comparable to the confidence proportion and interval of the results found by Mölnlycke (5.3% [2.3%; 10.1%])[3].

10.5. Interim analysis

There will be no interim analysis and therefore no reason to terminate the investigation based on statistical considerations.

10.6. Statistical reason for termination of investigation

Any deviations from the statistical plan will be documented in the clinical investigation report - CIR.

11. Data management

11.1. Data collection and data management

11.1.1. Data Collection in the clinical investigation

Data management and the final statistical analyses of all measurements described in this protocol are carried out by the Medical Affairs, Coloplast A/S.

Data will be collected through an electronic data capturing (EDC) system on electronic Case Report Form (eCRF), internet-based case report form. This system will be used to record all subject information collected in the investigation for secure data tracking and centralised data monitoring ("remote monitoring") done by monitors, as defined in the monitoring plan.

The EDC Rave system is used. The system is designed to be compliant with the FDA requirements of 21 CFR part 11. It is a validated data management system. The system has full audit trail and electronic signature. The data management system has restricted role-based access control allowing only qualified and trained personnel to enter the system.

The Principal Investigator or delegate will enter data in a part of the system referred to as the eCRF.

The sponsor will be responsible for training the investigator or delegate, in completion of the eCRF.

Principal Investigator, or delegate will perform primary data collection directly into the eCRF or drawn from source-document (medical records) reviews. The eCRF will be completed on a continuous basis starting from the point of enrolling the subject to final follow up.

The eCRF will be completed by the investigator, or delegate, who have signed the Site Personnel Signature and Delegation List and Clinical Investigation Training Log. It will be the responsibility of the Principal Investigator to ensure that all measurements and observations are correctly noted in the eCRF.

All assessments and observations throughout the investigation for each subject must be carefully recorded in an eCRF during the visit or immediately after. The eCRF makes it possible to enter data right away when they are obtained. This is the preferred way of collecting data.

In the unforeseen situation, where clinical investigation personnel cannot establish connection to the EDC system a paper CRF (pCRF) has been printed and supplied by sponsor. As soon as connection to the eCRF is established data should be entered.

Adverse events should be registered following the timelines described in the Adverse Event section.

The investigator will keep a separate list of the subjects' ID numbers, names, and addresses in a locked room/cabinet. Only data referred to in this clinical investigation plan will be recorded in the CRFs.

11.1.2. Database Management, Queries and Quality Control

The data management system has restricted role-based access control. The Principal Investigator or delegate must be trained in the system prior to getting access. The training is web-based and must be completed before access to the investigation is granted. Training will be documented in the data management system. Only the Principal Investigator, or delegate, will be authorised to enter data in the eCRF.

The monitor, using his/her personal login information shall verify all critical data points against the source documents and issue electronic queries for the authorised clinical site personnel to respond, as defined in the monitoring plan.
The Principal Investigator, using his/her personal login information shall sign each eCRF.
Automated, real time access to the data enable control on investigation compliance and safety assessments.

A critical quality control will be performed by the sponsor's data management team and queries issued where needed. Such queries will be reviewed by the monitor and must be resolved by the site personnel.

At the end of the investigation a formal data review meeting will be performed before the database will be locked.

A full audit trail ensures, that each user's (site personnel, monitor, sponsor, data manager) access to and actions in the system is tracked.

The Data Management Procedures are further described in the Data Management SOPs.

11.2. Remote monitoring

Remote (source data verification) and/or centralized (data review) monitoring is carried out by sponsor personnel or representatives (e.g., data management personnel, statisticians, or clinical monitors) at a location other than the site(s) at which the clinical investigation is being conducted (evaluation without visiting the investigation site). Remote monitoring processes can provide many of the capabilities of on-site monitoring as well as additional capabilities.

In addition to onsite monitoring visits, remote monitoring of the data entered in the e-CRF system could be used to achieve the following:

- Conduct activities such as: standard checks of range, consistency, and completeness of data and checks for unusual distribution of data, such as too little variance)
- Special attention will be given in case of frequent data anomalies or errors, protocol deviations or excessive dropouts.
- Augment on-site monitoring by performing monitoring activities that can only be accomplished using centralized processes (e.g., statistical analyses to identify data trends not easily detected by on-site monitoring)
- Monitor data quality through routine review of submitted data in real-time to identify missing data, inconsistent data, data outliers, and potential protocol deviations that may be indicative of systemic and/or significant errors in data collection and reporting at the site
- Verify source data remotely, provided that both source data and CRFs can be accessed remotely
- Conduct aggregate statistical analyses of investigational data to identify subject data that are outliers relative to others and to evaluate individual subject data for plausibility and completeness
- Conduct analyses of site characteristics, performance metrics (e.g., high screen failure rates, high frequency of eligibility deviations, and delays in reporting data), and clinical data to identify early on corrective actions needed for characteristics correlated with poor performance or noncompliance

11.3. Data retention

The Investigator file must be archived for a minimum period of 10 years after the final clinical investigation report has been signed.

12. Amendments to the Clinical Investigation Plan

No changes in the clinical investigation procedures shall be affected without mutual agreement between the Principal Investigator and the sponsor. The agreement of the changes must be documented by signing the corresponding clinical investigation plan amendments and registered in the Change Log.

All significant changes require notification to the EC. Substantial changes may require approval from the EC prior to implementation. (Example of significant change: Changes of inclusion criteria, end points or assessment methods)

13. Deviations from the Clinical Investigation Plan

Deviations to the Clinical Investigation Plan occurs when the activities during the clinical investigation do not comply with the EC approved investigation plan.

A minor deviation is defined as those that don't increase risk or decrease benefit or don't have a significant effect on the subject's rights, safety, or welfare; and/or on the integrity of the data. If a deviation increases risk or decreases benefit and/or; has a significant effect on the subject's rights, safety, or welfare and/or has a significant effect on the integrity of the data it is defined as a major deviation and the Investigator must inform the monitor immediately, and the Monitor will report and inform the Clinical Manager or designee immediately.

The investigator is not allowed to deviate from the Clinical Investigation Plan unless, under emergency circumstances or to protect the rights, safety, and welfare of the subject(s).

For the purposes of this investigation, any variance from the protocol is considered a deviation and is to be reported.

The Clinical investigation personnel will complete a deviation eCRF form for all data-related deviations and all deviations that are **not** related to the data (for example, an untrained nurse performing investigation procedures) are reported by the monitor in the Site Report – Periodic Monitoring and actions are addressed to the Investigator for completion.

If any deviations to the investigation plan are detected during the monitoring visit, the Monitor shall ensure the site reports all deviations in the eCRF or on the Deviation log in the Investigator File. Additionally, the monitor must report any deviation noted during the visit in the Periodic Monitoring Report.

Monitor will align with data management in each investigation, how data management will be informed about all deviations.

The following information about the deviation will be collected:

- Date the deviation took place.
- State what the deviation is related to.
- Does the deviation affect data integrity?
- Does the deviation affect the subject's safety?
- Clear and concise description of the event.
- Corrective action taken.

14. Device Accountability

All access to the investigational devices used in the clinical investigation is controlled by storage procedures and device accountability logs as described below. The investigational devices must only be used in this clinical investigation and only according to the CIP.

Sponsor keeps a device accountability log that states the physical location of all investigational devices.

The PI or an authorized designee keeps records documenting the receipt, use and return and disposal of the investigational devices, which includes:

- Date of receipt.
- Identification of each investigational device (batch no./serial no./unique code).
- The expire date, if applicable.
- The date(s) of use.

- Subject identification.
- The date on which the investigational device was returned/explanted from the subject, if applicable.
- The date of return unused, expired or malfunctioning investigational devices, if applicable.

15. Statement of compliance

The clinical investigation is conducted in accordance with:

- Ethical principles that have their origin in the Declaration of Helsinki, 1964, Last amended at the 59th WMA General Assembly, Brazil, October 2013.
- MDD 93/42/EEC as amended by Directive 2007/47/EC (commonly known as the Medical Device Directive).
- MDR (EU) 2017/745.
- ISO 14155:2020 "Clinical Investigation of medical devices for human subjects – Good clinical practices".
- Any applicable regional or national regulations will be specified in the country specific CIP.

15.1. Ethics committee and regulatory authorities

The Clinical investigation plan and/or other relevant documents are submitted to the appropriate EC. This clinical investigation will not begin until the required approval from the EC have been obtained. Any amendment to the pro-tocol will be submitted to the same EC.

Sponsor will notify the relevant regulatory authority and EC concerned of the end of the clinical investigation.

15.2. Other relevant authorities

E.g. Data Protection Agency: Clinical Regulatory Department in Coloplast A/S has obtained a general approval from the Danish Data Protection Agency to handle data collected in a clinical investigation.

15.3. Data protection

As part of the investigation Coloplast A/S, Holtedam 1, 3050 Humlebaek, Denmark ("Coloplast") will collect and process the personal information the subject provides for the investigation ("subject personal data"). This includes identification and contact information (which may be anonymised depending on the nature of the investigation) as well as information about product usage experience and your health. Coloplast will comply with the EU General Data Protection Regulation (GDPR) and the Danish act on data protection ("databeskyttelsesloven"), including in connection with transfer of data to third countries, cf. chapter V of GDPR, Coloplast will only process the subjects' personal data:

1. To conduct the investigation and carry out related research based on subject consent (primary use), cf. articles 6(1)(a) and 9(2)(a) of GDPR,
2. To comply with applicable legal obligations to e.g. ensure reliability and safety, cf. article 6(1)(c) in conjunction with article 9(1)(i) of GDPR, and
3. If separate consent is given for secondary use of subject personal data, cf. articles 6(1)(a) and 9(2)(a) of GDPR – carry out research outside the clinical protocol to improve Coloplast's products and services, and for use in education.

Part of Coloplast's processing is carried out on third-party platforms (clinical trial databases) and certain third parties are assisting Coloplast in the processing (e.g. the investigator). Such cases will imply a transfer of your personal data to the third parties, but solely for the specified purposes and with the third parties acting on instruction from Coloplast. Data may be collected and processed across the Coloplast network, which may entail processing of personal data outside the European Economic Area. In such cases, an adequate level of protection will be ensured by the third parties being subject to the standard contractual clauses on data protection adopted by the EU or to an EU-approved certification mechanism on data protection. For further information about this please the subject can always consult Coloplast's data protection officer (details below).

Subject personal data will be kept as long as required under applicable laws and regulations. The EU Medical Device Regulation obligates Coloplast to keep the data for a period of at least ten years after the investigation is completed, or, in the event that the device is subsequently placed on the market, at least ten years after the last device has been placed on the market. Subject personal data will be deleted at the end of the mandatory retention period.

If the subject has questions or queries regarding Coloplast's handling of personal information, the subject can always contact Coloplast's Data Protection Officer at dataprotectionoffice@coloplast.com. Complaints related to Coloplast's handling of subject personal information may similarly be sent to the Data Protection Officer, and the subject is also entitled to file a complaint with the relevant supervisory authority, which in the case of Denmark is the Danish Data Protection Agency (www.datatilsynet.dk).

The subject can write to privacyrequests@coloplast.com at any time to request:

- Access to personal data
- Correction of errors in personal data or to erase personal data
- Limit what can be done with personal data
- To receive personal data in machine-readable format (data portability).
- Withdrawal of consents the subject has given Coloplast to process personal data

15.4. Indemnity

All subjects are fully covered by Coloplast A/S insurance throughout the investigation.

15.5. Financial conditions

Coloplast A/S will compensate the Principal investigator involved in the clinical investigation for his time and resources spent on the investigation. All financial agreements with the Principal investigator involved in the clinical investigation will be specified in the sponsor investigator agreement.

The expenses include the salary to the Principal Investigator, the cost of external clinical support, investigation supplies, eCRF, Investigator and site personnel training.

The Principal Investigator and site personnel have no financial interests in the investigation.

The total budget for the investigation is covering 67 participants. The expenses are paid on an ongoing basis.

16. Informed consent process

Written informed consent is obtained from all subjects participating in the investigation after thorough written and verbal information. The information is given by the investigator or his/her representative in the subjects' native non-technical language. Each subject will be fully informed about the aim of the investigation, procedures, potential risks, or inconveniences and/or expected benefits, all anticipated adverse device effects and then have a minimum of 24h before deciding on participation. The subjects will be informed, that their participation is voluntary and that they may leave the investigation at any time, without this having any influence on their further treatment.

The informed consent signature form includes personally dated signatures of the subject and the PI or his/her representative responsible for conducting the informed consent process. A copy will be provided to the subject.

If new information is to be given during the investigation, sponsor will inform the investigators, and the new information is given to the subjects by the investigator. If new information becomes available that can significantly affect a subject's future health and medical care that information will be provided to the subject in written form. CM is re-sponsible for writing the information and providing the approved Subject Information and

Consent Form to investigators that will further provide it to the subjects. If applicable, all affected subjects shall be asked to confirm their continuing informed consent in writing.

17. Subject compensation

17.1. Compensation in case of injury

Product liability and No-Fault Clinical Investigation Insurance covering the duration of the clinical investigation are in place, to enable compensation in the event of an injury to a participating subject, see section 15.4.

17.2. Compensation for participating in the clinical investigation

Subjects will not be financially compensated for their time but may benefit from prevention of a sacral pressure ulcer.

18. Adverse events, adverse device effects and device deficiencies

18.1. Adverse events

An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, whether or not related to the investigational medical device(s) or the comparator(s), or the procedures involved. The adverse event shall be marked with the intensity mild, moderate or severe. This could include events such as headache or dizziness.

18.2. Adverse device effect

An adverse event, which is related to the use of the investigational medical device, is an adverse device effect, and should be marked as unlikely related, possible related, probable related or with causal relationship on the adverse event form.

The definition of an adverse device effect includes any event resulting from insufficiencies or inadequacies in the instruction for use, deployment, implantation, installation and operation, or any malfunction of the medical device, as well as any event resulting from use error or from intentional misuse of the device.

Table 6 lists anticipated adverse device effects that may occur, based on the IFU and their likely incidence rates based on adverse events reported in clinical studies[4].

Table 6

ANTICIPATED ADE	INCIDENCE RATES
Local pressure injury/Erythema*	1-10%
Skin irritation/inflammation/itching	0.1 %-1%
Maceration and/or local fungus infection of the skin	0.01-0.1%
Pain	0.01-0.1%
Blistering	0.01-0.1%
Allergic skin reaction	Not known

** Temporary redness/erythema upon removal of the sacral bandage is not considered an adverse device effect, however an abnormal development in intensity or duration should be considered as such.*

18.3. Device deficiency

A device deficiency is the inadequacy of the investigational medical device or comparator with respect to its identity, quality, durability, reliability, usability, safety or performance. This includes malfunctions, use errors

Only in cases, where rolling edges are observed more than normal, it should be registered as a device deficiency.

18.4. Serious adverse events (SAE)
A serious adverse event is an adverse event that:

- Led to death,
- Led to a serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:

1) a life-threatening illness or injury, or
2) a permanent impairment of a body structure or a body function including chronic diseases, or
3) in-patient or prolonged hospitalization, or
4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.

- Led to foetal distress, foetal death, a congenital abnormality or birth defect including physical or mental impairment.

This includes device deficiencies that might have led to a serious adverse event if:

1) Suitable action had not been taken, or
2) Intervention had not been made, or
3) Circumstances had been less fortunate.

These are handled under the serious adverse event reporting.

Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

18.4.1. Serious adverse device effect (SADE)
A serious adverse device effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

18.4.2. Anticipated serious adverse device effect (ASADE)
Anticipated serious adverse device effect is any effect that by its nature, incidence, severity or outcome has been previously identified in the risk analysis report.

18.4.3. Unanticipated serious adverse device effect (USADE)
An unanticipated serious adverse device effect is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

18.5. Medical care of subjects
Principal Investigator shall ensure that adequate medical care is provided, during and after participation in the clinical investigation, to a subject experiencing an adverse event. All ongoing ADEs, SAEs, SADEs and DDs, that could have led to a SAE at subject termination, will be followed according to the Risk Benefit analysis (see 8.2) An ongoing adverse event at subject termination visit is documented as the current status for the adverse event and will not be followed up.

The subjects shall be informed of any new significant findings occurring during the clinical investigation, including the need for additional medical care that can be required, and of the nature and possible cause of any adverse events experienced

Principal Investigator shall provide the subject with the necessary instructions on proper use, handling storage and return of the investigational device and comparator, when it is used or operated by the subject.

18.6. Reporting and timelines

18.7. Investigator's reporting responsibilities
- PI at each site must assess all (S)AE`s that occur at his/her site.

- All serious adverse events and serious adverse device effects must be reported to sponsor within 24 hours of the site becoming aware of the event.
- A device deficiency that could have led to a serious adverse event but did not because suitable action was taken, intervention had been made or because of fortunate circumstances should be reported to sponsor within 24 hours of the site becoming aware of the event.
- New findings and/or updates in relation to already reported serious events should also be reported to sponsor within 24 hours of the site becoming aware of the event.
- Device deficiencies and all adverse device effects related to CE marked Coloplast investigational product and/or comparator must be reported to sponsor within 24 hours of becoming aware of the event.

When reporting the SAE, the relationship to the test material shall be described whether the event is considered

- **Not related**, the event has no temporal relationship with the use of the test material or the procedures.
- **Unlikely related,** the relationship with the use of the test material seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- **Possible related,** the relationship with the use of the test material is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
- **Probable related,** the relationship with the use of the test material seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
- **Definitely related/Causal relationship,** the event has a temporal relationship with the test material use/application or procedures.

and the intensity of the event should be considered, as such:

- **Mild,** the intensity of the event is mild with no further action or intervention
- **Moderate,** the intensity of the event will lead to an action or intervention to solve the event
- **Severe,** the intensity of the event will lead to follow up on the action or intervention, as the effect of the action or intervention may not decrease the symptoms.

All above events must be reported by use of the relevant adverse event/serious adverse event/device deficiency form.

Please report to:
Coloplast A/S
Holtedam 1-3
3050 Humlebæk
Denmark

clinical-studies@coloplast.com and *dkckal@coloplast.com*

18.8. Sponsors reporting responsibilities

It is the responsibility of sponsor to ensure that the following are reported to national regulatory authorities immediately, but no later than 7 calendar days following the date of awareness by sponsor.

- All serious adverse events.
- All serious device effects.
- All device deficiencies that could have led to serious adverse events but did not because suitable action was taken, intervention had been made or because of fortunate circumstances.
- New findings and/or updates in relation to already reported events.

If the serious adverse event results in imminent risk of death, serious injury, or serious illness that requires prompt remedial action for other subjects, users or other persons or a new finding to such a serious adverse event, sponsor must immediately but no later than 2 calendar days after awareness by sponsor report the event to national regulatory authorities.

It is the responsibility of sponsor to inform all investigators in writing within 10 working days if device deficiencies, adverse events, adverse device effects, near-incidents, serious adverse events, serious adverse device effects or unanticipated serious adverse device effects lead to corrective actions (e.g. change of IFU).

19. Suspension or premature termination of the clinical investigation

Sponsor may suspend or prematurely terminate the entire clinical investigation for documented significant reasons.

If a suspicion of an unacceptable risk to subjects develops during the clinical investigation, sponsor will suspend the investigation while the risk is assessed. Sponsor will terminate the investigation if an unacceptable risk is confirmed. Sponsor will ensure that the premature termination will be justified in writing and will promptly inform the regulatory authorities and relevant EC(s). If monitoring or auditing of the clinical investigation identifies serious or repeated deviations, sponsor will suspend or terminate the conduct of the investigation. The sponsor or investigator will inform the regulatory authority as appropriate and notify the EC about the termination

If suspension or termination of the clinical investigation occurs, the investigator(s) will promptly inform the enrolled subjects. Sponsor will provide resources to fulfil the obligations from the CIP for follow-up on the subjects, as necessary.

20. Clinical Investigation Report

At completion of the investigation sponsor is responsible for writing the clinical investigation report. The report is retained on file. The report contains a critical evaluation of all data, which have been collected during the investigation. The report describes the methodology and design and a data analysis, including statistical preparation and conclusion.

Sponsor and Principal investigator must sign the final version of the clinical investigation report or an affidavit, indicating their agreement with the contents. If no coordinating investigator is appointed, then the signatures of the Principal Investigator(s) should be obtained.

The clinical investigation report must be submitted to EC.

21. Publication Policy

Publication policy is specified in Sponsor Investigator Agreement.

21.1. General

The investigation will be registered on a public accessible database, e.g. www.ClinicalTrial.gov, before recruitment of the first subject. The results of the investigation, positive as well as negative, may be communicated by abstracts, posters, or oral presentations provided that opportunity is given for sponsor to discuss the contents and any conclusions drawn, before the abstract, paper or visual presentations are finalised. In all cases the subject's identity will re-main confidential.

Sponsor will undertake to comment on the draft documents within 30 working days of receipt, but the final decision on the contents and format of the publication from the conclusions drawn, will remain with the authors.

No preliminary results will be published.

Data from the investigation is considered confidential until it is published according to the conditions of this CIP.

Sponsor may publish single subject case stories at any time during and after the investigation.

Sponsor reserves the right to use the data (published and unpublished) for reimbursement or regulatory purposes.

22. Suspension/termination of the clinical investigation

Sponsor will withdraw from sponsorship of the clinical investigation if:

- major non-adherence to the clinical investigation plan is occurring
- it is anticipated that the subject recruitment will not be adequate to meet the investigation objectives at least 75% of the subjects should be entered within the recruitment time.

In case sponsor withdraws, sponsorship for the subjects already recruited into the clinical investigation will continue. Suspension/termination of the clinical investigation

Sponsor will withdraw from sponsorship of the clinical investigation if

- major non-adherence to the clinical investigation plan is occurring
- it is anticipated that the subject recruitment will not be adequate to meet the investigation objectives at least 75% of the subjects should be entered within the recruitment time.

In case sponsor withdraws, sponsorship for the subjects already recruited into the clinical investigation will continue.

23. Bibliography

1. Moore ZE, Webster J. Dressings and topical agents for preventing pressure ulcers. Cochrane Database Syst Rev. 2013(8):Cd009362.

2. European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel and Pan Pacific Pressure Injury Alliance. Prevention and Treatment Pressure Ulcers/Injuries: Clinical Practice Guideline. The international guideline. Emily Haesler (Ed.). EPUPA/NPIAP/PPPIA 2019.

3. A randomised controlled trial of the effectiveness of soft silicone multi-layered foam dressings in the prevention of sacral and heel pressure ulcers in trauma and critically ill patients: The Border Trial. 2013. International Wound Journal. 12101. p. 302-308.

4. Clinical Evaluation Report: Biatain Silicone against pressure injuries. Vers. 8.0. March 2022.

24. Appendix 1: Instruction for Use

Biatain Silicone

Coloplast

Biatain Silicone Sacral
Silicone foam dressing

CE 0543

Coloplast A/S
Holtedam 1
3050 Humlebæk
Denmark

Instructions for use
IFU Master Biatain Silicone Sacral - PIP Version 6

Intended purpose
The product is intended for moist wound healing and exudate management

Indications
Biatain Silicone
- is indicated for a wide range of low- to highly exuding wounds. This includes acute wounds such as donor sites, post-operative wounds and traumatic wounds; and chronic wounds such as leg ulcers, pressure ulcers and non-infected diabetic foot ulcers
- the product can be used as part of a prophylactic therapy to help prevent skin damage, e.g. pressure injuries, postoperative blistering

Contra-indications
The Biatain Silicone Sacral 15 cm x 19 cm should not be used for patients with a body weight below 10 kg

The Biatain Silicone Sacral 25 cm x 25 cm should not be used for patients with a body weight below 15 kg

Warnings
Re-use of the single use product may create a potential harm to the user. Reprocessing, washing, disinfection and/or sterilisation may compromise product characteristics, causing additional risk of physical harm or infection to the user

Cautions
A health care professional should frequently inspect and manage infected wounds, diabetic wounds and wounds which are solely or partially caused by arterial insufficiency, in accordance with local guidelines

Do not use the product with oxidising solutions e.g. hypochlorite and hydrogen peroxide solutions, as this may cause product degradation. Ensure that any other evaporating solution is completely dried off before applying the product

The use of dressings as part of prophylactic therapy does not preclude the need to continue to develop and follow a comprehensive pressure ulcer prevention protocol, i.e. support surfaces, positioning, nutrition, hydration, skin care, mobility and regular controls

Do not cut the foam part of the product.

Do not use if package is damaged as sterility of the dressing may be compromised

Keep away from sunlight

Information
The product is a sterile, single use polyurethane foam dressing with a silicone adhesive

Biatain Silicone
- may be left in place for up to 7 days depending on the amount of exudate, dressing conditions and type of wound
- may be used together with Purilon Gel for autolytic debridement of necrotic tissue
- may be used on patients who are in treatment for a local or systemic infection at the discretion of a health care professional
- is suitable for use in combination with compression therapy

The product consists of
- a vapour permeable top film which is bacteria- and waterproof
- a lock away layer
- an absorbent polyurethane foam
- a perforated silicone adhesive
- turquoise protective films

If you experience a suspected allergic reaction or any other side effects, please contact your health care professional

Sterilised using ethylene oxide (EO)

Coloplast accepts no liability for any injury or loss that may arise if this product is used in a manner contrary to Coloplast's current recommendations

How to use

Preparation
Cleanse the wound and perwound skin in accordance with local guidelines, e.g. lukewarm water or physiological saline solution

Gently dry the perwound skin

If any film, cream, ointment or similar product is used, allow the perwound skin to dry before applying the product

Application
Select a product where the foam overlaps the wound edge by approximately 1-2 centimetres.

Use the protective films to avoid touching the adhesive side and to ensure aseptic application

Remove the center protective film

Apply the adhesive side towards the wound

Remove the remaining protective films, one at a time

Gently run your fingers around the edge of the product to ensure an even and smooth fit to the skin

Removal
The product should be changed when clinically indicated, when visible signs of exudate approach the edge of the foam or after 7 days.

Loosen the adhesive border before gently lifting the product away from the wound and removing the product.

For prophylactic therapy Biatain Silicone Sacral and Multishape may be left in place up to 7 days depending on the condition of the skin or as indicated by accepted clinical practice.

Disposal
The product is intended for single use only and should be disposed of in accordance with local guidelines, e.g. with normal household waste.

Do not flush the product down the toilet.

Reporting of incidents
If, during the use of this device or as a result of its use, a serious incident has occurred, please report it to the manufacturer and to your national authority.

Explanation of symbols


Do not use if package is damaged


Not made with natural rubber latex

Medical Device


Consult instructions for use

Sterilised using ethylene oxide


Keep away from sunlight

25. Appendix 2: Braden Scale Score

BRADEN SCALE – For Predicting Pressure Sore Risk

SEVERE RISK: Total score ≤ 9 **HIGH RISK**: Total score 10-12
MODERATE RISK: Total score 13-14 **MILD RISK**: Total score 15-18

RISK FACTOR	SCORE/DESCRIPTION				DATE OF ASSESS ➡ 1	2	3	4
SENSORY PERCEPTION Ability to respond meaningfully to pressure-related discomfort	**1. COMPLETELY LIMITED** – Unresponsive (does not moan, flinch, or grasp) to painful stimuli, due to diminished level of consciousness or sedation. OR limited ability to feel pain over most of body surface.	**2. VERY LIMITED** – Responds only to painful stimuli. Cannot communicate discomfort except by moaning or restlessness. OR has a sensory impairment which limits the ability to feel pain or discomfort over ½ of body.	**3. SLIGHTLY LIMITED** – Responds to verbal commands but cannot always communicate discomfort or need to be turned. OR has some sensory impairment which limits ability to feel pain or discomfort in 1 or 2 extremities.	**4. NO IMPAIRMENT** – Responds to verbal commands. Has no sensory deficit which would limit ability to feel or voice pain or discomfort.				
MOISTURE Degree to which skin is exposed to moisture	**1. CONSTANTLY MOIST**– Skin is kept moist almost constantly by perspiration, urine, etc. Dampness is detected every time patient is moved or turned.	**2. OFTEN MOIST** – Skin is often but not always moist. Linen must be changed at least once a shift.	**3. OCCASIONALLY MOIST** – Skin is occasionally moist, requiring an extra linen change approximately once a day.	**4. RARELY MOIST** – Skin is usually dry; linen only requires changing at routine intervals.				
ACTIVITY Degree of physical activity	**1. BEDFAST** – Confined to bed.	**2. CHAIRFAST** – Ability to walk severely limited or nonexistent. Cannot bear own weight and/or must be assisted into chair or wheelchair.	**3. WALKS OCCASIONALLY** – Walks occasionally during day, but for very short distances, with or without assistance. Spends majority of each shift in bed or chair.	**4. WALKS FREQUENTLY**– Walks outside the room at least twice a day and inside room at least once every 2 hours during waking hours.				
MOBILITY Ability to change and control body position	**1. COMPLETELY IMMOBILE** – Does not make even slight changes in body or extremity position without assistance.	**2. VERY LIMITED** – Makes occasional slight changes in body or extremity position but unable to make frequent or significant changes independently.	**3. SLIGHTLY LIMITED** – Makes frequent though slight changes in body or extremity position independently.	**4. NO LIMITATIONS** – Makes major and frequent changes in position without assistance.				
NUTRITION Usual food intake pattern [1]NPO: Nothing by mouth. [2]IV: Intravenously. [3]TPN: Total parenteral nutrition.	**1. VERY POOR** – Never eats a complete meal. Rarely eats more than 1/3 of any food offered. Eats 2 servings or less of protein (meat or dairy products) per day. Takes fluids poorly. Does not take a liquid dietary supplement. OR is NPO[1] and/or maintained on clear liquids or IV[2] for more than 5 days.	**2. PROBABLY INADEQUATE** – Rarely eats a complete meal and generally eats only about ½ of any food offered. Protein intake includes only 3 servings of meat or dairy products per day. Occasionally will take a dietary supplement OR receives less than optimum amount of liquid diet or tube feeding.	**3. ADEQUATE** – Eats over half of most meals. Eats a total of 4 servings of protein (meat, dairy products) each day. Occasionally refuses a meal, but will usually take a supplement if offered. OR is on a tube feeding or TPN[3] regimen, which probably meets most of nutritional needs.	**4. EXCELLENT** – Eats most of every meal. Never refuses a meal. Usually eats a total of 4 or more servings of meat and dairy products. Occasionally eats between meals. Does not require supplementation.				
FRICTION AND SHEAR	**1. PROBLEM**– Requires moderate to maximum assistance in moving. Complete lifting without sliding against sheets is impossible. Frequently slides down in bed or chair, requiring frequent repositioning with maximum assistance. Spasticity, contractures, or agitation leads to almost constant friction.	**2. POTENTIAL PROBLEM**– Moves feebly or requires minimum assistance. During a move, skin probably slides to some extent against sheets, chair, restraints, or other devices. Maintains relatively good position in chair or bed most of the time but occasionally slides down.	**3. NO APPARENT PROBLEM** – Moves in bed and in chair independently and has sufficient muscle strength to lift up completely during move. Maintains good position in bed or chair at all times.					
TOTAL SCORE	**Total score of 12 or less represents HIGH RISK**							

26. Appendix 3: International NPUAP/EPUAP Pressure Ulcer Classification System

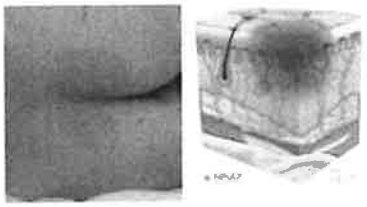
A pressure ulcer is localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear. A number of contributing or confounding factors are also associated with pressure ulcers; the significance of these factors is yet to be elucidated.

Category/Stage I: Nonblanchable Erythema

Intact skin with non-blanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its color may differ from the surrounding area.

The area may be painful, firm, soft, warmer or cooler as compared to adjacent tissue. Category/Stage I may be difficult to detect in individuals with dark skin tones. May indicate "at risk" individuals (a heralding sign of risk).

Category/Stage I Pressure Injury



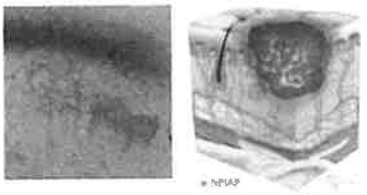
Category/Stage II: Partial Thickness Skin Loss

Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serumfilled blister.

Presents as a shiny or dry shallow ulcer without slough or bruising*. This Category/Stage should not be used to describe skin tears, tape burns, perineal dermatitis, maceration or excoriation.

**Bruising indicates suspected deep tissue injury.*

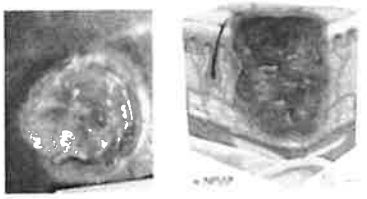
Category/Stage II Pressure Injury



Category/Stage III: Full Thickness Skin Loss

Full thickness tissue loss. Subcutaneous fat may be visible, but bone, tendon or muscle are not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining and tunneling. The depth of a Category/Stage III pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue and Category/Stage III ulcers can be shallow. In contrast, areas of significant adiposity can develop extremely deep Category/Stage III pressure ulcers. Bone/tendon is not visible or directly palpable.

Category/Stage III Pressure Injury

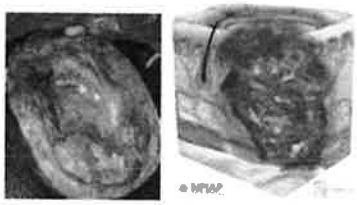


Category/Stage IV: Full Thickness Tissue Loss

Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed. Often include undermining and tunneling.

The depth of a Category/Stage IV pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue and these ulcers can be shallow. Category/Stage IV ulcers can extend into muscle and/or supporting structures (e.g., fascia, tendon or joint capsule) making osteomyelitis possible. Exposed bone/tendon is visible or directly palpable.

Category/Stage IV Pressure Injury

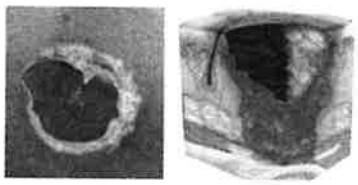


Unstageable: Depth Unknown

Full thickness tissue loss in which the base of the ulcer is covered by slough (yellow, tan, gray, green or brown) and/or eschar (tan, brown or black) in the wound bed.

Until enough slough and/or eschar is removed to expose the base of the wound, the true depth, and therefore Category/Stage, cannot be determined. Stable (dry, adherent, intact without erythema or fluctuance) eschar on the heels serves as 'the body's natural (biological) cover' and should not be removed.

Unstageable Pressure Injury
(covered in eschar or slough)



Suspected Deep Tissue Injury: Depth Unknown

Purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared to adjacent tissue.

Deep tissue injury may be difficult to detect in individuals with dark skin tones. Evolution may include a thin blister over a dark wound bed. The wound may further evolve and become covered by thin eschar. Evolution may be rapid exposing additional layers of tissue even with optimal treatment.

Suspected Deep Tissue Injury