GLOUCESTERSHIRE LEG ULCER SERVICE

Gloucestershire Hospitals NHS
NHS Foundation Trust

CLINICAL INVESTIGATION PLAN

Evaluation of the safety and effectiveness of the global treatment including multilayer compression therapy (Urgo KTwo®) in addition to an interactive dressing (UrgoStart® Plus) in the management of venous leg ulcers

PROTOCOL NUMBER: EUS23-4 **IRAS ID: 327680** **PROJECT REF NO: 23/003/GHT**

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SUMMARY

INTRODUCTION

Chronic venous insufficiency (CVI) of the lower limbs is a common condition affecting 5–30% of the adult population worldwide, with a prevalence that is consistently increasing with age (1-5).
The ultimate stage of CVI (the C6 stage) according to the CEAP classification (clinical, etiological, anatomical and pathophysiological) is represented by the venous leg ulcer (VLU), which can often take several months or even years to heal; only 30–75% of patients seem to achieve wound closure after six months of treatment, depending on the severity of the ulcer and the patients' health status (6,7).

According to guidelines, and based on systematic reviews, the management of these wounds requires a holistic approach, combining suitable local wound care with an adapted aetiological treatment based on an effective and high compression therapy applying 40 mmHg at the ankle in the acute decongestion phase of oedema and for the treatment of an active VLU (8).

Very positive clinical outcomes provided by a randomized controlled trial involving 187 patients comparing a four-layer bandage with a two-layer bandage compression system UrgoK2 (9) as well as a very large clinical evaluation including 702 patients treated under real-life conditions, have confirmed the efficacy and safety profile of this multicomponent compression system (10). Both of these clinical evaluations have supported the efficacy of this high compression therapy in healing VLUs, reducing lower limb oedema caused by CVI and improving the Quality of Life of patients. The real-life study even brought growing evidence supporting the use of this compression system, as a first-line intervention (higher healing rate when used in first intention) in the treatment of VLUs.

Venous leg ulcers are characterized by elevated and prolonged expressions of matrix metalloproteinases (MMPs) in the wound tissue and fluid which have been correlated to the impaired healing and chronicity and mixed arterial ulcers also have an impaired perfusion (11). Addressing this protease imbalance by reducing the high levels of MMPs could represent a possible therapeutic modality to improve ulcer healing (12-13).

Wound dressings including the Technology Lipido-Colloid with Nano Oligo Saccharide Factor (TLC-NOSF) are known for their protease inhibiting properties and positive impact on chronic wound healing; their efficacy and acceptability for patients and caregivers, when associated with good

standards of care, have been documented in a pooled data analysis from eight European non-interventional studies (real-life studies), including nearly 8,000 patients presenting with venous leg ulcers (14).

Additionally, clinical evidence in VLUs has been recently highlighted in the United Kingdom, by the National Institute of Health and Care Excellence (NICE), in its related evidence-base guidance (15). NICE stated that the interactive UrgoStart dressings (Technology Lipido-Colloid with Nano Oligo Saccharide Factor) improves wound healing in venous leg ulcers when used as part of overall management including compression therapy, and thus is likely to be cost-saving in addition to an improved quality-of-life. These recommendations were based on the clinical data provided through two randomized controlled trials which evaluated the impact on venous leg ulcers treated with UrgoStart dressings (16,17).

On this basis, we strongly believe that the combination of Urgo K2 and UrgoStart wound dressings could represent an optimal alternative to manage venous leg ulcers for which high compression application is needed. So, the objective of this clinical investigation is to assess the therapeutic safety and efficacy of this new “global solution” (high compression and interactive wound dressing) in such chronic wounds, when used as a first intention treatment.

1. STUDY DESIGN

This clinical investigation is an open non-comparative monocenter clinical trial conducted in England. The investigation will be conducted in the Gloucestershire Leg Ulcer Service, at Cheltenham General Hospital and Gloucestershire Royal Hospital (UK).

This clinical trial will include 60 patients; they will be outpatients, community treated, and will be followed for a maximum duration of twelve weeks.

The inclusion period will last a maximum of 12 months.

2. STUDY OUTCOMES

2.1. PRIMARY OUTCOME

The primary endpoint of this clinical investigation is to assess the efficacy of a global treatment for venous leg ulcers, comprising a combination of a multilayer high compression system, UrgoK2® in addition to an interactive dressing, named UrgoStart® Plus (Pad and Border).

The Main efficacy criteria will be complete ulcer closure (100% re-epithelialisation) after a maximum of 12 weeks treatment period.

2.2. SECONDARY OUTCOMES

The secondary criteria are to determine the following:

- Time to reach complete wound closure,
- Relative (and absolute) wound surface area reduction ($area_{t0}$-$area_{tlast}$),
- Percentage of patients with a ≥30% wound area reduction [($area_{t0}$-$area_{tlast}$)/$area_{t0}$ x100] at Week 4 (18,19).
- Evolution of the ankle circumference,
- Patient Quality of Life through a specific the WoundQuol Questionnaire,
- The safety of the tested procedure (compression therapy system and dressings) through the nature and number of emergent local adverse events (i.e., events not present at baseline),
- Patients' acceptability of the procedure, evaluated by the investigator and by the patient,
- The change frequency per week over the treatment period.

3. COMPOSITION AND CHARACTERISTICS OF THE STUDY TREATMENT

The study treatment is based upon a combination of a compression therapy system composed of a two layers compression therapy system (Urgo K2®) and an interactive wound dressing from the UrgoStart® range (UrgoStart® Plus Pad and UrgoStart® Plus Pad Border). Regarding the compression, UrgoK2® is a two-layer compression bandage system, which benefits from the exclusive technology of the pressure system. The pressure system has been specifically designed to aid the application of the recommended therapeutic pressure (average 40 mmHg) for venous leg ulcers presenting an ABPI (Ankle Brachial Pressure Index) superior to 0.8 value, from the first application.

3.1. THE TWO LAYER COMPRESSION SYSTEM

The Urgo K2® compression therapy system is indicated in the treatment of venous leg ulcers which require a high level of compression and presenting with Ankle Brachial Pressure Index (ABPI) > 0.85.

This compression system is described in Appendix 1 of this current clinical trial Protocol.

3.2. URGOSTART RANGE DRESSINGS

The UrgoStart® dressings represent a local treatment to enhance the healing process and to reduce healing time of chronic wounds such as leg ulcers, diabetic foot ulcers and pressure sores, due to the TLC-NOSF Healing Matrix, to be part of a good standard of care (including compression in the case of venous leg ulcers).

This dressings range (two different dressings) is described in Appendix 2 of this current clinical trial Protocol.

At any time of the 12 weeks treatment, a switch from one UrgoStart dressing to another one (Pad to Pad Border for example) can be done, at the convenience of the investigating caregiver.

3.3. CONCOMITANT TREATMENTS

3.3.1. General

The studied procedure (UrgoK2®/UrgoStart®) does not present any contra-indications to the use of a systemic treatment, irrespective of the therapeutic class.

The existence of general treatments at the time of inclusion in the investigation, along with any modifications during it, must be documented in the case report form (CRF).

3.3.2. Local treatments

Wounds will be cleansed with saline solution where appropriate.

The use of local antiseptics, if deemed necessary by the investigator, must be documented in the case report form.

Other local treatment (water, pastes, zinc pastes, corticosteroids, etc.) are permitted for application around the lesions: their use must be documented in the case report form.

4. PATIENT SELECTION

4.1. INITIAL SELECTION DIAGNOSIS

The patients recruited for this clinical investigation will be patients treated on an outpatient basis for a venous leg ulcer presenting with an ABPI>0.85 (venous origin).

4.2. INCLUSION CRITERIA

Related to the patient:

- Patient over 18 years old who has provided his/her written informed consent,
- Patient who is able and willing to commit to regular follow up with the investigating team for the purpose of the study, and in line with established service protocols for routine patient follow up until ulcer healed,
- Patient who agrees to adhere to the study protocol with respect to the type of multilayer compression system and primary wound dressing,

Related to the venous leg ulcer:

- Ulcer between 2 and 20 cm^2 in surface,
- Ulcer duration less than six weeks (“new ulcer”),
- Venous leg ulcer - Ankle Brachial Pressure Index > 0.85 at baseline, done in the previous three months and if not, at the inclusion of the patient),

4.3. EXCLUSION CRITERIA

Related to the patient:

- Patient participating in another clinical trial,
- Patient with known hypersensitivity to one of the components of the tested compression system Urgo KTwo Lite Latex free or the UrgoStart dressings,
- Patient who is unable to tolerate compression therapy,
- Patient presenting a neoplastic lesion treated by radiotherapy or chemotherapy or patients treated with immunosuppressive drugs or high-dose corticosteroids,
- Patient with a history of deep or superficial vein thrombosis in the 3 months prior to inclusion,
- Patient confined to bed.

Related to the leg ulcer:

- Ulcer with ABPI<0.85,
- Ulcer which is clinically infected,
- Ulcer surface area partially or totally covered by black necrosis plaque,
- Malignant ulcer,
- Ulcer less than 3 cm, from any edge, to another wound located on the same limb.

NB: In the case of a patient presenting with several ulcers located on the same limb, the investigator must select at the inclusion visit only one wound for the evaluation (target ulcer), which best meets the selection criteria. This ulcer will be distant from the edge of any other wound on the same limb by a minimum of 3 cm. The other wound(s) will be treated with the investigator's usual treatment procedures for the primary wound dressing (*i.e.,* the compression system being the same for one entire lower limb).

5. STUDY CONDUCT

5.1. Synoptic diagram of the investigation

For all included patients, the scheduled treatment duration is 12 weeks. Patients will be allocated to the Urgo K2 compression system and a wound dressing from the UrgoStart® range. Both devices must be applied according to manufacturers' recommendations as described in the respective device monographs (Appendix 1&2).

After obtaining the patient's written consent to participate and once all inclusion and exclusion criteria are met, patients will be included in the study. Patients will then be seen at Week 2 and Week 4 $\pm$ 3 days during the first month, and then every four weeks, until the 12th week for wound assessment or until complete wound closure if it happens before, with all the visits being documented in the case report form (CRF).

At each of these visits, the investigator will perform a clinical assessment and a will measure the wound with a ruler, and will also take a photographic record of the venous leg ulcer.

The treatment may be discontinued, temporarily or definitively, before the required 12 weeks have been completed if the investigator deems this to be necessary: this must be then documented in the Case Report Form (CRF).

A temporary discontinuation of the tested treatment (compression system or the primary dressing) must not exceed 2 weeks; after this time, it will become a permanent discontinuation.

In case of permanent discontinuation, the investigator has to follow-up the patient until Week 12, as expected in the protocol and to treat him at his entire convenience.

The acceptability of the study treatment will also be assessed at each visit planned in the protocol.

5.2. INCLUSION VISIT: DAY 0

Any patient presenting with a new venous leg ulcer (less than six weeks duration) and meeting all the selection criteria may be approached for inclusion in the study irrespective of previous local treatment for his chronic wound.

The patient must be informed of the nature of the study for which he/she is being selected and must sign a written informed consent form in duplicate, prior to any investigation relative to this study.

The investigator then considers that the patient is included in the investigation and must therefore document the Case Report Form.

1.2.1. Patient history

This includes:

- The patient's demographic characteristics,
- The patient's major medical and surgical history (including the comorbidities),
- Current general treatments.

1.2.2. Clinical assessment of the patient

This will be documented in the case report form and includes:

- Peripheral vascular condition, including pulses and ABPI measurement,
- Venous ulcer confirmed by duplex ultrasound scan
- Examination of the leg presenting with the ulcer,
- Number of ulcer(s) of the studied ulcerated limb,
- Ankle circumference.

1.2.3. Characteristics of the lesion

The following will be documented:

- The nature and location of the lesion,
- The clinical status of the wound (presence of sloughy tissue, granulation tissue and necrotic tissue, on the wound bed),
- The condition of the surrounding skin,
- The history of the lesion (duration, recurrence, previous treatment…).

1.2.4. Measurement of the wound

The surface area of the wound will be measured with a ruler (length and width) and noted in the CRF of the patient.

1.2.5. Photographic record

Photographs will be taken by the investigator at baseline and at every visit planned in the protocol till the end of the treatment period (Week 12 or before, if withdrawal or healing occurred), according to the investigator's normal procedures.

A ruler will be used when taking the photographic records.

At the end of this Inclusion visit, the investigator will give the Patient a letter for the nurse who will provide the care in the community, between two visits planned in the protocol. This letter will inform the community HCP about the study and will provide recommendations on how to use the products which are under evaluation.

The investigator, at the end of the inclusion visit, will give the patient an appointment for the next visit planned in the protocol, two weeks after the current one.

5.3. INTERMEDIATE ASSESSMENT

Over the 12 weeks of follow-up, intermediate assessments will be performed at the following frequency: W2, W4 and W8.

A period of two week is defined as 14 days (± 2 days), which means that:

- W2 is between the 12th and the 16th day of treatment,
- W4 is between the 26th and 30th day of treatment,
- W8 is between the 54th and 58th day of treatment.

At each visit planned in the protocol, the investigator will note the following in the Case Report Form:

- The characteristics of the lesion (if this one is still present),
- The occurrence of any local adverse event (LAE),

The investigator will also conduct the following:

- a measurement of the study lesion with a ruler,
- a photographic record of the study lesion.

The investigator will record the acceptability of the study procedure, including the following parameters:

- pain level at dressing changes,
- ease of application of the studied procedure (compression and dressing),
- odour, maceration and leakage of exudate,
- assessed qualitatively.

These elements will be documented in the Case Report Form each time a visit is dispensed in the investigating center, at the planned visits.

The investigator, at the end of each of those Intermediate visits will give the patient an appointment for the next visit planned in the protocol, from Week 2 to Week 4 and then after for the following ones, from Week 4 to Week 8 and after, Week 8 to Week 12, which corresponds to the final visit.

5.4. ASSESSMENT IN THE EVENT OF STUDY WITHDRAWAL BEFORE W12

A premature study withdrawal may occur for any of the following reasons:

- Withdrawal of informed consent,
- Healing of the tested wound; thus, the patient will have to consult the investigator as soon as possible after the onset of the wound closure to document the event and provide the exact date of the closure,
- Onset of a local adverse event requiring permanent discontinuation of the tested treatment,
- Intercurrent adverse event requiring withdrawal,
- Any other reason, to be documented.

A temporary discontinuation of the study treatment must not exceed two weeks; if it does so, it becomes a permanent discontinuation.

In case of permanent discontinuation of the treatment (studied compression system or the interactive dressing whatever), the investigator is asked to perform the planned protocol evaluations, at the same frequency, until the final evaluation (Week 12), whatever any local treatment applied.

On the day of permanent discontinuation, the investigator is asked:

- To make a clinical assessment,
- To measure the study lesion with a ruler,
- To make a photographic record,
- To measure the ankle circumference, in order to follow the evolution of any oedema of the lower limb, if existing.

5.5. FINAL ASSESSMENT AT THE 12TH WEEK

A complete assessment will be made by the investigator at the 12th week (W12), between the 82nd and 86th day of treatment for all those patients included in the investigation.

This assessment will include:

- A clinical assessment,
- A measurement of the study lesion with a ruler
- A photographic record,
- A measurement of the ankle circumference, in order to follow the evolution of any oedema of the lower limb, if existing.

6. ASSESSMENT CRITERIA

6.1. MAIN CRITERION

The main judgment criterion is the completely closed study ulcer (100% re-epithelialization) evaluated at last available study visit (12 weeks, at the latest).

6.2. SECONDARY CRITERIA

The secondary criteria are to assess or to measure the:

- Time to reach complete wound closure,
- Relative and Absolute wound surface area reduction ($area_{t0}$-$area_{tlast}$),
- Percentage of patients with a ≥30% wound area reduction [($area_{t0}$-$area_{tlast}$)/$area_{t0}$ * 100] at Week 4,
- Evolution of the ankle circumference,
- The Patient Quality of Life through a specific the WoundQuol Questionnaire,
- The safety of the procedure (nature and number of emergent local adverse events),
- Patients' acceptability to the studied procedure (compression system and dressing) evaluated by the investigator and by the patient,
- The dressing change frequency.

7. LOCAL ADVERSE EVENTS

Any local adverse event (LAE) occurring during the tested treatment, irrespective of its severity, must be recorded in the case report form, in the pages provided for this purpose.

The onset of an adverse event may lead to a withdrawal of the study treatment, either temporarily or definitively.

The following will be recorded:

- The nature and date of onset,
- The causal relationship with current treatment,
- The outcome,
- The therapeutic decision.

The occurrence of a local adverse event

- Does not necessarily represent a reason for premature study withdrawal,
- Leaves the investigator free to continue or to stop the study treatment, either temporarily or definitively, in this case replacing it with a treatment considered to be more appropriate, based on his/her clinician experience,
- Must be documented in the case report form and will be the subject of a clinical, and photographic assessment.

If an adverse event requires the investigator to discontinue definitively the study treatment, this must be documented in the Case Report Form, on the "Early termination before W12".

Any local adverse event involving the permanent discontinuation of treatment must be reported by the patient and/or the community HCP, to the principal investigator by phone within 48 hours and by email within 3 days.

If the occurrence of a local adverse event leads to a temporary discontinuation of the study treatment, this should not exceed 2 weeks; after that it becomes permanent and the investigator will then have to complete the "Early termination before Week 12" section in the Case Report Form.

The investigator could then document the description of this adverse event and its evolution in a specific materiovigilance document and send it to the manufacturer of the two tested devices (Vigilance-UrgoMedical@fr.urgo.com).

8. INTERCURRENT ADVERSE EVENTS

Any untoward intercurrent medical occurrence in a patient or clinical investigation subject administered an investigational product and which does not necessarily have a causal relationship

with this treatment will be considered as an Intercurrent Adverse Event. An intercurrent adverse event (IAE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporarily associated with the use of an investigational product, whether or not considered related to the tested procedure.

Any intercurrent adverse event occurring during the treatment will be recorded in the Case Report Form, in the pages provided for this purpose.

9. SERIOUS ADVERSE EVENTS

Any Serious Adverse Event (SAE) is any untoward medical occurrence that:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity,
- Corresponds to another important medical event,

will be reported by the patient and/or the community HCP to the principal investigator by telephone within 48 hours.

The investigator must inform the local ethics committee in accordance with the local regulations and guidelines and should inform the manufacturer (Laboratoires Urgo Medical) at the following email address: Vigilance-UrgoMedical@fr.urgo.com.

10. STATISTICAL ANALYSIS

10.1. NUMBER OF SUBJECTS

Given the uncontrolled nature of this clinical study, the data available in the literature in this area, and the treatment duration of twelve weeks for each patient, it appears that the total number of 60 patients is sufficient to provide a relevant answer to the primary endpoint. This has been agreed with our medical statistician who is independent of this study.

No statistical tests will be applied because this clinical study is non-comparative.

10.2. DATA MANAGEMENT AND STATISTICAL ANALYSIS

10.2.1. Statistical analysis plan (SAP)

The statistical analysis of this study will be performed by the principal investigator at the end of the trial, for all the primary and secondary objectives.

10.2.2. Data management

All CRFs will be reviewed by a health care giver with experience in wound management.

The data will be collected by using a password protected Microsoft Excel database specially prepared for this study. All data not lying within pre-established ranges without explanation from investigators will be queried.

The database will be considered as appropriate for analysis as soon as answers to all queries have been obtained.

10.3. GENERAL STATISTICAL CONSIDERATION ON DESCRIPTION OF VARIABLES

The distribution of parameters will be summarized using descriptive statistics according to characteristics of the study variable:

- Binary, nominal and ordered categorical variables will be summarized by their frequency distribution,
- Continuous variables will be summarized by their number of observations, mean, standard deviation, median, quartiles and range.

10.3.1. Definition of the populations

The following populations will be studied:

- The Intent to Treat population (ITT) is defined as all patients who received at baseline the allocated studied procedure and for whom a documented ulcer status (at minimum closed or not closed ulcer) is available at least one time after the inclusion of the patient.
- The Per Protocol population (PP) consists of all ITT patients, for whom no major protocol deviations were observed, and have been treated with the allocated procedure for a minimum of 4 weeks.
- The Safety population is defined as all included and treated patients (at least one documented application of studied systems).

10.3.2. STUDIED PATIENTS / SUBJECTS

<u>Disposition of patients / subjects</u>

The number of included patients, the number of patients who completed the planned medical visits and the number of patients who completed the overall study will be tabulated. The number of patients who discontinued prematurely the study will be also described.

Moreover, discontinued patients will be listed giving patient's number, age at inclusion, gender, last compression received, and reason for withdrawal and study duration.

A Subgroup analysis will be performed considering the ankle circumference (18-25cm group and 25-32cm group).

Protocol deviations; these will be listed by patient.

Moreover, the number of patients with at least one protocol deviation and the number of deviations will be tabulated by category and by term.

Patients Demographic and other baseline characteristics will be summarized using descriptive statistics. This analysis will be performed on Safety Population, ITT and PP populations (if different).

11. PROTOCOL MODIFICATIONS AND AMENDMENTS

No modification of this protocol can be made without the agreement of the principal investigator.

Any substantial modification/amendment must be sent for approval to the Ethics Committee.

12. REGULATORY OBLIGATIONS AND ADMINISTRATIVE CONDITIONS

In accordance with the principles of the Declaration of Helsinki (1964), revised in Tokyo (1975), Venice (1983), Hong Kong (1989), Somerset West (1996) and Edinburgh (2000), this investigation must be conducted according to Good Clinical Practices relative to the protection of individuals taking part in biomedical research. This may include an on-site audit and/or an inspection by representatives of the health authorities, at any time. The investigator must agree to the audit of the investigation's source documents by the representative of the health authorities

12.1. ETHIC COMMITTEE SUBMISSION

The Ethics Committee must be informed of any protocol amendment and its approval must be obtained if the amendment is liable to significantly affect the safety conditions of the patients taking part in the research.

The present protocol, patient information sheet and patient consent form and other documents will be submitted by the Investigator to the relevant Research Ethics Committee for Gloucestershire Hospitals NHS Foundation Trust.

12.2. PATIENT INFORMATION AND WRITTEN AND INFORMED CONSENT

The investigator will submit the patient information leaflet and written informed consent to the Ethics Committee for approval.

Signature of the consent forms must be obtained prior to patient enrolment in the study.

12.2.1. Patient Information Sheet

Every patient meeting the selection criteria must be informed by the investigator of the aims of the research, its methodology and its duration, the constraints and foreseeable risks, along with the benefits that he/she may reasonably expect from his/her participation.

The main points of the information provided to the patient must be included in the information document that the Investigator gives the patient before the start of the investigation.

The patient must know:

- that he/she may refuse to take part in the research,
- that he/she is able to withdraw from the study at any time without prejudice,
- that he/she will not have to bear any additional financial costs as a result of his/her participation in the investigation.

The investigator must answer any additional questions asked by the patient about the investigation at the time of selection and throughout the duration of the research.

12.2.2. Patient's Consent Form

Prior to inclusion in the investigation, the freely-given, express, informed consent of the patient must be obtained in writing in two originals. The patient keeps one copy and the investigator keeps the other.

12.3. PATIENT DATA

12.3.1. Data collection

The investigator must record the patients' individual data, independently of the Case Report Form.

The data must include identification of the patient, visit dates, information relative to vital signs, medical history, results of prescribed tests, any adverse events encountered or any other relevant comments. This information represents the "source data" (patient's medical file).

Any data recorded in the Case Report Form must also be present in the Source File (Patient Medical File).

The Case Report Form must be completed at the visits planned in the protocol.

The Consent Form must be placed in the patient's file throughout the investigation. Once the investigation has been completed, it must be placed in the Investigator's archive file, accompanied, at the end of the investigation, by a complete copy of the Case Report Form.

All original documents concerning laboratory data must be available in the patient files, since there is a possibility of errors or inaccuracies when transcribing original data into the Case Report Forms.

12.3.2. Information storage, archiving

Any correspondence linked to the clinical investigation must be stored in the Investigator's archive file.

Information concerning patients, source documents, case report forms, approval of the Ethics Committee and correspondence relating to the investigation must be filed and stored in the archive file for 15 years by the Investigator, in accordance with European regulations.

13. STUDY SCHEDULE

The investigators agree to comply with the following proposed schedule:

- September 2023: Initiation of the investigation,
- September 2024: End of the inclusion period,
- December 2024: End of the investigation,
- March 2025: Clinical Report of the trial.

14. SIGNATURES

I the undersigned, Mr. Colin DAVIES hereby undertake to conduct this clinical investigation as it is defined in this protocol, in accordance with Good Clinical Practices in compliance with the following proposed schedule:

- September 2023: Initiation of the investigation,
- September 2024: End of the inclusion period,
- December 2024: End of the investigation,
- March 2025: Clinical Report of the trial.

The Investigator

Date: ____ / ____ / _____ Signature:

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APPENDICES

APPENDIX (i)

URGO K2 Latex Free / URGO KTwo Latex Free

The application of this medical device must be carried out by a person trained in the application of compression bandages. Read these instructions for use carefully.

/ Urgo Medical

Application video available.

PRODUCT DESCRIPTION

URGO K2/URGO KTwo (or **URGO K2/URGO KTwo Latex Free**) is a two-layer multicomponent compression system, composed of a short stretch bandage and a long stretch bandage.

Its exclusive PresSure system technology, based on pressure indicators, guides application at the correct stretch and correct overlap, according to the selected kit.

KIT CONTENTS

URGO K2/URGO KTwo is composed of KTech (Layer 1) and KPress (Layer 2).
URGO K2/URGO KTwo Latex Free is composed of KTech (Layer 1) and KPress Latex Free (Layer 2).

- Layer 1:

KTech: white, short-stretch bandage; provides compression, protection.
Composition: wadding: viscose, polyester; knitted layer: polyamide, elastane.

- Layer 2:

KPress/KPress Latex Free: pink/beige, cohesive long-stretch bandage; provides the additional compression necessary to achieve the therapeutic pressure and secures the bandages in place.
KPress composition: acrylic, polyamide, elastane; cohesive material containing natural latex.
KPress Latex Free composition: cotton, polyester, polyamide, elastane; synthetic latex free cohesive material.

SIZES

URGO K2/URGO KTwo (or **URGO K2/URGO KTwo Latex Free**) is available in 2 sizes, for ankle circumferences: 18-25 cm and 25-32 cm.
URGO K2/URGO KTwo is available in 3 widths: 8 cm, 10 cm, and 12 cm.
URGO K2 Latex free/URGO KTwo Latex Free is available in 10 cm width only.

(Some kit widths may not be available in your country.)

PROPERTIES

- Comfortable day and night for improved patient concordance.
- Easy to wear shoes.
- Good ankle mobility.

- Easy, fast, and accurate application thanks to the PresSure System: the therapeutic pressure is achieved from the first application.
- High level of compression at the ankle (around 40 mmHg).

- High SSI (Static Stiffness Index): Continuous pressure thanks to a high working pressure and a moderate resting pressure, creating a massage effect for improved venous return and oedema reduction.
- The system can stay in place up to 7 days.

INDICATIONS

Treatment, in adults, of venous leg ulcer and/or lower limb oedemas where strong compression is recommended.

CONTRAINDICATIONS

- Moderate or severe arterial conditions, notably with recent Ankle Brachial Pressure Index (ABPI) <0.8.
- Patients suffering from *phlegmatia coerulea dolens*, septic phlebitis.
- Oedema from congestive cardiac failure.
- Epifascial arterial bypass.
- Known hypersensitivity to any of the components – in particular latex for **URGO K2/ URGO KTwo**.

PRECAUTIONS OF USE

- Single use: Do not wash to maintain the performances of the medical device.
- Do not sterilize.
- Do not use in direct contact with a wound.
- In the event of arterial bypass, cardiac failure, peripheral neuropathy (for example in case of diabetes), infected peri-ulcer dermatitis or acute cellulitis (erysipelas), use the compression system after specialist referral and under close medical monitoring.
- In case of ABPI ≥1.3, suspicion of media calcific sclerosis or history of revascularisation, an extensive vascular assessment is recommended before initiating the compression therapy.
- In case of infected leg ulcer, start treating infection in combination with compression therapy.
- The efficacy of **URGO K2/ URGO KTwo** (or **URGO K2/ URGO KTwo Latex Free**) has been tested and validated for the application of KTech and KPress (or KPress Latex Free) together.
- Follow the application method given below to achieve the recommended therapeutic pressure. The PresSure System has been specifically designed to guide the application of the bandages.
- This compression system should be worn continuously day and night until the next care at the discretion of the clinician.
- If experiencing discomfort, pain or skin reactions whilst wearing this product, patient should contact his/her healthcare professional.
- Any serious incident linked to the product must be reported to the manufacturer and the National Competent Authority.

INSTRUCTIONS FOR USE

Before applying the bandages

- If a wound is present, apply an appropriate dressing before applying KTech.
- Examine the shape of the leg and identify any areas at risk of excessive pressure (bony prominences). Protect and reshape leg with wadding if necessary.
- Measure the ankle circumference and choose the kit size accordingly (18-25 cm or 25-32 cm) **(Figure 1)**. For ankle circumference > 32 cm, the 25-32 cm kit may be used: the level of compression will approach the therapeutic pressure with the progressive oedema reduction.
- In the event of very stout legs, 2 kits may be used to cover the entire leg.
- It is preferable to apply the compression system first thing in the morning or after the patient's legs have been elevated for an hour to minimize any orthostatic oedema.
- Depending on the indication, assess the need for toe to knee or toe to thigh bandaging and choose the appropriate kit width according to the following application method.

Application method

"Below – knee" application

1. Position the foot at 90° angle - "toes to nose" **(Figure 2)**.
2. Ensure the wadding side of KTech is in contact with the skin, with the printed pressure indicators visible on the upper (towards the top of the leg) side (18-25 cm kit size) or at the middle (25-32 cm kit size) of the bandage. Start at the base of the toes, making one or two wraps around the foot to anchor the bandage with a moderate stretch, depending on vascular status, foot shape and presence of oedema **(Figure 3)**.
3. Take the heel, making a figure eight wrap around the ankle. Ensure that the heel is fully covered to avoid frictions **(Figure 4)**.
4. From the ankle, wrap up to the knee in spirals, stretching the bandage so that the pressure indicators form circles. To achieve correct overlap, cover pressure indicators (18-25 cm kit

size: 50% (1/2) overlap of the bandage width; 25-32 cm kit size: 2/3 overlap of the bandage width) **(Figure 5)**.
Finish 2 cm below popliteal space.
Cut off with a pair of scissors any excess bandage as extra wrapping will increase the pressure **(Figure 6)**. Secure with tape.

5. Apply KPress (or KPress Latex Free) over KTech using the same application technique as KTech. For patient comfort, allow a small border of KTech at the toes and knee so that only KTech is in direct contact with the skin.
   Once applied, press down gently on the bandage to ensure full cohesion **(Figure 7)**.

<u>"Toe to thigh" application</u>

If necessary, first bandage the toes using an appropriate bandage.
For full leg bandaging, use the same application technique as the "below-knee" application.
During the application, the knee should be slightly bent to ensure patient mobility.
Several KTech must be used to continue the application to the top of the thigh **(Figure I)**: when applying a new KTech, start by performing one turn around the previous KTech.
Cover the knee avoiding that the edge of KTech is positioned over the popliteal space to avoid skin lesions.

Cut off with a pair of scissors any excess of KTech and secure with tape.
Apply KPress (or KPress Latex Free) over KTech using the same sequence of bandages and application technique as KTech **(Figure II)**. Once applied, press down gently on the bandage to ensure full cohesion and secure with tape if necessary.

	DO NOT RE-USE
	CAUTION
	CONSULT INSTRUCTIONS FOR USE
	BATCH CODE
	USE-BY DATE
	CATALOGUE NUMBER
	MANUFACTURER
	MEDICAL DEVICE
	COMPRESSION LEVEL
	KIT SIZE
	**URGO K2/URGO KTwo:** PRESENCE OF NATURAL RUBBER LATEX
	**URGO K2 Latex Free/URGO KTwo Latex Free:** NOT MADE WITH NATURAL RUBBER LATEX
	BANDAGE WIDTH


Laboratoires URGO - 42 rue de Longvic - 21300 CHENOVE - France

UK Responsible Person:

Urgo Ltd - Sullington Road - Shepshed - Loughborough - LE12 9JG - United Kingdom

APPENDIX (ii)

UrgoStart Plus / UrgoStart Plus Non Border

DRESSING WITH SOFT-ADHERENT TLC-NOSF HEALING MATRIX TO REDUCE HEALING TIME AND WITH POLY-ABSORBENT FIBRES TO CLEAN THE WOUND

☐ DESCRIPTION:

UrgoStart Plus is an innovative, patented dressing developed by Laboratoires Urgo composed by two exclusive technologies, TLC-NOSF healing matrix and poly-absorbent fibres.

UrgoStart Plus is composed of:

- A soft-adherent TLC-NOSF matrix, composed of lipido-colloid particles, polymers and an exclusive component, NOSF (Nano-Oligo Saccharide factor) which reduces healing time. It is combined with polyacrylate poly-absorbent fibres, which guarantee wound cleaning (of slough, exudate, and bacterial residue)
- A super-absorbent layer
- A vapour permeable waterproof outer film.

This specific combination is a patented structure.

PROPERTIES:

UrgoStart Plus reduces healing time and cleans the wound of slough, exudate, and bacterial residue.

The TLC-NOSF healing matrix forms a gel when in contact with the wound and reduces healing time by inhibiting excess metallo-proteinases, which degrade the extracellular matrix. It also creates a moist environment and promotes the action of the key cells involved in the healing process (fibroblasts, keratinocytes, and macrophages).

When in contact with the wound, the poly-absorbent fibres in **Urgostart Plus** gel. The dressing absorbs and traps slough, exudate and bacterial residue present in the wound, for an autolytic desloughing. The poly-absorbent fibres offer a high level of cohesion of the dressing allowing it to be removed painlessly in one piece, without causing trauma to the wound.

The poly-absorbent pad and the super-absorbent layer in **UrgoStart Plus** ensure a high absorption and fluid management of exudate preventing maceration. The dressing can be used under compression bandage when prescribed.

UrgoStart Plus water proof backing is soft, very conformable and non-occlusive which allows the dressing to conform and adapt to each different wound. It also prevents fluid leakage and bacteria strikethrough. Its high vapour permeability characteristics allow the excess exudate to evaporate, preventing from the risk of maceration. The dressing can adapt to different body movements, ensuring patient comfort. Due to its transparency, it is possible to monitor fluid strikethrough enabling the dressing change to be performed only when needed.

UrgoStart Plus has multiple properties:

1) Healing properties:
   - Reduction of healing time combined with cleaning of all materials present in the wound (slough, exudate, bacterial residue)
   - Absorption of exudate
   - Management of minor bleeding wounds
   - Creation and maintenance of a moist wound environment that promotes healing
   - Atraumatic removal
   - Respect of peri-wound skin

2) Comfort and ease of use:
   - Painfree removal
   - Very conformable and easy to position due to soft-adherence
   - A vapour permeable waterproof outer film

The efficacy of TLC-NOSF on reduction of healing time has been demonstrated in randomised controlled clinical trials[1, 2, 3] and in a pooled analysis of observational studies[4].

[1] Edmonds M, et al. Sucrose octasulfate dressing versus control dressing in patients with neuroischaemic diabetic foot ulcers (EXPLORER): an international, multicentre, double-blind, randomised, controlled trial. Lancet Diabetes Endocrinol. 2018 Mar; 6(3):186-196.

[2] Meaume S, et al. A randomized-controlled, double-blinded prospective trial with a TLC-NOSF wound dressing, in the local management of venous leg ulcers. Wound Rep Reg. 2012; 20(4):500-511.

[3] Meaume S, et al. Quality of life in patients with leg ulcers: results from CHALLENGE, a double-blind randomized controlled trial. Journal of Wound Care. 2017; 26 (7): 368-379.

[4] Münter KC, et al. The reality of routine practice: a pooled data analysis on chronic wounds treated with TLC-NOSF wound dressings. J Wound Care. 2017 Feb; 26 (Sup2): S4-S15. Erratum in: J Wound Care. 2017 Mar 2; 26(3): 153.

INDICATIONS:

UrgoStart Plus is indicated for all stages (from the desloughing stage to complete healing) of exuding wounds, including chronic wounds (leg ulcers, pressure ulcers, diabetic foot ulcers) and long-standing acute wounds.

INSTRUCTIONS FOR USE:

- Wound preparation:
  - Clean the wound as per local protocol and rinse the wound with normal saline.
  - If an antiseptic has previously been used, rinse the wound carefully with normal saline before applying **Urgostart Plus.**
  - Dry the surrounding skin carefully.
  - The use of **Urgostart Plus** does not dispense with the need for mechanical debridement if required.

– Dressing application:
  - Gently remove the protective tabs.
  - Apply the soft-adherent side of **UrgoStart Plus** directly to the wound.
  - Apply a suitable bandage or compression bandage system when prescribed.

– Dressing changes:
  – Remove the dressing when it becomes saturated and clean the wound if necessary.

It is recommended to change **Urgostart Plus** every 1 to 2 days during the wound desloughing phase, then to adapt the renewal frequency according to the volume of exudate and the clinical progress of the wound. It can be left in place for up to 7 days.

Discard any unused parts of the dressing.

WARNINGS AND PRECAUTIONS FOR USE:

- The soft-adherent layer of **UrgoStart Plus** adheres to latex surgical gloves. Therefore, it is recommended that the tabs be used to facilitate application of the dressing.
- As it includes a super-absorbent layer, **UrgoStart Plus** should not be cut.
- If the wound shows signs of local infection, it is recommended that anti-microbial treatment (such as UrgoClean Ag) is used first before starting treatment with **Urgostart Plus**.
- If an atypical ulcer presents induration or over-granulation, treatment with **Urgostart Plus** should only be initiated after verifying that ulcer deterioration is absent, to prevent any delay in diagnosis.
- In the absence of clinical data regarding Epidermolysis Bullosa (even for longstanding lesions), the use of **Urgostart Plus** is not recommended.
- Stinging or even painful sensations may be reported at the start of the treatment. These are usually linked to the healing process and the need to suspend treatment is rare.
- During desloughing, the wound may appear to get larger due to the gradual elimination of slough.
- Concomitant use with a cream, an ointment, an emulsion is not recommended.
- **UrgoStart Plus** must not be used in a hyperbaric chamber.
- Sterile individual packaging, for single use only: re-using a disposable dressing can lead to the risks of infection.
- Do not re-sterilise the dressing.
- (*) Check that the sterile protector is intact before use. Do not use if package is damaged.

CONTRA-INDICATIONS:

- **UrgoStart Plus** facilitates the management of minor bleeding wounds. However, it should not be used for heavily bleeding wounds.
- In order not to delay any optimal treatment, **Urgostart Plus** is contra-indicated in cancerous wounds and wounds which may reveal a deep abscess.
- Do not use when there is a known sensitivity to **Urgostart Plus**.

APPENDIX (iii)

UrgoStart Plus Border

ADHESIVE DRESSING WITH SOFT-ADHERENT TLC-NOSF HEALING MATRIX TO REDUCE HEALING TIME AND WITH POLY-ABSORBENT FIBRES TO CLEAN THE WOUND

DESCRIPTION

UrgoStart Plus Border is an innovative, patented dressing developed by Laboratoires Urgo composed by two exclusive technologies, TLC-NOSF healing matrix and poly-absorbent fibres.

UrgoStart Plus Border is composed of:

- A soft-adherent TLC-NOSF matrix, composed of lipido-colloid particles, polymers and an exclusive component, NOSF (Nano-Oligo Saccharide factor) which reduces healing time. It is combined with polyacrylate poly-absorbent fibres, which guarantee wound cleaning (of slough, exudate, and bacterial residue),
- A super-absorbent layer,
- A vapour permeable waterproof outer film with silicone adhesive on the edges.

This specific combination is a patented structure.

PROPERTIES

UrgoStart Plus Border reduces healing time and cleans the wound of slough, exudate, and bacterial residue.

The TLC-NOSF healing matrix forms a gel when in contact with the wound and reduces healing time by inhibiting excess metallo-proteinases, which degrade the extracellular matrix. It also creates a moist environment and promotes the action of the key cells involved in the healing process (fibroblasts, keratinocytes, and macrophages).

When in contact with the wound, the poly-absorbent fibres in **UrgoStart Plus Border** gel. The dressing absorbs and traps slough, exudate and bacterial residue present in the wound, for an autolytic desloughing. The poly-absorbent fibres offer a high level of cohesion of the dressing allowing it to be removed painlessly in one piece, without causing trauma to the wound.

The poly-absorbent pad and the super-absorbent layer in **UrgoStart Plus Border** ensure a high absorption and fluid management of exudate preventing maceration. The dressing can be used under compression bandage when prescribed.

UrgoStart Plus Border water proof backing is soft, very conformable and non-occlusive which allows the dressing to conform and adapt to each different wound. It also prevents fluid leakage and bacteria strikethrough. Its high vapour permeability characteristics allow the excess exudate to evaporate, preventing from the risk of maceration. The dressing can adapt to different body movements, ensuring patient comfort. The silicone adhesive borders guarantee that the dressing adheres well, can be easily repositioned and also well tolerated by the skin. The adhesive border prevents the need of a secondary dressing. Due to its transparency, it is possible to monitor fluid strikethrough enabling the dressing change to be performed only when needed.

UrgoStart Plus Border has multiple properties:

3) Healing properties:
   - Reduction of healing time combined with cleaning of all materials present in the wound (slough, exudate, bacterial residue)
   - Absorption of exudate
   - Management of minor bleeding wounds
   - Creation and maintenance of a moist wound environment that promotes healing
   - Atraumatic removal
   - Respect of peri-wound skin

4) Comfort and ease of use:
   - Painfree removal
   - Very conformable and easy to reposition
   - A vapour permeable waterproof outer film with silicone adhesive on the edges

The efficacy of TLC-NOSF on reduction of healing time has been demonstrated in double-blind, randomised, controlled clinical studies [1,2,3] and in a pooled analysis of observational studies [4].

[1] Edmonds M, et al. Sucrose octasulfate dressing versus control dressing in patients with neuroischaemic diabetic foot ulcers (Explorer): an international, multicentre, double-blind, randomised, controlled trial. Lancet Diabetes Endocrinol. 2018 Mar;6(3):186-196.
[2] Meaume S, et al. A randomized-controlled, double-blinded prospective trial with a TLC-NOSF wound dressing, in the local management of venous leg ulcers. Wound Rep Reg. 2012; 20(4):500-511.
[3] Meaume S, et al. Quality of life in patients with leg ulcers: results from CHALLENGE, a double-blind randomized controlled trial. Journal of Wound Care. 2017; 26 (7): 368-379.
[4] Münter KC, et al. The reality of routine practice: a pooled data analysis on chronic wounds treated with TLC-NOSF wound dressings. J Wound Care. 2017 Feb; 26 (Sup2): S4-S15. Erratum in: J Wound Care. 2017 Mar 2; 26(3): 153

INDICATIONS

UrgoStart Plus Border is indicated for all stages (from the desloughing stage to complete healing) of exuding wounds, including chronic wounds (leg ulcers, pressure ulcers, diabetic foot ulcers) and long standing acute wounds.

The Sacral format is recommended for wounds in the sacrum region (pressure ulcers….).

INSTRUCTIONS FOR USE

Wound preparation:
- Clean the wound as per local protocol and rinse the wound with normal saline.
- If an antiseptic has previously been used, rinse the wound carefully with normal saline before applying **UrgoStart Plus Border**.
- Dry the surrounding skin carefully.
- The use of **UrgoStart Plus Border** does not dispense with the need for mechanical debridement if required.

Dressing application:
- Gently remove the protective tabs.
- Apply the soft-adherent side of **UrgoStart Plus Border** directly to the wound (the adhesive silicone border should be at least 1 cm away from the wound).
- Smooth the dressing.
- Apply a compression bandage system when prescribed.

Application of the sacral version:
- Place the dressing with the tip facing the sacral area.

Removal of the dressing:
- Press down on the healthy skin, lift on the corner of the dressing and remove it carefully.

Dressing changes:
- Remove the dressing when it becomes saturated and clean the wound if necessary.

It is recommended to change **UrgoStart Plus Border** every 1 to 2 days during the wound desloughing phase, then to adapt the renewal frequency according to the volume of exudate and the clinical progress of the wound. It can be left in place for up to 7 days.
Discard any unused parts of the dressing.

WARNINGS AND PRECAUTIONS FOR USE

- As the **UrgoStart Plus Border** includes a super-absorbent layer, the central pad should not be cut. However, the adhesive edges can be cut if necessary, using sterile scissors to fit different wound or body shapes.
- If the wound shows signs of local infection, it is recommended that anti-microbial treatment such as UrgoClean Ag is used first before starting treatment with **UrgoStart Plus Border**.
- If an atypical ulcer presents induration or over-granulation, treatment with **UrgoStart Plus Border** should only be initiated after verifying that ulcer deterioration is absent, to prevent any delay in diagnosis.
- Regarding Epidermolysis Bullosa (even for longstanding lesions), the use of **UrgoStart Plus Border** is not recommended.
- Stinging or even painful sensations may be reported at the start of the treatment. These are usually linked to the healing process and the need to suspend treatment is rare.
- During desloughing, the wound may appear to get larger due to the gradual elimination of slough.
- Any excess hair should be removed to ensure the dressing has a good contact with the wound.
- In case of concomitant use with a cream, an ointment, an emulsion, let the skin dry out before applying the dressing.
- **UrgoStart Plus Border** must not be used in a hyperbaric chamber.
- Sterile individual packaging, for single use only: re-using a disposable dressing can lead to the risks of infection.
- Do not re-sterilise the dressing.
- (*) Check that the sterile protector is intact before use. Do not use if package is damaged.

CONTRA-INDICATIONS

- **UrgoStart Plus Border** facilitates the management of minor bleeding wounds. However, it should not be used for heavily bleeding wounds.
- In order not to delay any optimal treatment, **UrgoStart Plus Border** is contra-indicated in cancerous wounds and wounds which may reveal a deep abscess.
- Do not use when there is a known sensitivity to **UrgoStart Plus Border**.

APPENDIX (iv)

PARTICIPANT INFORMATION SHEET

Evaluation of the safety and effectiveness of the global treatment including multilayer compression therapy (Urgo KTwo®) in addition to an interactive dressing (UrgoStart® Plus) in the management of venous leg ulcers

PROTOCOL NUMBER: EUS23-4 **IRAS ID: 327680** **PROJECT REF NO: 23/003/GHT**

Patient Name: _____

Introduction and brief summary

You are being invited to take part in a clinical investigation (known as a research study). Before you decide to enroll in this clinical study, it is important for you to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully and discuss it with friends, relatives and your family doctor if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What involved?

There are a number of compression bandage systems used to treat venous leg ulcers; they are the cornerstone of the treatment of these lesions as they treat the cause of the vascular disease; among them, the multilayer Urgo K2 is effective and safe in the management of venous leg ulcers. A dressing is used to cover the ulcer in order to promote the wound healing process; the NICE (National Institute of Health Care Excellence) Guidance edited in January 2019, stated that the UrgoStart dressing improves wound healing in venous leg ulcers and thus is likely to be cost-saving in addition to reported quality-of-life benefits. This study is being conducted so that we can assess the combination of the two devices for the treatment of your venous leg ulcer, which is very commonly performed in routine but has not yet been assessed in a clinical trial. The clinical study itself will last approximately 12 months (recruitment of all the 60 expected participants) but your participation in this trial will be for a maximum of 12 weeks or until your ulcer has healed (whichever comes first).

What are the two products that are being tested?

The procedure being tested is a combination of a high compression bandage system and a wound dressing. The compression system known as Urgo K2 has been available in UK for the past fifteen years and helps to promote the healing process of venous leg ulcers. This compression system is the most widely used in patients like yourself, with venous leg ulcers, in the UK.

The UrgoStart® dressings are marketed in UK and are indicated in the local management of chronic wounds (leg ulcers, pressure ulcers, diabetic foot ulcers) and longstanding acute wounds. They have shown through clinical trials all over the world that they enhance the healing process of these chronic wounds and thus, shorten the healing time and improve the quality of life of the treated patients, when integrated in a good standard of care (including compression therapy in the venous leg ulcers), as it was stated by the NICE in UK, in January 2019.

Why have I been chosen?

The research team proposes you to participate the study because you have a venous leg ulcer which could be suitable for treatment with the Urgo K2® compression bandage system and the UrgoStart dressing as a primary dressing to locally treat your leg ulcer. A total of 60 patients will be asked to participate in the study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form and you are still free to withdraw at any time and without giving any reason to the investigator.
If you decide not to take part, this will not affect the standard of care you will receive from the research team who will continue to treat your leg ulcer.
If you do decide to take part in the study, your treatment will last for a maximum of 12 weeks. You will see the leg ulcer nurse specialist regularly during the 12 weeks of follow-up. This means you will need to make a maximum of 5 visits to see your leg ulcer nurse specialist; it is the same number of visits that you would normally make even if you were not participating in this study.

At each of the visits, the investigator will assess the size of your ulcer by taking a measurement of the ulcer (this procedure should not cause you any discomfort) and will also take a photograph of the ulcer (at each visit planned in the protocol) and examine it - both painless procedures. The investigator will also ask you some simple questions about how you have found the compression system and the dressing you are being treated with. The visits should not be any longer than the usual visits you have been used to. If you need to see your GP or another medical professional about your ulcer, or if the compression system needs to be changed in between the scheduled visits you will need to let your leg ulcer nurse specialist know about this. You can phone him or her on the number given belo*w.*

You are free to withdraw from the study at any time. If you do decide to withdraw from the study, we will keep and continue to use all your previously collected data. We will, however not collect any further data about you.

What are the alternatives for diagnosis or treatment?

There are other treatments available to locally treat your venous leg ulcer. These include other similar types of compression systems and other dressings but it is stated that UrgoStart enhances

the healing process more than the commonly used neutral dressings (NICE Guidance. January 2019).

What are the side effects of taking part?

It is possible that you may be sensitive to any of the materials in any of the two devices (Urgo K2 or UrgoStart dressings). The symptoms may include redness, soreness, itching, damage to your skin and underlying tissues caused by the compression therapy system and/or the wound dressing. If you suffer from any of these or any other symptoms or become concerned in any way about your leg you should contact the research team on the number given below.

What are the possible benefits of taking part?

We hope this combination, Urgo K2 / UrgoStart Plus, will promote the healing process of your venous leg ulcer and will make your ulcer heal faster. However, this cannot be guaranteed. The information we get from this study may help us to treat future patients with leg ulcers better.
You will not be paid to take part in this study.

What are the possible disadvantages and risks of taking part?

There are no anticipated disadvantages or risks of taking part in this study. Indeed, the treatment that you will be receiving will remain the same whether you take part or not.

What if new information becomes available?

Sometimes during the course of a study, new information becomes available about the treatment that is being studied. If this happens, your leg ulcer nurse specialist will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, you will continue to receive the same high standard of care for your ulcer. If you decide to continue in the study, you will be asked to sign an updated consent form.
Also, on receiving new information, the research team might consider it to be in your best interests to withdraw you from the study. Your nurse will explain the reasons and arrange for your care to continue.

What happens when the study comes to an end?

Once the study is finished for you, at the end of 12 weeks, you will continue to be treated with an appropriate compression system and dressing. You may wish to continue the treatment you are currently receiving; the decision will be made by yourself in discussion with your clinician.

Will my taking part in this study be kept confidential?

If you consent to take part in the study, any of your medical records may be inspected by the investigator of the study for purposes of analyzing the findings. They may also be looked at by people designated by the investigator and from regulatory authorities to check that the study is being carried out correctly. Your name, however, will not be disclosed.

All information which is collected about you during the course of the study will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognized from it. Information will be recorded on a password protected computer database by the investigator. However, this will not contain your name and confidentiality will be maintained at all times.

With your permission, we also wish to inform your GP that you are taking part. In giving your consent you are stating that you have no objection to any of the above.

The results of the study may be published in an appropriate journal or presented at an appropriate medical meeting. If you would like to see the results of the study you should let the research team know so that they can provide the information to you. You will not be identified in any publication or results from the study.

Will the use of my data meet GDPR rules?

GDPR stands for the General Data Protection Regulation. In the UK we follow the GDPR rules and have a law called the Data Protection Act. All research using patient data must follow UK laws and rules. Universities, NHS organizations and companies may use patient data to do research to make health and care better.

When companies do research to develop new treatments, they need to be able to prove that they need to use patient data for the research, and that they need to do the research to develop new treatments. In legal terms this means that they have a 'legitimate interest' in using patient data.
Universities and the NHS are funded from taxes and they are expected to do research as part of their job. They still need to be able to prove that they need to use patient data for the research. In legal terms this means that they use patient data as part of 'a task in the public interest'.
If they could do the research without using patient data, they would not be allowed to get your data.

Researchers must show that their research takes account of the views of patients and ordinary members of the public. They must also show how they protect the privacy of the people who take part. An NHS research ethics committee checks this before the research starts.

Who is organizing and funding the research?

The study is being organized by the Gloucestershire Leg Ulcer Service and sponsored by Gloucestershire Hospitals NHS Foundation Trust.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by The South West - Cornwall & Plymouth Research Ethics Committee.

Who can I contact if I have a complaint?

If you want to complain about how researchers have handled your information, you should contact the research team. If you are not happy after that, you can contact the Data Protection Officer. The research team can give you details of the right Data Protection Officer.
If you are not happy with their response or believe they are processing your data in a way that is not right or lawful, you can complain to the Information Commissioner's Office (ICO) (www.ico.org.uk or 0303 123 1113).

If you are not satisfied or would like support with resolving your concerns, you may choose to speak in confidence with a member of the Patient Advice and Liaison Service (PALS) at the hospital. The PALS team listen to the concerns of patients, carers and visitors and can help negotiate prompt solutions on your behalf. The PALS team can be contacted at:

PALS office, Ground Floor, Tower Block, Gloucestershire Royal Hospital
(Monday to Friday, 9am to 4pm)
Phone: 0800 019 3282
Email: ghn-tr.pals.gloshospitals@nhs.net

THANK YOU VERY MUCH FOR CONSIDERING TO TAKE PART IN OUR RESEARCH.

For further information on this study, please contact:

Mr. Colin Davies
Principle Investigator
Clinical Lead (Leg Ulcers) / Associate Lecturer
Gloucestershire Leg Ulcer Service
Unit 5 Pullman Court, Great Western Road
Gloucester, GL1 3ND

☎ 0300 422 3684 (Office)
☎ 0300 422 3480 (Secretary)
☎ 07432 109334 (Moblie)
✉ colin.davies1@nhs.net

APPENDIX (v)

PATIENT CONSENT FORM

Patient Identification Number for this trial: ☐☐

Evaluation of the safety and effectiveness of the global treatment including multilayer compression therapy (Urgo KTwo®) in addition to an interactive dressing (UrgoStart® Plus in the management of venous leg ulcers

PROTOCOL NUMBER: EUS23-4 **IRAS ID: 327680** **PROJECT REF NO: 23/003/GHT**

Name of Lead Researcher: Mr. Colin Davies, Clinical Lead (Leg Ulcers)

	Please initial box
I confirm that I have read and understand the information sheet dated 25th July 2023 for the above study and have had the opportunity to ask questions.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
I understand that relevant sections of my medical notes and data collected during the study may be looked at by Regulatory authorities where it is relevant to my taking part in this research. I give my permission for these individuals to have access to my records.	☐
I understand that my data will be held on a computer. I give my permission for this data to be held on computer by these parties.	☐
I give my permission for you to contact my General Practitioner (GP).	☐
I agree to take part in the above study.	☐

_____	_____	_____
Name of Patient	Date	Signature
_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature
Mr. Colin DAVIES	_____	_____
Researcher	Date	Signature

***1 for patient (copy); 1 for medical notes (copy); 1 for participant's GP (copy); 1 for researcher (original)**

APPENDIX (vi)

LETTER TO THE COMMUNITY HEATH CARE PROFESSIONAL

Patient Identification Number for this trial: | | |

Evaluation of the safety and effectiveness of the global treatment including multilayer compression therapy (Urgo KTwo®) in addition to an interactive dressing (UrgoStart® Plus in the management of venous leg ulcers

PROTOCOL NUMBER: EUS23-4 **IRAS ID: 327680** **PROJECT REF NO: 23/003/GHT**

Practice Nurse / Community Nurse
Email: (insert)

Dear Colleague,

Your patient, ... has been seen by us for the management of his/her venous leg ulcer. As part of a clinical trial protocol, we have invited him/her to participate in a prospective, monocentre clinical trial, which has received a favourable opinion from the South West - Cornwall & Plymouth Research Ethics Committee.

This study evaluates the efficacy and tolerance of a specific procedure composed of a high compression system (Urgo K2) and an interactive wound dressing (UrgoStart Plus) for the local treatment of venous leg ulcers. After informing the patient of the nature of this study and how this study will be conducted and, after obtaining their written informed consent in accordance with Good Clinical Practice, the patient has agreed to participate in the study.

Thus, his/her ulcer should be treated locally with the UrgoStart Plus Pad, in combination with the Urgo K2 multilayer compression system. The treatment period is 12 weeks during which five clinical evaluations are scheduled by our team; at the initial visit (Day 0) and at the follow-up visits Week 2/ Week 4/Week 8 and Week 12.

Therefore, in between clinical assessments, we would appreciate it if you would carry out the care of the patient's ulcer according to the protocol that we have initiated and according to the instructions for use of the compression system given to him/her and the UrgoStart Plus Pad, used as a primary dressing.

In accordance with the protocol of this study, any modification or discontinuation of the trial treatment must be initiated by the investigating centre and any serious adverse event

(hospitalization, life-threatening event...) occurring during the study should be documented by our investigating centre.
Thus, we would also be grateful if you could inform us as soon as possible of any event relating to the treated lesion which you feel may compromise the follow-up of the treatment.

This clinical study does not involve any foreseeable risk for your patient, the expected benefit is an improvement in the condition of his/her ulcer which will result in a reduction of the surface area of the ulcer or even in its complete closure, and in a shorter period of time.
We thank you very much for your active participation in this clinical study. Please do not hesitate to contact me if you require any further information.

Yours faithfully,

Mr Colin Davies MSc, BSc(Hons) FAETC, NMP, RGN
Clinical Lead (Leg Ulcers) / Associate Lecturer
Gloucestershire Leg Ulcer Service
Unit 5 Pullman Court
Great Western Road
Gloucester
GL1 3ND

Telephone number: 0300 422 3684

**Send as email attachment to Practice Nurse / Community Nurse*

APPENDIX (vii)

LETTER TO THE GENERAL PRACTITIONER

Patient Identification Number for this trial: | | |

Evaluation of the safety and effectiveness of the global treatment including multilayer compression therapy (Urgo KTwo®) in addition to an interactive dressing (UrgoStart® Plus in the management of venous leg ulcers

PROTOCOL NUMBER: EUS23-4 **IRAS ID: 327680** **PROJECT REF NO: 23/003/GHT**

GPs Name
GP Practice
GP Address

Dear Dr (insert name)

Your patient, ..., NHS number: …….. has been seen by us for the management of his/her venous leg ulcer. As part of a clinical trial protocol, we have invited him/her to participate in the above prospective, monocentre clinical trial, which has received a favourable opinion from the South West - Cornwall & Plymouth Research Ethics Committee.

This study evaluates the efficacy of a specific procedure composed of a high compression system (Urgo K2) and an interactive wound dressing (UrgoStart Plus) for the local treatment of venous leg ulcers. After informing the patient of the nature of this study and how this study will be conducted and, after obtaining their written informed consent in accordance with Good Clinical Practice, the patient has agreed to participate in the study.

A copy of the information sheet is enclosed for your information.

If you know of any reason why your patient should not take part in this study – please contact us.

Yours faithfully,

Mr Colin Davies MSc, BSc(Hons) FAETC, NMP, RGN
Clinical Lead (Leg Ulcers) / Associate Lecturer
Gloucestershire Leg Ulcer Service
Unit 5 Pullman Court, Great Western Road
Gloucester GL1 3ND
Telephone number: 0300 422 3684

APPENDIX (viii)

WOUNDQUOL QUALITY OF LIFE QUESTIONNAIRE

Evaluation of the safety and effectiveness of the global treatment including multilayer compression therapy (Urgo KTwo®) in addition to an interactive dressing (UrgoStart® Plus) in the management of venous leg ulcers

PROTOCOL NUMBER: EUS23-4 **IRAS ID: 327680** **PROJECT REF NO: 23/003/GHT**

Wound-QoL-17 questionnaire on quality of life with chronic wounds

With the following questions, we aim to find out how your chronic wound(s) affect(s) your quality of life.

Please tick one box per line !

In the last seven days …		**not at all**	**a little**	**moderately**	**quite a lot**	**very much**
1	…my wound hurt	O	O	O	O	O
2	…my wound had a bad smell	O	O	O	O	O
3	…there was a disturbing discharge from the wound	O	O	O	O	O
4	…the wound has affected my sleep	O	O	O	O	O
5	…the treatment of the wound has been a burden to me	O	O	O	O	O
6	…the wound has made me unhappy	O	O	O	O	O
7	…I have felt frustrated because the wound is taking so long to heal	O	O	O	O	O
8	…I have worried about my wound	O	O	O	O	O
9	…I have been afraid of the wound getting worse or of new wounds appearing	O	O	O	O	O
10	…I have been afraid of knocking the wound	O	O	O	O	O
11	…I have had trouble moving about because of the wound	O	O	O	O	O
12	…climbing stairs has been difficult because of the wound	O	O	O	O	O
13	…I have had trouble with day-to-day activities because of the wound	O	O	O	O	O
14	…the wound has limited my leisure activities	O	O	O	O	O
15	…the wound has forced me to limit my activities with others	O	O	O	O	O
16	…I have felt dependent on help from others because of the wound	O	O	O	O	O
17	…the wound has been a financial burden to me	O	O	O	O	O

"Wound-QoL-17" questionnaire on Health-related Quality of Life in Chronic Wounds | Version English (UK), Augustin et al. 2017, Blome et al. 2014

APPENDIX (ix)

SYNOPSIS OF THE CLINICAL TRIAL

	Inclusion visit Day 0	**Follow-up visits W2 / Week 4 / Week 8**	**Termination before W12, whatever reason**	**End of the study or Week 12**
INVESTIGATOR				
Informed consent	X	-	-	-
Inclusion criteria validation	X	-	-	-
Exclusion Criteria validation	X	-	-	-
Ankle Brachial Pressure Index Vascular Assessment	X*	-	-	-
Wound clinical assessment	X	X	X	X
Measurement of the Wound	X	X	X	X
Photographic record	X	X	X**	X**
PATIENT				
Acceptability	-	X	X	X
Quality of Life Questionnaire	X	-	X	X

**ABPI to be assessed at baseline if not available in the 3 previous months.*

***A photographic record of the treated ulcer will be taken also in case of occurrence of a local adverse event.*