ActiGraft
Instructions for Use

RedDress Ltd.

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EC REP

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CE 0425

1.0 The ActiGraft

1.1 Components

The ActiGraft includes:

1. Blood withdrawal (phlebotomy) kit containing:

- Gloves, nitrile, powder-free
- Tourniquet, 18" length
- Sterile blood draw/infusion set, 21G winged with 7" Tube with holder
- Sterile alcohol pad 2" x 2"
- Gauze pad
- Bandage
- 2 sterile ACDA (each containing 1.5ml of ACDA) vacuum tubes of 8.5ml total volume each for blood collection.

2. Coagulation initiation and accelerator kit (WBC preparation kit) containing:

- 5 mL sterile vial containing 3.6ml of 10% calcium gluconate (manufactured by RedDress Ltd.)
- 30 mL sterile syringe with 18G needle – for puncturing coagulation mold
- 18G Safety needle for blood injection
- Coagulation mold (clotting tray) – a sterile, biocompatible one-size (6cm diameter) blister made of 400µ PETG sealed with a Tyvek cover and sterilized, containing:
  - 28 mg pharmaceutical grade kaolin powder
  - Medical-grade cotton gauze
- A 600 µm PETG biocompatible sterile clot extraction ring
- Face Mask

3. Wound dressing single-use components for topical patient application (provided sterile):

- Gloves, nitrile, powder-free
- Drape

- Gauze
- Non adherent dressing
- Wound measuring aid
- Optifoam
- Tape, Ø .5" circle band-aid.
- Medi-Strip

1.2 Intended Use / Indications for Use

The ActiGraft is intended to be used at point-of-care for the safe and rapid preparation of Whole Blood Clot (WBC) gel from a small sample of a patient's own peripheral blood. Under the supervision of a healthcare professional, the WBC gel produced by the ActiGraft is topically applied for the management of exuding cutaneous wounds, such as leg ulcers, pressure ulcers, diabetic ulcers, and mechanically or surgically-debrided wounds.

1.3 Use of the system

The ActiGraft should be used in conjunction with standard of care procedures for comprehensive wound management such as:

- Removal of necrotic or infected tissue
- Off-loading
- Compression therapy for venous stasis ulcers
- Establishment of adequate blood circulation
- Management of wound infection
- Wound cleansing
- Nutritional support, blood glucose control for subjects with diabetic ulcers
- Bowel/bladder care for subjects with pressure ulcers at risk for contamination
- Management of underlying disease

1.4 Contraindications

The ActiGraft is contraindicated in patients with the following types of wounds:

- wounds due to malignancy
- wounds with active clinically diagnosed infection

1.5 Precautions

- Some blood-contacting components of the ACTIGRAFT have been sterilized by Ethylene Oxide, which can cause serious allergic reactions in some sensitized individuals.
- Throughout the processing and application of ActiGraft, use universal precautions as defined by the facility policy and procedure manual. All parts of the procedure shall be performed in such a manner as to minimize splashing, spattering, and generation of potential droplets.
- Calcium gluconate should only be used with ACTIGRAFT kit
- Calcium gluconate (Preservative Free): Use only if solution is clear and seal intact.

- Calcium Gluconate Note: Supersaturated solutions are prone to precipitation. The precipitate, if present, may be dissolved by warming the vial to 60C to 80C, with occasional agitation, until the solution becomes clear. Shake vigorously. Allow to cool to room temperature before dispensing. Use Calcium Gluconate only if clear immediately prior to use.

1.6 Pre-Clinical Investigations

A pre-clinical study was performed, to evaluate the safety and efficacy of RD1 on wound healing when repeatedly applied to full thickness dermal wounds in pigs. Given the shared indications and principles of operation, and very similar technological characteristics, between the ACTIGRAFT and RD1 Systems, the results apply equally to the ActiGraft. Four healthy and previously unused pigs were selected. Six full thickness dermal wounds were created on each pig, 3 on each side. The wounds on 3 pigs (18 wounds) were treated with the whole blood clot matrix produced by the RD1 System, and the wounds on one pig (6 wounds) were treated with a control (saline-soaked gauze). The treatment duration was 18 days, with re-applications occurring on days 6 and 12. *Results:* A significantly higher percentage of wound area reduction was observed on day 18 in the RD1 wounds (66%) compared to 41% in the control wounds ($p<0.0001$). Greater re-epithelialization was also observed in the RD1 intervention group. No product-related adverse findings were observed. Kaolin could not be differentiated microscopically in the wound beds.

1.7 Clinical Investigations

RedDress conducted two prospective clinical studies to evaluate the safety and clinical performance of the RD1 System output for the management of various chronic wounds. The clinical evidence is equally applicable to support the safety and effectiveness of the ActiGraft for the same intended use, given the similarities between the devices.

Study 1: This prospective, open-label, and uncontrolled study evaluated the safety and clinical performance of RD1 in the treatment of chronic wounds. The study included 9 lower-body wounds in seven patients with multiple and serious comorbidities, including three venous ulcers, four pressure ulcers, one tear wound and one amputation wound. The wounds were 4 to 12 weeks in duration, from 0.9 to 28.1 cm^2 in size, and had not responded to previous treatments. Patients were treated weekly with RD1 for 9 weeks, or until healing was complete. Efficacy: Seven of the 9 wounds healed completely (77%) during the nine weeks of the study period. In 1 venous ulcer with a non-healing fistula, 76% wound closure was achieved. One pressure ulcer treatment was terminated at 82% wound closure, because an unexpected mechanical trauma resulted in deterioration. Safety: Across the 30 RD1 procedures and applications performed, there were no blood draw related adverse events (AEs), and there was only 1 non-related AE, that of the patient who had mechanical trauma.

Study 2: A prospective, open-label, uncontrolled study evaluated the safety and efficacy of RD1 in treatment of chronic diabetic foot ulcers at three wound care clinics in the U.S. Forty-one subjects with diabetic foot ulcers (DFUs) were screened for two weeks. 20 subjects with 20 DFUs were enrolled at 3 sites beginning in June 2014. Wounds treated weekly for up to 12 weeks with the RD1 device in addition to standard of care (debridement, offloading, and infection management).

Four subjects had to discontinue the intervention due to ulcer deterioration or infection, and 2 subjects were not compliant with the protocol. This resulted in 20 subjects for the ITT (intent-to-treat) analysis and 18 for the PP (per protocol) analysis.

Wounds included UT grade 1 (75%), located on the foot (60%), and new (70%). Mean wound age was 36.4 weeks, and mean initial area and depth were 2.5 cm^2 and 2.4 mm, respectively. Eighty-five percent of all wounds were debrided on the first day of screening, and wounds were debrided an average of 4.9 times during treatment. 149 complete RD1 procedures were performed on the 20 wounds during the study. Safety: There were a total of 32 AEs, of which 2 were serious adverse events (SAEs) and 2 were device-related adverse events (DRAEs). The 2 SAEs were not related to the device or study wounds. The 2 DRAEs were possibly device-related AEs, determined as such due to location of AE, in the same subject involving a left hallux infection with subsequent increased pain involving the same hallux and foot. There were no complications involving venous access either in the preparation of the RD1 or for other procedures. The mean AE rate for both ITT and PP populations was 1.6. With respect to severity, 21 AEs were classified as mild (65%), 9 (29%) as moderate, and 2 (6%) as severe. In the ITT population, 4 out of 20 subjects (20%) were impacted in regard to use of the RD1 device by AEs; in 3 subjects this resulted in device discontinuation, and in 1 subject it resulted only in an interruption. Efficacy: The proportion of wounds healed in the ITT and PP populations was 13/20 (65%) and 13/18 (72%), respectively. There were 4 ulcer recurrences following initial healing, with 2 occurrences resulting in unhealed wounds (same for both ITT and PP populations). Mean time to heal was 59 days in the ITT population and 56 days in the PP population. Percentage wound area reduction (PAR) for the ITT population at 4 and 12 weeks was 61.3% and 66.6%, respectively; the figures for the PP population were comparable at 4 weeks but better at 12 weeks: 60.0% and 76.1%, respectively.

2.0 ACTIGRAFT Preparation

Follow the instructions below to use the ActiGraft:

1. Mark patient name on the Kit.
2. Measure the ulcer/wound maximal length (edge to edge) using the tape.
3. Open the ActiGraft cardboard box.
4. Draw patient blood using the gloves, tourniquet, sterile alcohol pad, sterile blood draw/infusion set, IV butterfly needle, and 2 vacuum tubes; after blood withdrawal, place a gauze pad and bandage over the phlebotomy site on the patient's skin.
   Note – Blood withdrawal and handling should be performed according to standard blood withdrawal precaution guidelines.
5. Document patient details and time of draw on the vacuum tubes.
6. Place the vacuum tubes back into the kit.
7. When you are ready to re-initiate the coagulation process, continue;
8. Make sure the ActiGraft Kit box is horizontal.
9. Pierce the Coagulation Mold with the syringe and needle twice, next to the upper center – the first puncture will serve for blood injection and the second puncture will serve as an outlet for air when you inject blood into the Coagulation Mold.

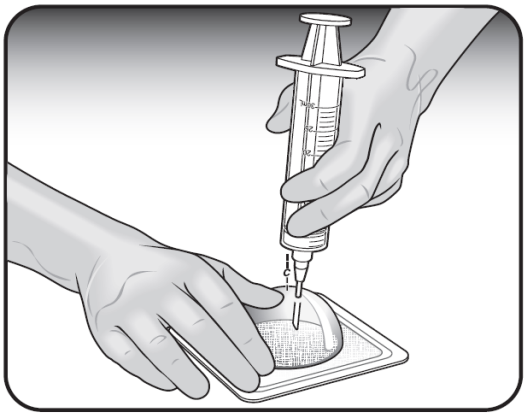


Figure 1 – Pierce a hole with the needle next to the upper center of the Coagulation Mold

10. Mix gently each of the 2 tubes containing blood.
11. Change the needle on the syringe to a safety needle.
12. Wear a face mask
13. Draw the blood from the 2 tubes into the 30 ml syringe.
14. Draw the whole content of the Calcium Gluconate into the syringe containing the blood.
15. Insert the needle to one of the existing pierced holes in the blister in the central top hub.

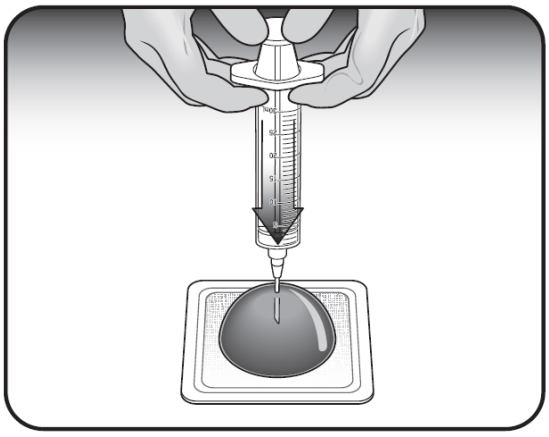


Figure 2 – Inserting the needle to existing pierced hole in the center to inject the blood

16. inject the blood into the coagulation blister slowly.
17. Assure air is coming out of the blister via the puncture hole as you inject the blood to prevent rupture of the inner seal by pressure.
18. After injection of blood, clean the pierced hub and adhere the round sterile band aid over the pierced hub to prevent leakage.
19. Mix the blood with the Kaolin by shaking and turning the coagulation blister.
20. Place the Blister back in the Kit assuring it is horizontal.
21. Wait minimum 12 minutes for complete coagulation to occur.
22. Tilt the blister to ensure the blood has coagulated.
23. Turn over the blister to open it.
24. Open first only the outer square seal all around the blister – do not open the round seal with the gauze.

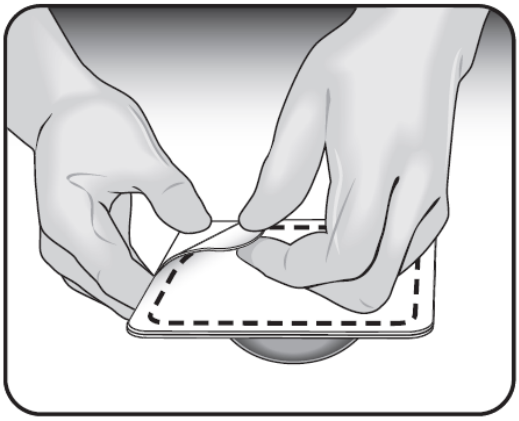


Figure 4 – First open only the outer square seal – marked with dotted line in the picture

25. Only after completely opening the square outer seal you may begin to open the round seal.
26. Hold the gauze firmly to the transparent blister while pulling the white Tyvek paper, all around the circle seal.

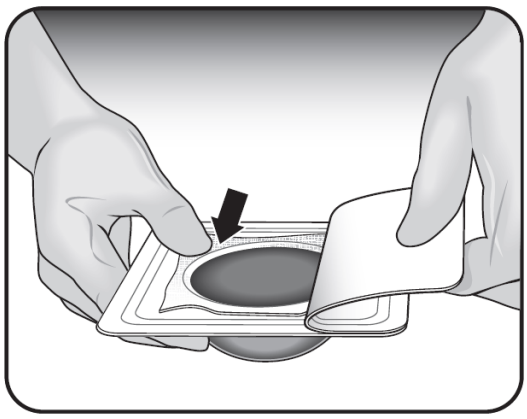


Figure 5: Open the inner round seal Tyvek while holding the gauze in place

27. Once the Tyvek paper is completely removed, the gauze should still be adhered to the blister all around the circle seal.
28. Use the clot extraction ring to push the gauze closely to the seal to release it; press the extraction ring all around assuring all gauze edges are released from the blister seal.

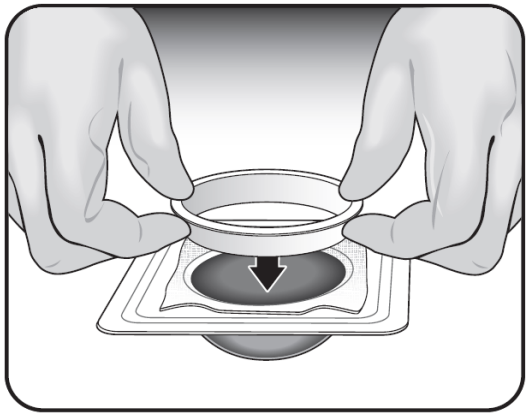


Figure 6: Press the extraction ring down over the WBC

29. The ActiGraft Whole Blood Clot (WBC) is now resting inside the blister, ready for application.

Handling and placing the WBC:

30. Wear sterile gloves.
31. Gently remove the WBC from the clotting tray by holding it from its rim. Use both hands.
32. Place the WBC over the wound with the embedded gauze facing upwards (distal).
33. The WBC may be shaped, if needed, by cutting it with sterile scissors. Cutting should be performed on the tray or while being held in the gloved hand.

Note: Make sure that the ActiGraft is large enough to cover the entire wound, extending at least as far as the wound edges.

Affixing the WBC:

34. Anchor the WBC to the wound by its rim with a sterile adhesive Curad Medi-Strips; you may place Medi-Strips over the WBC itself.

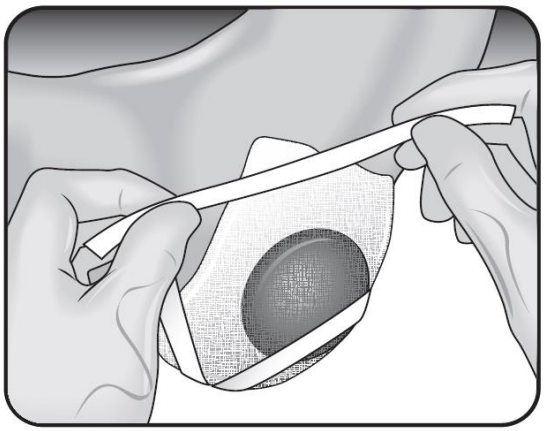


Figure 7- Affixing the WBC.

35. Place a primary non-adherent dressing supplied in the ACTIGRAFT kit over the WBC and over the Medi-Strips.
36. Place the Optifoam (secondary absorbent foam dressing) supplied in the ACTIGRAFT kit over the non-adherent dressing.

WBC Removal (after approximately 7 days):

37. Wear sterile gloves.
38. Remove the remaining WBC by pulling it gently off the wound.
39. In case of adhesions, wet the WBC with saline to facilitate gentle removal.
40. Discard the remaining WBC properly.

3.0 Storage Conditions

Store in the original container at a controlled room temperature of 15°C (59°F) – 25°C (77°F). Protect from freezing and avoid excessive heat.

4.0 Shelf Life

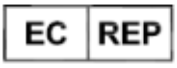
1 Year from date of manufacturing

5.0 Disposal instructions

Dispose of all blood, tools, needles and materials according to local requirements.

6.0 Symbols Glossary

The following symbols are used in the labels/labeling for the ActiGraft, in accordance with ISO 7000, *Graphical Symbols for use in equipment – Registered symbols* and ISO 15223-1, *Medical devices – Symbols to be used with medical device labels – General requirements.*

Symbol	Description	Symbol	Description
	Manufacturer		Do not use if package is damaged
	Authorized representative in the European Community		Fragile, handle with care
	Date of Manufacture		Keep away from sunlight
	Use-By Date		Keep dry
	Batch Code		Temperature limit
	Catalogue Number		Do not re-use
	Serial Number		Consult instructions for use
	Sterile		Prescription Use Only
			Caution