ActiGraft Pro Instructions for Use

ActiGraft PRO
Autologous Wound Care System

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⚠ **Caution: Federal Law (U.S.A.) restricts this device to sale by or on the order of a Physician.**

1.0 The ActiGraft Pro

1.1 Components

The ActiGraft Pro Box includes:
1. Blood withdrawal (phlebotomy) components:

- 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
- 1 sterile 16ml ACDA vacuum tube for blood collection

2. Coagulation initiation and accelerator kit containing:

- 30 mL sterile syringe
- Coagulation mold punch tool
- 18 G safety needle for blood transfer
- Coagulation mold (clotting tray) – a sterile, biocompatible one-size (6cm diameter) blister made of 400µ PETG sealed with a Tyvek cover and sterilized, containing:
  - 85 mg calcium gluconate powder
  - 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):

- Drape
- Gauze
- Non adherent dressing
- Hydrophilic foam dressing
- Tape, Ø .5" circle band-aid.
- Medi-Strips

1.2 Product Information

ActiGraft Pro is an autologous blood derived product for chronic, non-healing wounds (including diabetic wounds) which constructs a whole blood clot (WBC) gel that contains whole cells: white cells, red cells, plasma, platelets, fibrin, stem cells, and fibrocyte precursors. The gel is used by physicians in clinical settings to treat chronic, non-healing wounds, open cutaneous wounds, and soft tissue. The procedure includes administration, dressings, phlebotomy, mixing, and other preparatory procedures, per treatment.

1.3 Intended Use/Indications for Use

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

1.4 Use of the System

The ActiGraft Pro 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 and blood glucose control for subjects with diabetic ulcers
- Bowel/bladder care for subjects with pressure ulcers at risk for contamination
- Management of underlying disease

1.5 Contraindications

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

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

1.6 Precautions

- Some blood-contacting components of the ActiGraft Pro have been sterilized by Ethylene Oxide, which can cause serious allergic reactions in some sensitized individuals.
- Throughout the processing and application of ActiGraft Pro, 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.
- If a patient complains of an increase in pain in the days following ActiGraft Pro application, even if the clot is complete and intact, consider removing the clot to expose the wound and investigate for potential infection in the wound or in the surrounding areas.

1.7 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.

1.8 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 cm2 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 were 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%). The mean wound age was 36.4 weeks, and mean initial area and depth were 2.5 cm2 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 regarding the 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). The 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 Pro Preparation

Follow the instructions below to use the ActiGraft Pro:

1. Mark the box with the patient's name.
2. Measure the ulcer/wound maximal length (edge-to-edge) using the tape.
3. Open the ActiGraft Pro cardboard box.
4. Lightly shake/gently agitate the anticoagulant fluid inside the ACDA tube before drawing blood to allow the fluid to cover the inside of the tube.

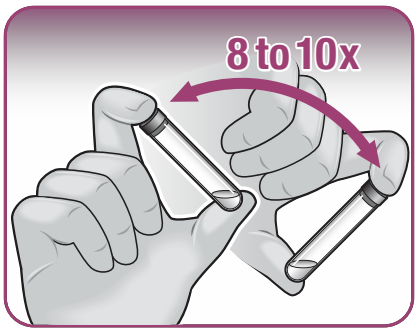


Figure 1: Lightly agitate the ACDA tube before drawing blood

5. Using gloves, tourniquet, sterile alcohol pad, sterile blood draw/infusion set, and IV butterfly needle, draw patient blood into the vacuum tube containing anticoagulant (ACDA). 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.

6. Lightly shake/gently agitate the tube **IMMEDIATELY** after blood collection to allow adequate mixing with the anticoagulant in the tube. Not doing so, or inadequate mixing may result in partial clotting of blood that will impact blood transfer into the mold.

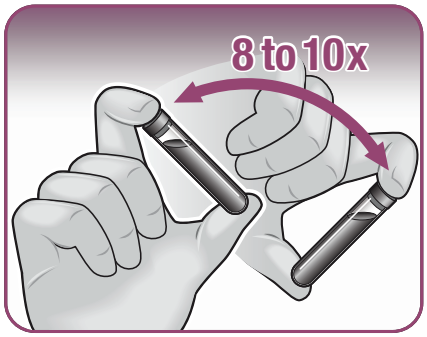


Figure 2: Gently agitate the ACDA tube immediately after blood draw

7. Document patient details and time of draw on the vacuum tube.
8. Make sure the ActiGraft Pro box is kept horizontal.
9. Remove the Coagulation Mold punch tool cover and pierce the coagulation mold once, next to the upper center.

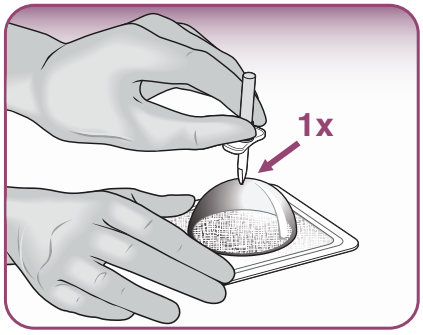


Figure 3: Pierce blister once with Coagulation Mold Punch Tool for air outlet

10. Discard the coagulation mold punch tool after puncturing the coagulation mold once.
11. Gently mix the vacuum tube containing blood.
12. Wear a face mask.
13. Attach a safety needle to the syringe.

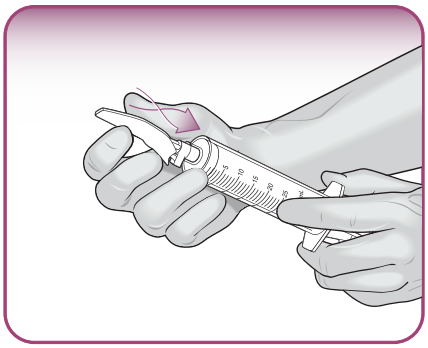
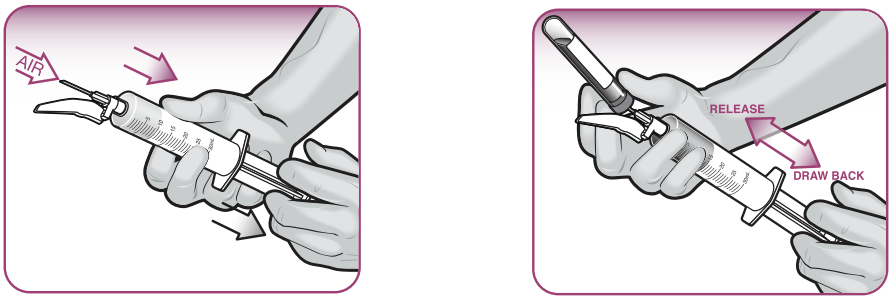


Figure 4: Attach safety needle to the syringe

14. Draw the blood from the tube into the 30 ml syringe using these instructions:
    a. Draw 10ml of air into the syringe before inserting the needle to the ACDA tube.
    b. Insert the needle to the tube half-way only and not all the way.
    c. The tube should be facing up and the syringe down when drawing the blood.
    d. Start pulling and releasing the syringe plunger to draw the blood from the tube.
    e. Do not push the plunger forward, do not apply positive pressure into the ACDA tube.
    f. When blood draw is complete, hold the plunger in a pull position and extract the needle.



Draw 10ml of Air beforehand Pull & release the plunger to draw blood

Figure 5: Blood draw from ACDA tube instructions

15. Transfer the blood into the coagulation mold: Insert the needle to the existing pierced hole in the blister in the central top hub.

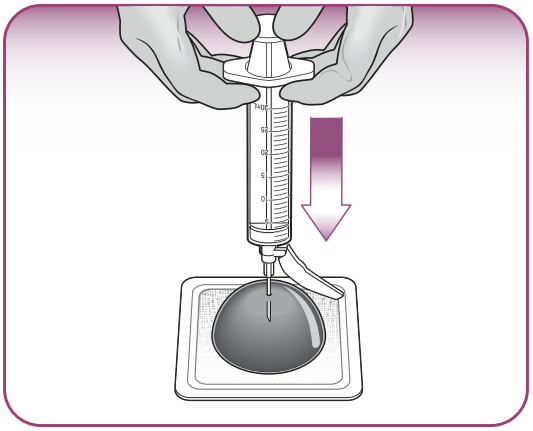


Figure 6: Inject blood through the existing coagulation mold hole

16. Ensure 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.
17. After injection of blood, clean the pierced hub and adhere the round sterile band aid over the pierced hub to prevent leakage.
18. Mix the blood with the Kaolin and Calcium gluconate for at least 20 seconds by shaking and turning the coagulation mold.
19. Place the coagulation mold on a surface assuring it is horizontal.
20. Wait for a minimum of 5 minutes for complete coagulation to occur.
21. Tilt the coagulation mold to ensure the blood has coagulated.
22. Turn over the Coagulation Mold to open it.
23. First open only the outer square seal all around the coagulation mold– do not open the round seal with the gauze.

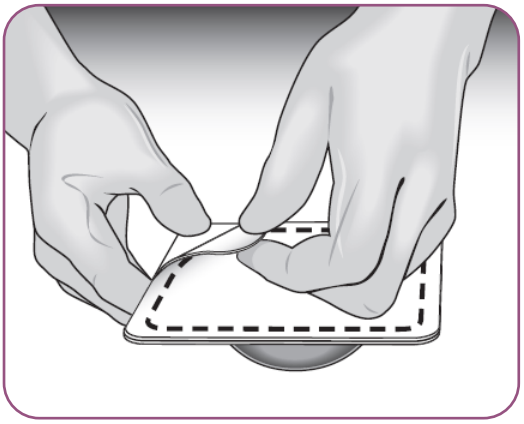


Figure 7: Open only the outer square seal first – marked with dotted line in the figure above

24. Completely open the square outer seal first before you begin to open the round seal.
25. Hold the gauze firmly to the transparent part while slowly and gradually pulling the white Tyvek paper, all around the circle seal.

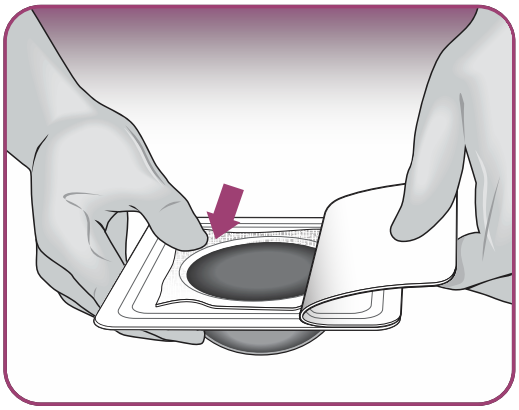


Figure 8: Open the inner round sealTyvek while holding the gauze in place

26. Once the Tyvek paper is completely removed, ensure the gauze is still adhering to the coagulation mold all around the circle seal.
27. 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 coagulation mold seal. Some Calcium gluconate powder may be visual on the clot's back surface.

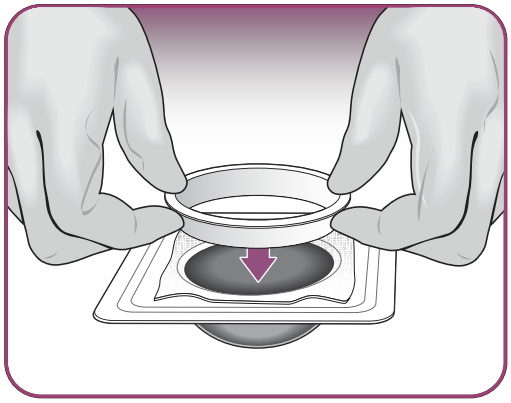


Figure 9: Press the extraction ring down over the clot

28. The ActiGraft Pro Whole Blood Clot (WBC) is now resting inside the coagulation mold, and is ready for application.

Handling and Applying the WBC:

29. Wear sterile gloves.
30. Gently remove the WBC from the clotting tray by holding it from its rim. Use both hands.
31. Place the WBC over the wound with the embedded gauze facing upwards (distal).
32. 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 WBC is large enough to cover the entire wound, extending at least as far as the wound edges.

Affixing the WBC:

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

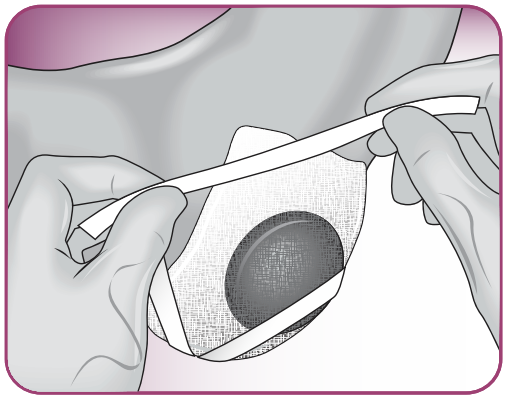


Figure 10: Affixing the WBC

34. Place a primary non-adherent dressing supplied in the ActiGraft Pro box over the WBC and the Medi-Strips.
35. Apply the Hydrophilic foam dressing (secondary absorbent foam dressing) supplied in the ActiGraft Pro box over the non-adherent dressing.

WBC Removal (after approximately 7 days):

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

3.0 Storage Conditions

Store in the original container at a controlled room temperature of 5°C (41°F) – 30°C (86°F). Protect it from freezing and avoidexcessive heat.

4.0 Disposal instructions

According to labels

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 Pro, 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
EC REP	Authorized representative in the European Community		Fragile, handle with care
	Date of Manufacture		Keep away from sunlight
LOT	Use-By Date		Keep dry
LOT	Batch Code		Temperature limit
REF	Catalogue Number		Do not re-use
SN	Serial Number		Consult instructions for use
STERILE	Sterile	Rx only	Prescription Use Only
			Caution