QuikClot® INTERVENTIONAL®

Instructions for Use

Manufactured by:
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Patents: Z-Medica.com/patents.aspx

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CE
2797

EC REP
Emergo Europe
Prinsessegracht 20
2514 AP
The Hague
The Netherlands

Rx ONLY

REF 183

Please contact Z-Medica Customer Service to determine if this product is available for sale in your market / country.

Description
QuikClot® Interventional® consists of a pad to be used in conjunction with 3M Tegaderm™ adhesive bandage or equivalent. The pad is a soft, white, sterile, hydrophilic hemostatic dressing and is packaged for aseptic removal. This product contains kaolin.

Indications
QuikClot Interventional is applied topically as an adjunct to manual compression and is indicated for the local management and control of surface bleeding from vascular access sites, percutaneous catheters or tubes utilizing introducer sheaths up to 12 Fr. or up to 7 Fr. for patients on drug/induced anti-coagulation treatment.

Contraindications
QuikClot Interventional has not been tested on patients with bleeding disorders due to underlying disease (liver, kidney, or others) and is not indicated for these populations.

Warnings
QuikClot Interventional has been tested in clinical trials and its efficacy has been shown only in patients treated with anticoagulation medications: heparin, clopidogrel bisulfate and warfarin. The efficacy of QuikClot Interventional in the presence of other anticoagulation medications is not known.

Precautions
- For external use only
- Sterility not guaranteed if package is damaged or opened
- Discard if package is damaged
- Avoid contact with eyes
- Use aseptic techniques
- Do not re-sterilize
- Reuse will cause risk of infection and loss of efficacy
- Longer compression time may be required for patients who are hypertensive, obese, or on drug-induced anticoagulant therapies

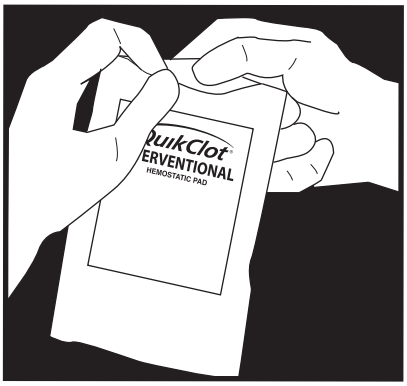
Storage Conditions
Keep dry. Keep from heat (including storage in direct sunlight or in direct contact with heat sources). Store at temperatures of 77° (25°C) or less.

Rx ONLY means prescription use only

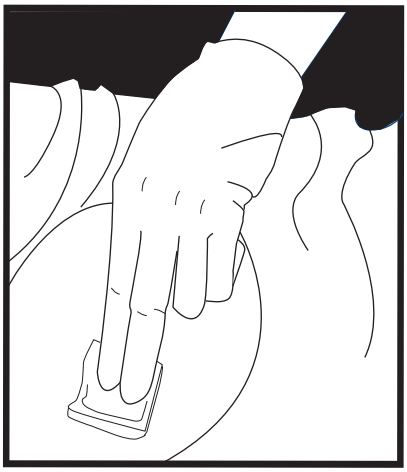
SBS means sterile barrier system

MD means medical device

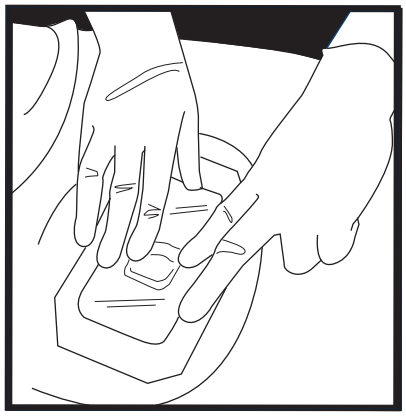
Instructions for Use



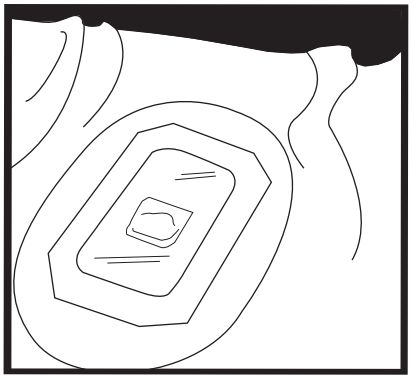
(1) Remove hemostatic pad from packaging and place pad into sterile field, using aseptic technique. Do not wet the pad with saline before using it.



(2) Place the hemostatic pad on the puncture site. Apply manual compression on the pad for at least 5 minutes or until bleeding stops. Note: Arterial punctures using large dilators will require longer manual compression time. Following placement of the hemostatic pad, health care professionals are encouraged to continue to use the standard of care at their institution regarding site care, time to ambulation and time to patient discharge.



(3) Without moving or lifting the pad, apply Tegaderm adhesive bandage or equivalent over pad while maintaining manual compression on the pad. Secure adhesive bandage to skin.



(4) The hemostatic pad should be changed every 24 hours or more often, if required. To change bandage, gently peel away adhesive bandage and gently remove pad.

PRECLINICAL DATA

Animal testing has been performed to demonstrate compatibility of the QuikClot and drug/induced anticoagulant therapy.

<table>
<tr><td>Study Name/Description</td><td>Pre-clinical evaluation of QuikClot in an anticoagulated swine model.</td></tr>
<tr><td>Objective</td><td>To evaluate the efficacy of kaolin, the active ingredient in Z-Medica's QuikClot in controlling bleeding in animals treated with common drugs such as Coumadin and Plavix.</td></tr>
<tr><td>Number of sites/investigators (OUS/US)</td><td>One site (US) and one investigator.</td></tr>
<tr><td>Number of animals/wounds</td><td>Ten pigs were divided in 2 groups (five animals each):
One group received Plavix at 75 mg/day orally for > 5 days. The second group received daily doses of Coumadin until INR was > 3.
187 intra-abdominal vascular injuries (splenic, liver and mesenteric) were tested. Injuries consisted of surgically inflicted wounds with mixed arterial and venous bleeding. The size of the wounds were 5 cm in length and 3-5 mm in depth for liver and spleen and 2 mm of depth for the mesentery.</td></tr>
<tr><td>Procedure</td><td>In combination with manual pressure, QuikClot was applied to a series of wounds to the liver, spleen, mesentery and femoral artery and compared to standard surgical gauze. The study was prospective, open label, randomized 1:1 between QuikClot and control.
Manual compression was applied over the wounds for 5 minutes and then released.</td></tr>
<tr><td>Success/Failure criteria</td><td>Success = complete bleeding cessation within 5 minutes.
Failure = persistent bleeding at 5 minutes.</td></tr>
<tr><td>Study results</td><td>Animals treated with Coumadin and QuikClot showed successful control of bleeding in 94.5% of wounds. Animals treated with Coumadin and control gauze showed control of bleeding in 24% of wounds.
Animals treated with Plavix and QuikClot showed successful control of bleeding in 91.2% of wounds. Animals treated with Plavix and control gauze showed control of bleeding in 29.7% of wounds.
QuikClot versus Control in Coumadin treated Pigs (n=5)
<table>
<tr><td></td><td>Pass</td><td>Fail</td><td>Total</td></tr>
<tr><td>Test</td><td>52</td><td>3</td><td>55</td></tr>
<tr><td>Control</td><td>9</td><td>29</td><td>38</td></tr>
<tr><td></td><td></td><td></td><td>93</td></tr>
</table>
QuikClot versus Control in Plavix treated Pigs (n=5)
<table>
<tr><td></td><td>Pass</td><td>Fail</td><td>Total</td></tr>
<tr><td>Test</td><td>52</td><td>5</td><td>57</td></tr>
<tr><td>Control</td><td>11</td><td>26</td><td>37</td></tr>
<tr><td></td><td></td><td></td><td>94</td></tr>
</table></td></tr>
<tr><td>Adverse events</td><td>No animals died because of bleeding. The wounds where QuikClot did not control bleeding completely within 5 minutes required some additional manual compression time to achieve hemostasis.</td></tr>
</table>

CLINICAL DATA

Several peer reviewed clinical publications support the use of QuikClot in human patients on drug/induced anticoagulant therapy.

<table>
<tr><td>Study Name/Description</td><td>Trabattoni D, et al. A New Kaolin-based Hemostatic Bandage Use after Coronary Diagnostic and Interventional Procedures. Int J Cardiol. 2012;156(1):53-54.</td></tr>
<tr><td>Number of sites/investigators (OUS/US)</td><td>One site (OUS) and three investigators.</td></tr>
<tr><td>Number of subjects</td><td>40 subjects</td></tr>
<tr><td>Inclusion/Exclusion</td><td>Patients undergoing diagnostic angiography or Percutaneous Coronary Intervention (PCI) via a femoral artery approach.
Exclusion not described in publication.</td></tr>
<tr><td>Procedure</td><td>Prospective single arm pilot trial of QuikClot in cardiac catheterization.
Introducer sheath size 6 Fr (90%) or 7 Fr (10%).
Femoral artery sheath removed once the ACT < 180 seconds.
All patients were treated with QuikClot after arterial sheath removal.</td></tr>
<tr><td>Study endpoints and assessment protocol</td><td>Complete bleeding cessation at 5 minutes and safe ambulation at 4 hours.</td></tr>
<tr><td>Duration of follow-up</td><td>30 days</td></tr>
<tr><td>Patient demographics</td><td>75% male, age 68+/-11 years</td></tr>
<tr><td>Patient condition</td><td>Patient undergoing diagnostic angiogram (62%) or PCI (38%) via femoral artery approach using 6F (90%) or 7F (10%) sheath.
<table>
<tr><td></td><td>QuikClot (n=40)</td></tr>
<tr><td>LMW Heparin</td><td>2.5%</td></tr>
<tr><td>Aspirin + Clopidogrel</td><td>27.5%</td></tr>
<tr><td>Aspirin</td><td>60%</td></tr>
<tr><td>Aspirin + Warfarin</td><td>5%</td></tr>
<tr><td>IV Heparin</td><td>38%</td></tr>
<tr><td>No anticoagulation</td><td>5%</td></tr>
</table></td></tr>
<tr><td>Study results</td><td>Mean ACT value at hemostasis 138 ± 24 sec (range 95-186 sec).
Mean cumulative hemostasis time 4.9±1.05 min.
Diagnostic procedures 4.2±0.9 min.
Interventional procedures 5.3±0.95 min.
Ambulation time 4 h for all patients.</td></tr>
<tr><td>Adverse events</td><td>One PCI patient required extra compression time to achieve hemostasis and developed a small (< 5cm) hematoma.</td></tr>
</table>

CLINICAL DATA

<table>
<tr><td>Study Name/Description</td><td>Politi L, et al. Randomized Clinical Trial on Short-Time Compression with Kaolin Filled Pad: A New Strategy to Avoid Early Bleeding and Subacute Radial Artery Occlusion after Percutaneous Coronary Intervention. J Internat Card. 2011; 24(1):65-72.</td></tr>
<tr><td>Number of sites/investigators (OUS/US)</td><td>One site (OUS) and ten investigators.</td></tr>
<tr><td>Number of subjects</td><td>120 subjects divided in 3 groups:
Group 1 (QuikClot 15 minute compression, n=50), Group 2 (control – 15 minute compression, n=20), Group 3 (control 2 hour compression, n=50).</td></tr>
<tr><td>Inclusion/Exclusion</td><td>All patients undergoing transradial elective diagnostic or interventional coronary procedures between November 1, 2009 and January 31, 2010.
Abnormal Allen's test before puncture excluded.
Failure to provide written informed consent excluded.</td></tr>
<tr><td>Procedure</td><td>QuikClot was applied to the radial artery over the sheath which was then removed.
Pressure was maintained for 15 minutes and then completely relaxed.</td></tr>
<tr><td>Study endpoints and assessment protocol</td><td>The main end-point was subacute Radial Artery Occlusion (RAO).
The secondary end-point was failure of the closure technique (death, MI or major bleeding occurring in hospital).
Groups 1 and 2: 15 minute assessment for bleeding.
Group 3: 2 hour assessment for bleeding.
All groups: Radial artery patency assessed at 24 hours using Barbeau's Test.</td></tr>
<tr><td>Duration of follow-up</td><td>Until patient discharge and follow-up visit. Follow-up at 6 months was done for patients who developed RAO.</td></tr>
<tr><td>Patient demographics</td><td>Age (years) Group 1 = 64.16 ± 11.53, Group 2 = 61.30 ± 14.22, Group 3 = 59.72 ± 14.23
Male Group 1 = 37 (74%), Group 2 = 14 (70%), Group 3 = 36 (72%)
Weight (kg) Group 1 = 76.42 ± 11.13, Group 2 = 80.00 ± 14.96, Group 3 = 82.02 ± 13.26</td></tr>
<tr><td>Patient condition</td><td>
<table>
<tr><th></th><th>QuikClot</th><th>Control Group 1</th><th>Control Group 2</th></tr>
<tr><td>Aspirin</td><td>46 (92%)</td><td>19 (95%)</td><td>50 (100%)</td></tr>
<tr><td>Clopidogrel</td><td>10 (20%)</td><td>2 (10%)</td><td>11 (22%)</td></tr>
<tr><td>LMW Heparin</td><td>8 (16%)</td><td>5 (25%)</td><td>5 (10%)</td></tr>
<tr><td>Warfarin</td><td>6 (12%)</td><td>5 (25%)</td><td>5 (10%)</td></tr>
<tr><td>IV heparin</td><td>100%</td><td>100%</td><td>100%</td></tr>
<tr><td>No anticoagulation</td><td>0%</td><td>0%</td><td>0%</td></tr>
<tr><td colspan="4">Several patients received multiple therapies</td></tr>
</table>
</td></tr>
<tr><td>Study results</td><td>While a total of 150 patients were planned to be enrolled, the study stopped enrolling group 2 subjects after the 20th patient due to unethically high rates of bleeding.
None of the patients enrolled in Group 1 (QuikClot) developed RAO the main outcome variable.
Among patients enrolled in Group 2, RAO occurred in 1 case (5%) and among Group 3 in 5 cases (10%).</td></tr>
<tr><td>Adverse events</td><td>Active bleeding after compression removal:
Group 1: 10 patients (20%)
Group 2: 18 (90%)
Group 3: 1 (2%)
In all cases, hemostasis was achieved with a supplementary compression for 2 hours that did not produced any RAO in Group 1.</td></tr>
</table>

CLINICAL DATA

<table>
<tr><td>Study Name/Description</td><td>Trabattoni D, et al. A New Kaolin-based Haemostatic Bandage Compared with Manual Compression for Bleeding Control after Percutaneous Coronary Procedures; Eur Radiol, 2011 Aug 21(8): 1687-91.</td></tr>
<tr><td>Number of sites/investigators (OUS/US)</td><td>One site (OUS) and six investigators.</td></tr>
<tr><td>Number of subjects</td><td>200 subjects. Prospective randomized trial of QuikClot (n=100) vs. manual compression (n=100)</td></tr>
<tr><td>Inclusion/Exclusion</td><td>Undergoing angiography or Percutaneous Coronary Intervention (PCI)via a femoral approach.
Patients with baseline INR > 1.4 excluded.
Patients who had previous arterial access at the same femoral site within 30 days excluded.</td></tr>
<tr><td>Procedure</td><td>Femoral arterial sheath removed once the ACT < 180 seconds.
Patients randomized to receive QuikClot or manual compression after femoral sheath removal.
Patient ambulation at 4 hours.</td></tr>
<tr><td>Study endpoints and assessment protocol</td><td>Complete bleeding cessation at 5 minutes and safe ambulation at 4 hours.</td></tr>
<tr><td>Duration of follow-up</td><td>30 days</td></tr>
<tr><td>Patient demographics</td><td>Male 70% QuikClot vs. 60% control.
Mean age (years) 65.7±13 QuikClot vs. 73.6±6.2 control.
Weight (kg) 73.9±12 QuikClot vs. 71.2±15 control.
Diagnostic procedure (n=98) or PCI (n=102).
Introducer sheath size 6 Fr (90%) or 7 Fr (10%).</td></tr>
<tr><td>Patient condition</td><td>
<table>
<tr><td></td><td>QuikClot</td><td>Control</td></tr>
<tr><td>LMW Heparin</td><td>4%</td><td>2%</td></tr>
<tr><td>Aspirin + Clopidogrel</td><td>29%</td><td>26%</td></tr>
<tr><td>Aspirin</td><td>60%</td><td>60%</td></tr>
<tr><td>Aspirin + Warfarin</td><td>7%</td><td>3%</td></tr>
<tr><td>IV Heparin</td><td>51%</td><td>49%</td></tr>
<tr><td>No anticoagulation</td><td>0%</td><td>9%</td></tr>
</table>
</td></tr>
<tr><td>Study results</td><td>Mean ACT value at hemostasis 146 ± 24 sec (range 98 – 198 sec).
Hemostasis with QCI bandage 5.4 ± 1.5 min.
Hemostasis with manual compression 25 ±15 min, p<0.001.
No hemostasis failure in either group.</td></tr>
<tr><td>Adverse events</td><td>Major Bleeding: 1 patient in each group.
Haematoma > 5 cm: 1 patient* QuikClot vs. 2 patients control.
Pseudoaneurysm: 1 patient* QuikClot vs. 1 patient control.
*Same patient</td></tr>
</table>