

**PREVENA PLUS[™] 125 THERAPY UNIT WITH
PREVENA PLUS[™] 150ML CANISTER AND
ACCESSORIES**

**INSTRUCTIONS FOR USE
FOR CLINICIANS ONLY**

DISCLAIMER OF WARRANTY AND LIMITATION OF REMEDY

KCI HEREBY DISCLAIMS ALL EXPRESS OR IMPLIED WARRANTIES, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, ON THE KCI PRODUCT(S) DESCRIBED IN THIS PUBLICATION. ANY WRITTEN WARRANTY OFFERED BY KCI SHALL BE EXPRESSLY SET FORTH IN THIS PUBLICATION OR INCLUDED WITH THE PRODUCT. UNDER NO CIRCUMSTANCES SHALL KCI BE LIABLE FOR ANY INDIRECT, INCIDENTAL, OR CONSEQUENTIAL DAMAGES AND EXPENSES, INCLUDING DAMAGES OR INJURY TO PERSON OR PROPERTY, DUE IN WHOLE OR IN PART TO THE USE OF THE PRODUCT OTHER THAN THOSE FOR WHICH DISCLAIMER OF WARRANTY OR LIMITATION OF LIABILITY IS EXPRESSLY PROHIBITED BY SPECIFIC, APPLICABLE LAW. NO PERSON HAS THE AUTHORITY TO BIND KCI TO ANY REPRESENTATION OR WARRANTY EXCEPT AS SPECIFICALLY SET FORTH IN THIS PARAGRAPH.

Descriptions or specifications in KCI printed matter, including this publication, are meant solely to generally describe the product at the time of manufacture and do not constitute any express warranties except as set forth in the written limited warranty included with this product. Information in this publication may be subject to change at any time. Contact KCI for updates.

TABLE OF CONTENTS

Product Description	5
Indication for Use and Limitations	5
Important Information for Users.....	5
Optimum Use Conditions.....	6
Warnings.....	6
Precautions	7
PREVENA™ Dressing Application Instructions	8
Connecting the PREVENA™ Dressing to the PREVENA PLUS™ 125 Therapy Unit.....	9
PREVENA PLUS™ 125 Therapy Unit Components	9
PREVENA PLUS™ Canister Installation	10
Connecting to a PREVENA™ Dressing with SENSAT.R.A.C.™ Tubing Set	10
Connecting to a PREVENA™ Therapy V.A.C.® Connector and Non SENSAT.R.A.C.™ Dressing	11
Beginning Therapy.....	11
Unit Troubleshooting.....	13
Therapy Life Indicators	13
Duration of PREVENA PLUS™ Therapy	13
Alerts.....	14
Correcting a Leak Condition.....	15
PREVENA CUSTOMIZABLE™ OR PREVENA PLUS CUSTOMIZABLE™ Dressing.....	15
PREVENA PEEL & PLACE™ or PREVENA RESTOR™ Dressing	15
Check Canister Tubing Connection.....	16
Indications That a Leak Condition Has Been Corrected.....	16
Battery Charging.....	17
Canister Removal and Replacement	18
PREVENA PLUS™ 125 Therapy Unit Disposal	18
Instructions for Patients	19
Daily Use	19
Sleeping.....	19
Showering and Bathing	19
Strenuous Activity.....	19
Cleaning.....	19
Warnings and Important Information for Users - PREVENA PLUS™ 125 Therapy Unit	20
PREVENA PLUS™ 125 Therapy Unit Electromagnetic Compatibility	21
Included Power Supplies	26
Customer Contact Information	27

PREVENA PLUS™ 125 Therapy Unit Specifications	27
Summary of Clinical Information.....	28
References.....	45
Bibliography of Published Studies.....	47
Symbols Used	49

INSTRUCTIONS FOR USE PREVENA PLUS™ 125 THERAPY UNIT

KCI CUSTOMER CONTACT INFORMATION IS LOCATED IN THE BACK OF THIS GUIDE.

PRODUCT DESCRIPTION

The PREVENA PLUS™ 125 Therapy Unit, Canister and associated accessories are compatible with PREVENA PEEL & PLACE™ Dressings, PREVENA CUSTOMIZABLE™ Dressings and PREVENA RESTOR™ Dressings.

INDICATION FOR USE AND LIMITATIONS

PREVENA™ 125 and PREVENA PLUS™ 125 Therapy Units manage the environment of closed surgical incisions and remove fluid away from the surgical incision via the application of -125mmHg continuous negative pressure. When used with legally marketed compatible dressings, PREVENA™ 125 and PREVENA PLUS™ 125 Therapy Units are intended to aid in reducing the incidence of seroma; and in patients at high risk for post-operative infections, aid in reducing the incidence of superficial surgical site infection in Class I and Class II wounds.

- The device is not intended to treat surgical site infection or seroma.
- Safety and effectiveness in pediatric population (<22 years old) have not been evaluated.
- Safety and effectiveness in Class III (Contaminated) and Class IV (Dirty/Infected) wounds have not been demonstrated. Furthermore, Class IV surgical wounds are not expected to be closed primarily, and the subject device should only be used on closed surgical incisions.
- The device has not been demonstrated to reduce deep incisional and organ space surgical site infections.
- The device has not been demonstrated to be effective in reducing the incidence of surgical site infection and seroma in all surgical procedures and patient populations; therefore, the device may not be recommended for routine use to reduce the incidence of surgical site infection and seroma.
- Please refer to the 'Summary of Clinical Information' section for the specific surgical procedures and patient populations included in the clinical studies. Surgeons should continue to follow the 'Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection'² and the 'American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines'¹ for best practices in preventing surgical site infection.

Clinical studies have been conducted on KCI Negative Pressure Incision Management Systems. Refer to the **Summary of Clinical Information** and the **Bibliography of Published Studies** in the back of this guide.

IMPORTANT INFORMATION FOR USERS

CAUTION: The PREVENA PLUS™ Incision Management System should be applied and removed only by qualified physicians, nurses or caregivers.

As with any prescription medical device, failure to carefully read and follow all instructions and safety information prior to use may lead to improper product performance and could result in failure of the wound to heal.

PREVENA™ Dressings, Therapy Units, Canisters and accessories are disposable and are for single use only. Re-use of disposable components may result in wound contamination and/or infection.

CAUTION: Do not use the PREVENA PLUS™ 125 Therapy Unit with V.A.C.® Dressings or V.A.C.® Therapy System accessories.

OPTIMUM USE CONDITIONS

For maximum benefit the PREVENA PLUS™ Incision Management System should be applied immediately post surgery to clean surgically closed wounds. It is to be continuously applied for a minimum of two days up to a maximum of seven days. It can transition home with the patient.

The PREVENA PLUS™ Incision Management System will not be effective in addressing complications associated with:

- ischemia to the incision or incision area
- untreated or inadequately treated infection
- inadequate hemostasis of the incision
- cellulitis of the incision area

The PREVENA PLUS™ Incision Management System should not be used to treat open or dehisced surgical wounds.

The V.A.C.® Therapy System should be considered for treatment of these wounds.

The PREVENA PLUS™ Incision Management System should be used with caution in the following patients:

- patients with fragile skin surrounding the incision as they may experience skin or tissue damage upon removal of the PREVENA™ Dressing
- patients who are at an increased risk of bleeding from the incision associated with the use of anticoagulants and/or platelet aggregation inhibitors

WARNINGS

The PREVENA PLUS™ Incision Management System is not intended to manage open or dehisced wounds.

Bleeding: Before applying the PREVENA PLUS™ Incision Management System to patients who are at risk of bleeding complications due to the operative procedure or concomitant therapies and/or co-morbidities, ensure that hemostasis has been achieved and all tissue planes have been approximated. If active bleeding develops suddenly or in large amounts during therapy, or if frank blood is seen in the tubing or in the canister, the patient should leave the PREVENA™ Dressing in place, turn off the therapy unit and seek immediate emergency medical assistance.

Infected Wounds: As with any wound treatment, clinicians and patients/caregivers should frequently monitor the patient's wound, periwound tissue and exudate for signs of infection or other complications. Some signs of infection are fever, tenderness, redness, swelling, itching, rash, increased warmth in the wound or periwound area, purulent discharge or strong odor. Infection can be serious, and can lead to complications such as pain, discomfort, fever, gangrene, toxic shock, septic shock and/or fatal injury. Some signs or complications of systemic infection are nausea, vomiting, diarrhea, headache, dizziness, fainting, sore throat with swelling of the mucus membranes, disorientation, high fever, refractory and/or orthostatic hypotension or erythroderma (a sunburn-like rash). Silver in the interface layer of the PREVENA™ Dressing is not intended to treat infection, but to reduce bacterial colonization in the fabric. If infection develops, PREVENA PLUS™ Therapy should be discontinued until the infection is treated.

Allergic Response: The PREVENA™ Dressing has an acrylic adhesive coating and a skin interface layer with silver, which may present a risk of an adverse reaction in patients who are allergic or hypersensitive to acrylic adhesives or silver. If a patient has a known allergy or hypersensitivity to these materials, do not use PREVENA™ Dressings. If any signs of allergic reaction, irritation or hypersensitivity develop, such as redness, swelling, rash, hives, blisters or significant pruritus, patient should consult a physician immediately. If bronchospasm or more serious signs of allergic reaction appear, the patient should turn off the therapy unit and seek immediate emergency medical assistance.

Defibrillation: Remove the PREVENA™ Dressing if defibrillation is required in the area of dressing placement. Failure to remove the dressing may inhibit transmission of electrical energy and/or patient resuscitation.

Magnetic Resonance Imaging (MRI): All KCI Therapy Units, including the PREVENA PLUS™ 125 Therapy Unit, are MR unsafe. Do not take therapy units into the MR environment. PREVENA™ Dressings can typically remain on the patient with minimal risk in an MR environment. Interruption of PREVENA PLUS™ Therapy during MRI may reduce the effectiveness of PREVENA PLUS™ Incision Management System. PREVENA™ Dressings pose no known hazards in an MR environment with the following conditions of use: static magnetic field of 3 Tesla or less, spatial gradient field of 720 Gauss/cm or less and maximum whole-body-averaged specific absorption rate (SAR) of 3W/kg for 15 minutes of scanning.

Diagnostic Imaging: The PREVENA™ Dressing contains metallic silver that may impair visualization with certain imaging modalities.

Hyperbaric Oxygen Therapy (HBO): Do not take the PREVENA PLUS™ 125 Therapy Unit or PREVENA™ Dressings into a hyperbaric oxygen chamber. They are not designed for this environment and should be considered a fire hazard. If PREVENA PLUS™ Therapy is reinitiated after HBO treatment, do not readhere the same dressing; a new dressing must be applied.

Canister Full: If at any time while using the PREVENA PLUS™ 125 Therapy Unit the canister becomes full of fluid, indicated by a therapy unit alert or visual inspection, the patient should turn off the therapy unit and contact the treating physician for additional instruction.

Standard Operation: Do not use accessories or materials not labeled for use with the PREVENA PLUS™ 125 Therapy Unit. For a list of acceptable dressings with which the PREVENA PLUS™ 125 Therapy Unit may be used, see the **Product Description** section.

PRECAUTIONS

Standard Precautions: To reduce the risk of transmission of bloodborne pathogens, apply standard precautions for infection control with all patients, per institutional protocol, regardless of their diagnosis or presumed infection status.

PREVENA™ DRESSING APPLICATION INSTRUCTIONS

NOTE: While the concomitant use of surgical drains is allowable with the PREVENA PLUS™ Incision Management System, the system must not be used as an outlet or reservoir for the drain.

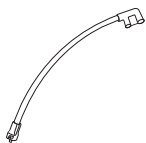
Application instructions for the PREVENA PEEL & PLACE™, PREVENA CUSTOMIZABLE™ and PREVENA RESTOR™ Dressings are provided in the dressing cartons. Refer to those instructions for complete dressing application information.

NOTE: When using PREVENA™ Dressings without a SENSAT.R.A.C.™ Dressing tubing set, the PREVENA™ Therapy V.A.C.® Connector (provided in the dressing pouch or ordered as a separate component) must be used to connect the tubing set to the PREVENA PLUS™ Canister tubing.

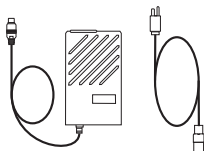
CAUTION: Do not use the PREVENA PLUS™ 125 Therapy Unit with V.A.C.® Dressings or V.A.C.® Therapy System accessories.

CONNECTING THE PREVENA™ DRESSING TO THE PREVENA PLUS™ 125 THERAPY UNIT

PREVENA PLUS™ 125 THERAPY UNIT COMPONENTS



PREVENA PLUS™ Connector - used to connect the PREVENA PLUS™ Canister to the PREVENA™ Therapy V.A.C.® Connector.



PREVENA PLUS™ 125 Therapy Unit Power Supply and Power Cord - a charging system provided with the PREVENA PLUS™ 125 Therapy Unit to charge the internal battery.



PREVENA PLUS™ 150 mL Canister - a sterile reservoir for collection of wound fluids



PREVENA PLUS™ 125 Therapy Unit - delivers negative pressure to the surgical area. The unit is battery and electrically powered. The non-sterile PREVENA PLUS™ 125 Therapy Unit Carrying Case is provided to facilitate patient mobility.

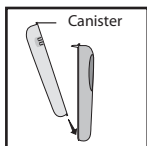
PREVENA PLUS™ CANISTER INSTALLATION

The canister used with the PREVENA PLUS™ 125 Therapy Unit is a single-use, sterile, 150 mL container with graduated markings of approximately 50 cc/mL increments.

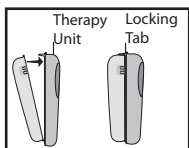
NOTE: If the canister is not fully engaged, the PREVENA PLUS™ 125 Therapy Unit will alert.

NOTE: Only use the recommended PREVENA PLUS™ 125 Therapy Unit Canister with this product.

NOTE: Never reuse a canister.



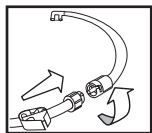
1. Remove the canister from the sterile package.
2. Hold therapy unit and canister, vertically or horizontally, one in each hand, and slide bottom of canister into slot on bottom of therapy unit.



3. Close canister against therapy unit. The upper locking tab will click when canister is secured.

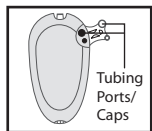
CONNECTING TO A PREVENA™ DRESSING WITH SENSAT.R.A.C.™ TUBING SET

When using PREVENA™ Dressings with a SENSAT.R.A.C.™ Tubing set:

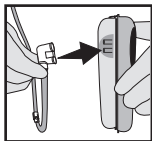


1. Connect the SENSAT.R.A.C.™ Tubing to the PREVENA PLUS™ Connector:

- Push the connectors together
- Twist the connectors to lock



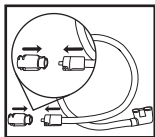
2. Connect the PREVENA PLUS™ Connector to the canister by aligning and plugging the connector at end of the tubing onto the tubing ports on the side of canister. Push together firmly. Ensure clamp on tube is open and positioned away from the patient.



3. Begin therapy.

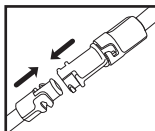
CONNECTING TO A PREVENA™ THERAPY V.A.C.® CONNECTOR AND NON SENSAT.R.A.C.™ DRESSING

When using PREVENA™ Dressings without a SENSAT.R.A.C.™ Dressing tubing set:



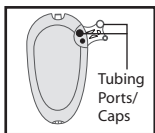
1. Connect the PREVENA™ Therapy V.A.C.® Connector to the PREVENA PLUS™ Connector:

- Push the connectors together
- Twist the connectors to lock

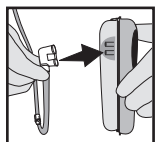


2. Connect the dressing tubing to the PREVENA™ Therapy V.A.C.® Connector:

- Push the connectors together
- Twist the connectors to lock

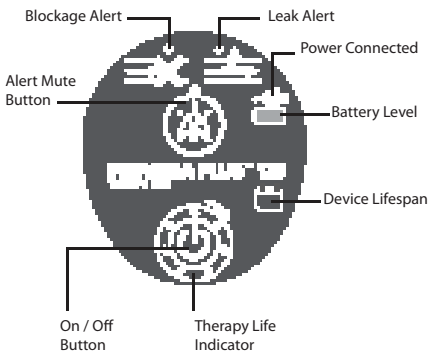


3. Connect the PREVENA PLUS™ Connector to the canister by aligning and plugging the connector at end of the tubing onto the tubing ports on the side of canister. Push together firmly. Ensure clamp on tube is open and positioned away from the patient.



4. Begin therapy.

BEGINNING THERAPY



1. Ensure the PREVENA™ Dressing has been applied as described in the individual PREVENA™ Dressing Application Instructions provided in dressing cartons.

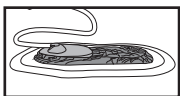


2. To begin therapy, press and hold center of the **On/Off** button for three seconds. The PREVENA PLUS™ 125 Therapy Unit, while in operation, may have a moderate sound emanating from the unit. All seven Therapy Life Indicators will illuminate with a green LED, indicating therapy is running.

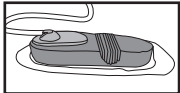
NOTE: To interrupt therapy or turn unit off, press and hold center of the **On/Off** button for three seconds.

Once therapy is on for one hour non-stop, the seven day lifespan begins and continues even if unit is turned off.

3. With therapy on, assess dressing to ensure integrity of seal.

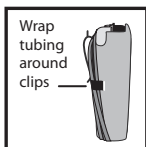


- The dressing should have a wrinkled appearance and the foam bolster should be compressed.

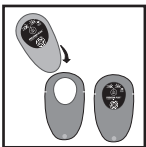


- If the foam bolster is not compressed or the therapy unit alerts, see the **Alerts** section.

4. If there is any evidence of a leak, check the dressing seals, tubing connectors, and canister connection, and ensure clamp is open. Refer to the **Correcting a Leak Condition** section for more information.

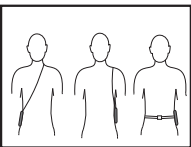


5. Secure excess tubing to prevent interference with patient mobility.



6. If desired, place the therapy unit into the carrying case. Ensure display is visible through the opening in the carrying case.

7. The carrying case comes with both an adjustable strap and belt clip for carrying. The belt clip and additional clips on each side and at the bottom of the carrying case provide a place where excess tubing may be wrapped and stored to help prevent/minimize tripping and strangulation.

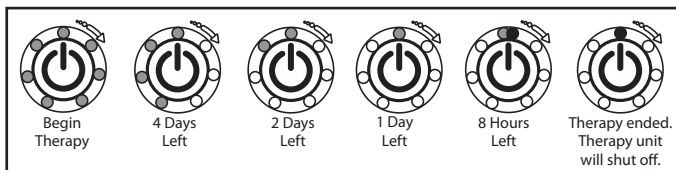


CAUTION: Do not wear or wrap strap around neck. Do not wrap tubing around neck.

UNIT TROUBLESHOOTING

If the PREVENA PLUS™ 125 Therapy Unit will not power on, make sure batteries are charged (see **Battery Charging** section). If the therapy unit still will not turn on, contact KCI.

THERAPY LIFE INDICATORS



NOTE: Grey represents green indicators and black represents yellow indicators.

The therapy life indicators provide a visual display of the seven (7) day therapy life cycle and the therapy life remaining. When therapy begins all seven green LEDs are illuminated. During therapy, after each 24-hour period an indicator will turn off. When eight hours of therapy time remains, the last indicator will illuminate with both a green and yellow LED simultaneously. When therapy time is about to expire, the last indicator will illuminate with a yellow LED and an alert will sound for approximately two minutes, then the therapy unit will shut off.

At the end of therapy, the therapy unit must be replaced with a new unit or alternative therapy must be used. Patients should be instructed to contact the treating physician or caregiver if therapy unit turns off and cannot be restarted before therapy is scheduled to end.

NOTE: Once therapy is on for one hour non-stop, the seven day lifespan begins and continues even if the unit is turned off.

DURATION OF PREVENA PLUS™ THERAPY

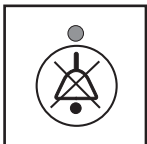
- Therapy should be continuous for a minimum of two days up to a maximum of seven days.

NOTE: The PREVENA PLUS™ 125 Therapy Unit will automatically time-out after seven days of therapy. Once therapy is on for one hour without stopping, the seven day lifespan begins and continues even if the unit is turned off.

- Patients should be instructed to contact their treating physician and not to turn therapy off unless:
 - advised by the treating physician
 - bleeding develops suddenly or in large amounts during therapy
 - there are signs of allergic reaction or infection
 - the canister is full of fluid
 - system alerts must be addressed
- Patient should be instructed to contact the treating physician if therapy unit turns off and cannot be restarted before therapy is scheduled to end, or if canister becomes full of fluid.
- At end of therapy, patient should return to treating physician for dressing removal.






ALERTS

Audible Alerts - All audible alerts will sound two beeps, escalating and repeating every 15 seconds, which will increase in volume through four cycles. The fourth cycle will produce the loudest audible beep and will repeat until the alert condition is corrected.



Alert Mute Button - Press and hold center of the **Alert Mute** button for three seconds during an alert condition to silence the audible alert for two minutes. When pressed, the **Alert Mute** button will illuminate to indicate mute has been selected. The alert will re-occur after two minutes unless the alert condition has been corrected.

The therapy unit will sound audible and display visual alerts as follows:

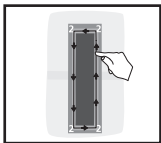
Alert Type	ID and Resolution
<p>Blockage Alert</p> 	<ul style="list-style-type: none"> • A solid yellow LED above the blockage symbol will turn on. • Audible blockage alert will sound two beeps repeating every 15 seconds. • When the blockage condition is resolved, audible and visual alerts will turn off. <p>To Correct Alert Check for a full canister. Check for kinked tubing. Ensure tubing clamp is open (SENSAT.R.A.C.™ Dressing only).</p>
<p>Leak Alert</p> 	<ul style="list-style-type: none"> • A solid yellow LED above the leak symbol will turn on. • Leak alert will sound two beeps repeating every 15 seconds. • When the leak condition is corrected, audible and visual alerts will turn off. <p>To Correct Alert See the Correcting a Leak Condition section in this guide.</p>
<p>Low Battery Level Alert</p> 	<ul style="list-style-type: none"> • A solid yellow LED on the battery level indicator will turn on. • Alert will sound two beeps repeating every four minutes. • A low battery alert indicates approximately two hours of therapy remain; charge batteries IMMEDIATELY to prevent disruption of therapy. • When battery is charged, audible and visual alerts will turn off. <p>To Correct Alert Charge battery; see the Battery Charging section in this guide.</p>
<p>Therapy Ended</p> 	<ul style="list-style-type: none"> • A solid yellow LED at the top of the Therapy Life Indicator will turn on. • The therapy unit will sound eight beeps, followed by a continuous beep for five seconds, then the therapy unit will turn off. • Notify the treating physician or caregiver: If the therapy unit has completed the seven day therapy and has timed out, and an attempt is made to turn the therapy unit on, the therapy unit will sound an alert for three seconds then shut off.
<p>System Fault Alert</p> 	<ul style="list-style-type: none"> • All LEDs will turn on and flash. • Two beeps sound, repeating every 15 seconds. <p>To Correct Alert Power the therapy unit off and then on again. If alert continues contact the treating physician or caregiver.</p>

CORRECTING A LEAK CONDITION

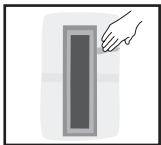
When the therapy unit detects a significant leak, a visual and audible leak alert will activate (see **Alerts** section).

See the PREVENA™ Dressings Clinician Guide for additional information

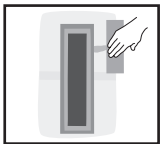
PREVENA CUSTOMIZABLE™ OR PREVENA PLUS CUSTOMIZABLE™ DRESSING



1. Press down through drape onto the adhesive seal all the way around to ensure seal.



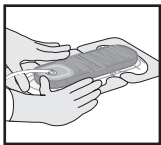
2. Use fingers to smooth out any creases or wrinkles.



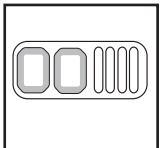
3. Use excess KCI Drape along the outer edge of drape to seal leaks.

PREVENA PEEL & PLACE™ OR PREVENA RESTOR™ DRESSING

(Illustrations in the steps below show the PREVENA PEEL & PLACE™ Dressing.)

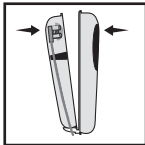


1. With therapy unit on, slowly press firmly around dressing edge to ensure good contact between adhesive and skin.

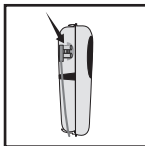


2. If a leak is identified, use PREVENA™ Patch Strips (located in dressing package) to help seal leaks around dressing. If large wrinkles are present, place patch strips so they run in line along the length of the wrinkle and not across the wrinkle.

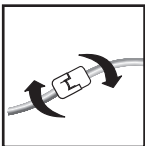
CHECK CANISTER TUBING CONNECTION



1. Ensure canister is securely locked onto the therapy unit. When canister is installed, a distinct click will be heard indicating it has been properly installed.



2. Check dressing tubing connector at canister.



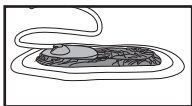
3. Check tubing connectors to ensure they are fully engaged and locked.

INDICATIONS THAT A LEAK CONDITION HAS BEEN CORRECTED

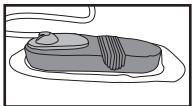
NOTE: Upon correcting a leak condition, a small delay will occur before the therapy unit senses the correction and silences the alerts.

The therapy unit will continue the alert until condition is corrected. When leak condition has been corrected, audible alerts will stop, and visual alerts will turn off.

The PREVENA™ Dressing will be compressed.



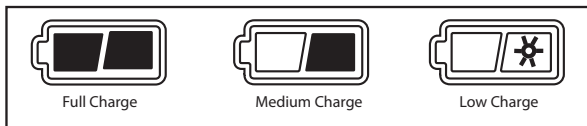
- Dressing compressed - system pressure acceptable.



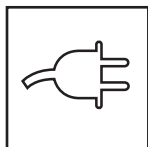
- Dressing not compressed - system pressure not acceptable.
Return to the **Correcting a Leak Condition** section to continue pressure correction steps.

BATTERY CHARGING

The PREVENA PLUS™ 125 Therapy Unit is battery-operated to facilitate patient mobility. The battery charge indicator on the user interface will display three levels of charge.

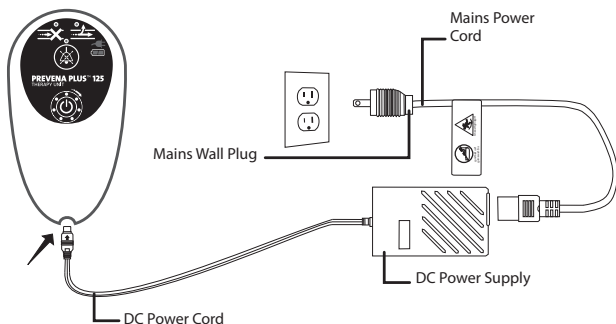


- Full charge (approximately nine hours remain)
- Medium charge (approximately two - seven hours remaining)
- Low charge. When low charge is indicated approximately two hours of therapy remain. Charge unit immediately to avoid disruption of therapy.



When the PREVENA PLUS™ 125 Therapy Unit is plugged into a power supply, the Power Connected icon turns yellow, indicating power is connected and system is charging. The icon will turn green when fully charged.

NOTE: Upon receipt, the PREVENA PLUS™ 125 Therapy Unit battery may not be fully charged.



NOTE: The rechargeable battery used in the PREVENA PLUS™ 125 Therapy Unit is not user accessible or replaceable.

1. Plug the mains power cord into a wall outlet.
2. Plug the other end of the mains power cord into the DC power supply.
3. Plug the DC power cord into the bottom of the therapy unit.
4. A fully discharged battery will recharge in approximately six hours.

CAUTION: Use only the charging system provided with the PREVENA PLUS™ 125 Therapy Unit. Using any other charging system may damage the therapy unit.

CAUTION: Power cords may present a tripping hazard. Ensure that power cords are out of areas where people walk.

NOTE: Power cords may have different wall plug configurations depending on country requirements.

CANISTER REMOVAL AND REPLACEMENT

1. Turn therapy off.
2. Slide dressing tubing clamp close to where tubing plugs into canister. Close clamp (SENSAT.R.A.C.™ Dressing only).
3. Unplug tubing from canister tubing ports.
4. Close canister tubing ports with attached cap.
5. Remove therapy unit from carrying case, if in use.
6. Press tab on canister to remove used canister from therapy unit.
7. Install new canister (see the **PREVENA PLUS™ Canister Installation** section).
8. Return therapy unit to carrying case if desired.
9. Reattach dressing tubing to canister tubing ports.
10. Release tubing clamp (SENSAT.R.A.C.™ Dressing only).
11. Turn therapy on.

NOTE: Dispose of used canister according to institution and local environmental regulations.

PREVENA PLUS™ 125 THERAPY UNIT DISPOSAL

At the end of therapy, the patient should return the PREVENA PLUS™ 125 Therapy Unit to the physician for disposal. Dispose of all waste according to local requirements. Improper disposal may run the risk of regulatory non-compliance.

INSTRUCTIONS FOR PATIENTS

Review the following information with the patient prior to discharge. This information is summarized in the PREVENA PLUS™ Incision Management System Patient Guide which must be provided to the patient at discharge.

DAILY USE

The PREVENA PLUS™ 125 Therapy Unit is portable and small enough that it may be worn beneath clothing during normal patient activities as approved by the treating physician.

CAUTION: Advise patient to NOT SUBMERGE therapy unit or dressing in liquid and to ensure therapy unit is not pulled into a tub or sink where it may become submerged.

CAUTION: The PREVENA PLUS™ Incision Management System is a medical device not a toy. Keep away from children, pets and pests as they can damage the dressing and therapy unit and affect performance. Keep therapy unit free of dust and lint.

SLEEPING

Instruct patient to:

- place the therapy unit in a position where tubing will not become kinked or pinched.
- ensure therapy unit will not be pulled off a table or fall to the floor during sleep.

SHOWERING AND BATHING

- Do not use the PREVENA PLUS™ 125 Therapy Unit while bathing/showering or where it can fall or be pulled into a tub, shower or sink.
- Do not reach for a product that has fallen into water. Unplug the unit immediately if plugged into an electrical source. Disconnect unit from dressing and contact treating physician or caregiver.
- Light showering is permissible, bathing is not. Before showering, disconnect the dressing from the therapy unit. For a SENSAT.R.A.C.™ Dressing, clamp the tubing then disconnect the dressing from the therapy unit.
- Dressing may be exposed to common shower soaps and rinsed with indirect shower stream. Do not submerge dressing. This may lead to wound maceration. Do not remove dressing.
- When towel drying, avoid disturbing or damaging the dressing.

STRENUOUS ACTIVITY

Advise patient as to when and at what level physical activities may be resumed. It is recommended that patients avoid strenuous activity while using the PREVENA PLUS™ Incision Management System.

CLEANING

Advise patient that the therapy unit and carrying case can be wiped with a damp cloth using a mild household soap solution that does not contain bleach.

WARNINGS AND IMPORTANT INFORMATION FOR USERS - PREVENA PLUS™ 125 THERAPY UNIT

In order for KCI products to perform properly, KCI recommends the following conditions. Failure to comply with these conditions will void any applicable warranties.

- Use this product only in accordance with these instructions and applicable product labeling.
- Assembly, operations, extensions, re-adjustments, modifications, technical maintenance or repairs must be performed by qualified personnel authorized by KCI.
- Ensure the electrical installation of the room complies with the appropriate national electrical wiring standards. To avoid the risk of electrical shock, this product must be connected to a grounded power receptacle.
- Cell phones or similar products could affect the therapy unit. Move the therapy unit away from these devices if interference is suspected.
- Do not operate this product if it has a damaged power cord, power supply or plug. If these components are worn or damaged, contact KCI.
- Do not drop or insert any object into any opening or tubing of this product.
- Do not connect this product or its components to devices not recommended by KCI.
- Do not modify the therapy unit or dressing. Do not connect the therapy unit or dressing to other devices being used.
- Use only PREVENA™ Dressings with this product.
- Keep this product away from heated surfaces.
- Equipment not suitable for use in presence of flammable anesthetic mixture with air, oxygen or nitrous oxide or in an environment in which the concentration of oxygen is: a) greater than 25% for ambient pressures up to 110 kPa; or b) the partial pressure of oxygen is greater than 27.5 kPa at ambient pressures exceeding 110 k.
- Avoid spilling fluids on any part of this product.
- Do not make any changes to the settings on the therapy unit without instructions from the treating physician.
- Small Parts - Choking Hazard
- The PREVENA PLUS™ Incision Management System is a medical device, not a toy. Keep away from children, pets and pests as they can damage the dressing and therapy unit and affect performance. Keep the therapy unit free of dust and lint as they can also damage the dressing and therapy unit and affect performance.

WARNING: The PREVENA PLUS™ 125 Therapy Unit has no serviceable parts and should not be opened, disassembled or otherwise modified by the user, and should be replaced as a unit. All assembly, operations, adjustments, modifications, maintenance and repairs must be carried out by qualified personnel authorized by KCI.

Electric Shock Hazard - Do not open any electrical cover on the therapy unit. There are no serviceable parts. Refer to qualified KCI service personnel.

Fluids remaining on the electronic controls can cause corrosion that may cause the electronic components to fail. Component failures may cause the unit to operate erratically, possibly producing potential hazards to patient and staff. If spills do occur, unplug the unit immediately and clean with an absorbent cloth. Ensure there is no moisture in or near the power connection and power supply components before reconnecting power. If the product does not work properly, contact KCI.

PREVENA PLUS™ 125 THERAPY UNIT ELECTROMAGNETIC COMPATIBILITY

The following are guidance and manufacturer's declarations regarding EMC for the PREVENA PLUS™ 125 Therapy Unit.

- The PREVENA PLUS™ 125 Therapy Unit needs special precautions regarding EMC and needs to be installed and put into service according to the EMC information provided in the following pages.

WARNING: This equipment is intended for use by healthcare professionals only. As with all electrical medical equipment, this equipment may cause radio interference or may disrupt the operation of nearby equipment. It may be necessary to take mitigation measures such as re-orienting or relocating the PREVENA PLUS™ 125 Therapy Unit or shielding the location.

- Portable and Mobile RF communications equipment, RFID readers, electronic article surveillance (anti-theft) equipment and metal detectors can affect the performance of the PREVENA PLUS™ 125 Therapy Unit. Please use the guidelines and recommendations specified in Tables 204 and 206.
- Other medical equipment or systems can produce electromagnetic emissions and therefore can interfere with the functionality of the PREVENA PLUS™ 125 Therapy Unit. Care should be used when operating the PREVENA PLUS™ 125 Therapy Unit adjacent to or stacked with other equipment. If adjacent or stacked use is necessary, the PREVENA PLUS™ 125 Therapy Unit and the other equipment should initially be observed to verify normal operation in the configuration in which it will be used.
- The electrical cables, external power supplies and accessories listed or referenced in this manual have been shown to comply with the test requirements listed in the following tables. Care should be taken to use only manufacturer-recommended cables, power supplies and accessories with the PREVENA PLUS™ 125 Therapy Unit. If a third-party supplier offers cables, external power supplies and electrical accessories for use with the PREVENA PLUS™ 125 Therapy Unit and they are not listed or referenced in this manual, it is the responsibility of that third-party supplier to determine compliance with the standards and tests in the following tables.
- The use of electrical cables and accessories other than those specified in this manual or referenced documents may result in increased electromagnetic emissions from the PREVENA PLUS™ 125 Therapy Unit or decreased electromagnetic immunity of the PREVENA PLUS™ 125 Therapy Unit.
- Portable and mobile RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the PREVENA PLUS™ 125 Therapy Unit including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result. More precisely, the minimum recommended separation distance should be calculated from the equation applicable to the frequency of the transmitter, as noted in the guidance below.
- NOTE: This equipment has been tested and found to comply with the limits for medical devices to IEC 60601-1-2: 2014 4th edition. These limits and test levels are intended to provide reasonable safety with regard to electromagnetic disturbances when the device is used in a typical medical installation.

Table 201

Guidance and Manufacturer's Declaration - Electromagnetic Emissions		
The PREVENA PLUS™ 125 Therapy Unit is intended for use in the electromagnetic environment specified below. The customer or the end user of the PREVENA PLUS™ 125 Therapy Unit should assure that it is used in such an environment.		
Emission Test	Compliance	Electromagnetic Environment - Guidance
RF emissions - CISPR 11 (Radiated & Conducted)	Group 1	The PREVENA PLUS™ 125 Therapy Unit uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions - CISPR 11 (Radiated & Conducted)	Class B	The PREVENA PLUS™ 125 Therapy Unit is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/flicker emissions IEC 61000-3-3	Complies	

Table 202

Guidance and Manufacturer's Declaration - Electromagnetic Immunity			
The PREVENA PLUS™ 125 Therapy Unit is intended for use in the electromagnetic environment specified below. The customer or the end user of the unit should assure it is used only in such an environment.			
Immunity Test	EN/IEC 60601 Test Level	Compliance Level	Intended Electromagnetic Environment
Electrostatic discharge (ESD) IEC 61000-4-2	±8 kV contact ±15 kV air	±8 kV contact ±15 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/burst IEC 61000-4-4	±2 kV for power supply lines 100 kHz repetition frequency ±1 kV for input/output lines 100 kHz repetition frequency	±2 kV for power supply lines 100 kHz repetition frequency ±1 kV for input/output lines 100 kHz repetition frequency	Mains power quality should be that of a typical commercial or home healthcare environment.
Surge IEC 61000-4-5	±1 kV differential mode (line - line) ±2 kV common mode (line - earth)	±1 kV differential mode (line - line) ±2 kV common mode (line - earth)	Mains power quality should be that of a typical commercial or home healthcare environment.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	Dips: 0% Ut for 1 cycle 70% Ut for 25 cycles at 50 Hz or 30 cycles at 60 Hz Single phase: at 0° Interruptions: 0% Ut for 250 cycles at 50 Hz or 300 cycles at 60 Hz	Dips: 0% Ut for 1 cycle 70% Ut for 25 cycles at 50 Hz or 30 cycles at 60 Hz Single phase: at 0° Interruptions: 0% Ut for 250 cycles at 50 Hz or 300 cycles at 60 Hz	Product has internal battery backup. If the user of the PREVENA PLUS™ 125 Therapy Unit requires continued operation during power mains interruptions, it is recommended that the unit be powered from an uninterruptible power supply or a battery.
Power frequency (50Hz/60Hz) magnetic field IEC 61000-4-8	30 A/m 50 Hz or 60 Hz	30 A/m 50 Hz or 60 Hz	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or home healthcare environment.
NOTE: Ut is the A.C. mains voltage prior to application of the test level.			

Table 204


Guidance and Manufacturer's Declaration - Electromagnetic Immunity			
The PREVENA PLUS™ 125 Therapy Unit is intended for use in the electromagnetic environment specified below. The customer or the end user of the unit should assure it is used in such an environment.			
Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment Guidance
<p>Conducted RF IEC 61000-4-6</p> <p>Radiated RF IEC 61000-4-3</p>	<p>3Vrms 150kHz to 80 MHz</p> <p>6Vrms in ISM and amateur radio bands between 150 kHz and 80 MHz</p> <p>80% AM at 1kHz</p> <p>10 V/m 80 MHz to 2.7 GHz</p> <p>80% AM at 1kHz</p>	<p>3Vrms 150kHz to 80 MHz</p> <p>6Vrms in ISM and amateur radio bands between 150 kHz and 80 MHz</p> <p>80% AM at 1kHz</p> <p>10 V/m 80 MHz to 2.7 GHz</p> <p>80% AM at 1kHz</p>	<p>Portable and mobile RF communications equipment should be used no closer to any part of the PREVENA PLUS™ 125 Therapy Unit, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.</p> <p>Recommended separation distance</p> $d = 1.2\sqrt{P}$ $d = 0.35\sqrt{P} \quad 80\text{MHz to } 800 \text{ MHz}$ $d = 0.7\sqrt{P} \quad 800\text{MHz to } 2.7\text{GHz}$ <p>where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended minimum separation distance in meters (m).</p> <p>Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey^a, should be less than the compliance level in each frequency range.</p> <p>Interference may occur in the vicinity of equipment marked with the following symbol:</p> 
NOTE 1: At 80MHz and 800MHz, the higher frequency range applies.			
NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from objects, structures and people.			
<p>^a Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the PREVENA PLUS™ 125 Therapy Unit is used exceeds the applicable RF compliance level above, the unit should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the PREVENA PLUS™ 125 Therapy Unit.</p>			

Table 205

Guidance and Manufacturer's Declaration - Electromagnetic Immunity						
The PREVENA PLUS™ 125 Therapy Unit is intended for use in the electromagnetic environment specified below. The customer or the end user of the unit should assure it is used in such an environment.						
Test Frequency (MHz)	Band ^a (MHz)	Service ^a	Modulation ^b	Maximum Power (W)	Distance (m)	Immunity Test Level (V/m)
385	380 - 390	TETRA 400	Pulse modulation ^b 18 Hz	1,8	0,3	27
450	430 - 470	GMRS 460, FRS 460	FM ^c ±5 kHz deviation 1 kHz sine	2	0,3	28
710	704 - 787	LTE Band 13, 17	Pulse modulation ^b 217 Hz	0,2	0,3	9
745						
780						
810	800 - 960	GSM 800/900, TETRA 800, IDEN 820, CDMA 850, LTE Band 5	Pulse modulation ^b 18 Hz	2	0,3	28
870						
930						
1 720	1 700 - 1 990	GSM 1800; CDMA 1900; GSM 1900; DECT; LTE Band 1, 3 4, 25; UMTS	Pulse modulation ^b 217 Hz	2	0,3	28
1 845						
1 970						
2 450	2 400 - 2 570	Bluetooth WLAN, 802.11 b/g/n, RFID 2450, LTE Band 7	Pulse modulation ^b 217 Hz	2	0,3	28
5 240	5 100 - 5 800	WLAN 802.11 a/n	Pulse modulation ^b 217 Hz	0,2	0,3	9
5 500						
5 785						
NOTE: If necessary to achieve the Immunity Test Level, the distance between the transmitting antenna and the ME Equipment or ME System may be reduced to 1 m. The 1 m test distance is permitted by IEC 61000-4-3.						
^a For some services, only the uplink frequencies are included.						
^b The carrier shall be modulated using a 50% duty cycle square wave signal.						
^c As an alternative to FM modulation, a 50% pulse modulation at 18 Hz may be used because while it does not represent actual modulation, it would be worst case.						

Table 206

Recommended separation distances between portable and mobile RF communications equipment and the PREVENA PLUS™ 125 Therapy Unit			
The PREVENA PLUS™ 125 Therapy Unit is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the PREVENA PLUS™ 125 Therapy Unit can help prevent electromagnetic interference by maintaining a minimum distance between the portable and mobile RF communications equipment (transmitters) and the unit as recommended below, according to the maximum output power of the communications equipment.			
Rated maximum output power of transmitter in watts (W)	Separation distance according to frequency of transmitter in meters (m)		
	150 kHz to 80 MHz $d = 1.2 \sqrt{P}$	80 MHz to 800 MHz $d = 0.35 \sqrt{P}$	800 MHz to 2.5 GHz $d = 0.7 \sqrt{P}$
0.01	.12	.04	.07
0.1	.38	.11	.22
1	1.2	.35	.7
10	3.8	1.1	2.2
100	12	3.5	7
For transmitters rated at a maximum output power not listed above, the recommended separation distance d in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.			
NOTE 1: At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.			
NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			

INCLUDED POWER SUPPLIES

Part Number	Description	Manufacturer	Max Length
44001674	Power Supply, 5V, 10W	Inventus Power	1.03 m
413628	Cord, V.A.C.® Power, US	Consolidated Wire	2.08 m

The use of electrical cables and accessories other than those specified in the supplied instructions for use or referenced documents may result in increased electromagnetic emissions from the PREVENA PLUS™ 125 Therapy Unit or decreased electromagnetic immunity of the PREVENA PLUS™ 125 Therapy Unit.

CUSTOMER CONTACT INFORMATION

For questions regarding this product, supplies, maintenance or additional information about KCI products and services, please contact KCI or a KCI authorized representative, or:

In the US call 1-800-275-4524 or visit www.ancelity.com

Outside the US visit www.kci-medical.com

KCI USA, Inc. 12930 IH 10 West, San Antonio, TX 78249

PREVENA PLUS™ 125 THERAPY UNIT SPECIFICATIONS

Dimensions:..... 3.5" W x 6.4" H x 2.16" D (8.9 x 16.3 x 5.49 cm)
Weight (with empty canister attached):..... ~.64 lbs (~.29 kg)
Pressure:..... 125 mmHg (16.7 kPa)
Canister Volume:..... 150 mL

Electrical:

Battery Run Life:..... ~8.5 hours
Battery Charge Time:..... ~6 hours from a fully discharged state
External Power Supply Input:..... 100-240VAC 0.5A-0.3A 50 - 60 Hz
External Power Supply Output:..... 5V, 2.0 A
Patient and Enclosure Leakage Current:..... <100 Microamps

Environmental Conditions:

Storage/Transport Conditions

Temperature Range:..... 0°F (-18°C) to 140°F (60°C)
Relative Humidity Range:..... 0%-95% non-condensing

Operating Conditions

Temperature Range:..... 41°F (5°C) to 104°F (40°C)
Relative Humidity Range:..... 15% - 93% non-condensing
Atmospheric Pressure:..... 1060 hpa (-1253 ft/-381.9 m) to 700 hpa (9878 ft/3010 m)
Expected Service Life..... 7.5 days

IEC Classification

Medical Equipment

Type BF, Applied Part

Class II

IP22 - Protection against solid objects greater than 12.5 mm and against liquid water falling for short periods of time.

The dressing components of the PREVENA PLUS™ 125 Incision Management System are considered Applied Parts under IEC 60601-1.

Conforms to AAMI ES60601-1:2005 +A1:2012, IEC 60601-1-6 Ed.3.1:2013, IEC 60601-1-8 Ed.2.1:2012, IEC 60601-1-11 Ed.2.0:2015, CSA C22.2#60601-1:2014 Ed.3

SUMMARY OF CLINICAL INFORMATION

A systematic literature review and associated meta-analyses were used to support the safety and effectiveness of the PREVENA™ Incision Management Systems over closed incisions in reducing the incidence of surgical site infections (SSIs) and seromas versus conventional wound dressings. The systematic literature search was performed using PubMed, The Cochrane Library, OVID, EMBASE, ScienceDirect, and alternative resources such as Google searches and QUOSA. Search terms included: (“negative pressure wound therapy” OR “negative pressure” OR “negative pressure therapy” OR “NPWT”) AND (“PREVENA™” OR “ciNPT” OR “prophylactic NPWT” OR “preventative NPWT” OR “incision management” OR “incisional management” OR “closed incision negative pressure wound therapy” OR “closed incision negative pressure therapy”).

Six (6) independent reviewers performed the study selection. Titles of manuscripts and abstracts that met the search criteria were logged and investigated for duplicates. The abstracts and manuscripts were assessed for inclusion and exclusion criteria (Table 2) by a subset of two (2) independent reviewers. When discordance was identified, the two reviewers deliberated until a consensus was reached.

Table 1. Inclusion and exclusion criteria for the systematic literature review

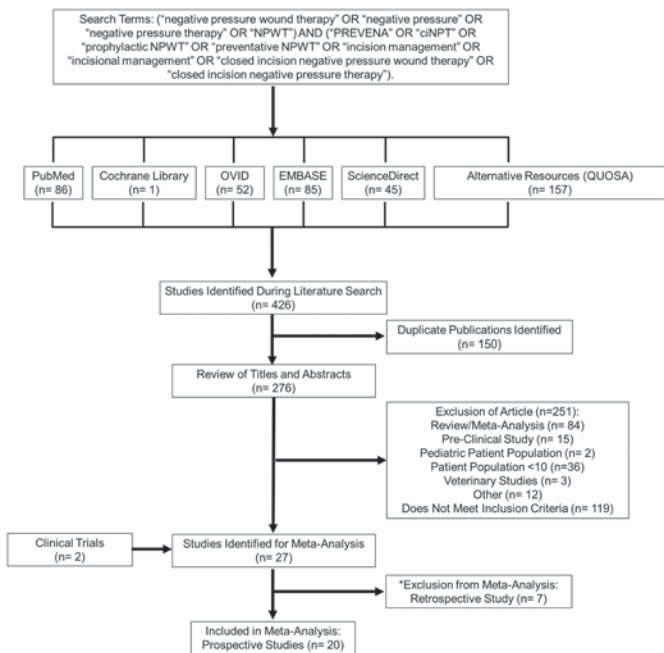
Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none">• Abstract or manuscript written in English• Published or unpublished study• Studies that compare the use of PREVENA™ Incision Management Systems using -125 mmHg pressure with legally marketed compatible dressing over closed incisions to conventional wound dressings (e.g., occlusive gauze dressing)• Contained an endpoint/outcome of surgical site infection (SSI), dehiscence, seroma, hematoma, or post-operative pain• Studies that followed the subjects/patients for a minimum of 30 days for the SSI endpoint• Studies that followed the subjects/patients for a minimum of 10 days for the seroma endpoint	<ul style="list-style-type: none">• Meta-analysis studies• Pre-clinical studies (i.e., animal or bench science assessments)• Studies on pediatric patients (age <18 years)• Studies with less than 10 patients• Veterinary studies

For abstracts and manuscripts that met all the inclusion criteria and none of the exclusion criteria, they were examined critically to: i) assess whether containing reference of any other articles that meet the inclusion criteria and ii) extract study characteristics by at least two additional independent reviewers. Registered studies at ClinicalTrials.gov were also reviewed using the same search criteria for completed and terminated studies. The Cochrane Collaboration tool was used for assessing risk of bias.

A total of 426 studies resulted from the initial search. After 150 duplicate publications were removed, a total of 276 unique studies were assessed for inclusion. An additional 251 articles were excluded based on the pre-specified inclusion/exclusion criteria (Table 2), which was comprised of 64 review/meta-analysis, 15 pre-clinical studies, 2 pediatric patient populations, 3 veterinary studies, 12 other

(protocol, technical report, subsequent study included in the meta-analysis, and comment), and 119 that did not meet all inclusion criteria. Lastly, seven (7) articles identified as retrospective studies were removed to minimize bias and ensure only the highest level of evidence for the meta-analyses.

Figure 1. Summary of study selection for the meta-analyses



Ultimately, twenty (20) prospective studies, including two (2) KCI USA, Inc.-sponsored, unpublished clinical studies from ClinicalTrials.gov, were included in the meta-analyses for SSI and seroma characterization. A total of up to 6,403 evaluable patients were included in these meta-analyses with 1,367 in the PREVENA™ Incision Management Systems therapy (treatment) group and 5,036 in the conventional wound dressing (control) group.

The two (2) KCI USA, Inc.-sponsored, unpublished clinical studies from ClinicalTrials.gov can be summarized as follows:

NCT01341444 was a randomized, single center, interventional trial evaluating the safety and effectiveness of PREVENA™ Incision Management Systems on closed surgical incisions in subjects who had undergone open renal transplant surgery. Subjects were randomized 1:1 to receive either the PREVENA™ Therapy (treatment group) or a silver-impregnated occlusive dressing (control group). The purpose of the study was to compare surgical site complications, which include incisional fluid accumulation, dehiscence, and surgical site infections, between the PREVENA™ Therapy (treatment group) and conventional occlusive dressing (control group). The measurement outcome was the incidence of surgical site complications up to 30 days (+/- 2 days)

post renal transplant surgery. Due to enrollment difficulties, KCI decided to terminate the study after enrolling 63 of 88 subjects. There were a total 28 subjects in the treatment group with 0 surgical site infections (0%) and 30 subjects in the control group with 2 surgical site infections (6.7%). Adverse events were reported: 25 subjects in the treatment group reported at least 1 adverse event and 24 subjects in the control group reported at least 1 adverse event. In the treatment group, 11 subjects reported at least 1 serious adverse event, and in the control group, 13 subjects reported at least one serious adverse event. None of the reported adverse events were related to the PREVENA™ Therapy or conventional wound dressings used.

NCT02195310 was a randomized, multi-center, open label, interventional trial evaluating the safety and effectiveness of PREVENA™ Incision Management System (treatment group) on closed sternal midline incisions in patients at high risk for surgical site occurrences to a control group treated with conventional wound dressings, such as gauze with tape, pressure dressing with additional packing and tape, and silver-impregnated dressings. The purpose of the study was to assess the performance of PREVENA™ Incision Management System versus conventional wound dressings on closed median sternal incisions in subjects undergoing cardiac surgery. The primary endpoint was the incidence of surgical site infections (SSI) within 30 days postoperatively per CDC guidelines²¹. Five hundred twenty subjects were expected to be randomized 1:1. An interim data review was conducted on 257 subjects (128 PREVENA™ subjects, 129 control subjects). The conditional power from this analysis was below 60%. Since the calculated SSI rates from the interim data review were outside the ranges of the sample size assumptions, the study was terminated early due to the lack of evidence to support the objectives and assumptions of the study. A final analysis was conducted on 299 subjects; 145 subjects for the PREVENA™ arm and 154 subjects for the control arm. The incidence rate of SSI in the PREVENA™ arm was 9.0% (13 subjects) and in the SOC arm was 10.4% (16 subjects). There was a 1.5-fold higher rate of SSI in control subjects with a Body Mass Index (BMI) >35 kg/m². In the treatment group, 6/68 subjects with a BMI >35 kg/m² had an SSI (8.8%) and 10/75 control subjects with a BMI >35 kg/m² had an SSI (13.3%). Adverse events were reported. See 'Safety' section below for more detail. There were 286 (83.6%) of subjects that experienced at least one adverse event. In the treatment group, 83.8% subjects experienced an adverse event, while 83.4% of the control group subjects experienced an adverse event. There were 18 subjects that experienced a treatment related adverse event. In the treatment group, 16 (9.2%) subjects experienced a treatment related adverse event, while 2 (1.2%) subjects in the control group experienced a treatment related adverse event. There were 118 serious adverse events. In the treatment group, 36.4% of subjects experienced a serious adverse event, while 32.5% of the control subjects experienced a serious adverse event. There were no device-related serious adverse events in either the treatment or control group.

Surgical Site Infection (SSI)

Sixteen (16) prospective studies were included in the meta-analyses for SSI, which are summarized in Table 3 below. Nine (9) studies are randomized controlled trials, which are considered level I evidence. The remaining seven (7) studies are considered level II evidence, which include five (5) prospective treatment and historical controls studies and two (2) prospective observational studies that alternated patient assignment into either the treatment or control group (i.e., not randomized).

Table 3. Characteristics of studies included in the SSI meta-analyses

Study/Level of Evidence	Study Design	Surgical Procedure	Subjects' Risk Factors	Study Duration	Incisional Dressings Used	No. of Subjects	Treatment Duration Days
Cantero 2016 ³ Level II	Prospective & Historical Controlled	Diverting loop ileostomy reversal	NR	30 Days	PREVENA™ System	17	5-7
					Conventional Wound Dressing	43	1-2, then daily
DiMuzio 2017 ⁴ Level I	RCT	Elective vascular surgery [†]	BMI > 30kg/m ² , pannus, immunosuppressant disorder, reoperation, prosthetic frafr, HbA _{1c} >8	30 Days	PREVENA™ System	59	NR
					Standard Gauze Dressing	60	NR
Grauhan 2013 ⁶ Level II	Prospective Observational	Median sternotomy [†]	BMI Mean Treatment: 37kg/m ² , Control: 36kg/m ² , Diabetes; COPD; LVEF	90 Days	PREVENA™ System	75	6-7
					Conventional Wound Dressing	75	1-2
Grauhan 2014 ⁷ Level II	Prospective & Historical Controlled	Median sternotomy	NR	30 Days	PREVENA™ System	237	6-7
					Conventional Sterile Wound Tape Dressing	3508	1-2
Gunatillake 2017 ⁸ Level I	RCT	Cesarean delivery	BMI Mean Treatment: 46.3kg/m ² , Control: 46.8kg/m ² , Diabetes	42+/- 10 Days	PREVENA™ System	39	5-7
					Steri-strips, Sterile Gauze, Tegaderm™	43	1-2

Study/Level of Evidence	Study Design	Surgical Procedure	Subjects' Risk Factors	Study Duration	Incisional Dressings Used	No. of Subjects	Treatment Duration Days
Lavryk 2016 ¹⁰ Level II	Prospective Observational	Reoperative colorectal surgery [†]	Diabetes; Hx of smoking	30 Days	PREVENA™ System	55	7 +/- 2
Lee AJ 2016 ¹¹ Level I	RCT	CABG with harvesting of GSV [†]	Diabetes; smoking; COPD; HTN; CHF; LVD; Aortic Stenosis; AF; CVD; Dyslipidemia; CKF; PVD; Hypothyroidism; Arthritis; Gout; Asthma	42 Days	PREVENA™ System	101	NR
Lee K 2017 ¹² Level I	RCT	Femoral to distal artery bypass; femoral endarterectomy; femoral artery crossover, other [†]	BMI Mean Treatment : 29kg/m ² ; Control: 29kg/m ² ; Diabetes; Hx of smoking; COPD; CAD; LVD; HTN; CKD; Anticoagulation; Ischemic tissue loss	30 Days and 90 Days	PREVENA™ System	53	First day of discharge up to 8 days
Matatov 2013 ¹³ Level II	Prospective & Historical Controlled	Femoral cutdown for vascular procedures	BMI Mean Treatment: 26kg/m ² ; Control 27kg/m ² ; Diabetes; Hx of smoking; COPD; CAD; CHF; HTN; Renal insufficiency; Anemia	30 Days	PREVENA™ System	41 (52 wounds)	5-7
NCT01341444 Level I	RCT	Renal transplant [†]	BMI Mean Treatment: 29.0kg/m ² ; Control: 28.72kg/m ² ; Diabetes; Tobacco use	30 Days	Primapore or Dermabond Adhesive	49 (63 wounds)	3
					PREVENA™ System	28	5
					Standard Incisional Dressing	30	3

Study/Level of Evidence	Study Design	Surgical Procedure	Subjects' Risk Factors	Study Duration	Incisional Dressings Used	No. of Subjects	Treatment Duration Days
NCT02195310 Level I	RCT	Median sternotomy (elective cardiac surgery) [†]	BMI Mean Treatment: 35.64kg/m ² ; Control: 35.27kg/m ² ; Diabetes; Immunosuppressant Disorder; Hx of Smoking; Dialysis; Planned Bilateral Mammary Artery; Chronic Lung Disease; CKD; Previous Chest Wall Radiotherapy; Breast Size D; Age > 75 years; LVEF<30%	30 Days	PREVENA™ System Traditional Sterile Wound Dressing (included gauze with tape, pressure dressings and silver impregnated dressings)	145 154	4-7 2-3
Newman 2017 ¹⁴ Level I	RCT	Total hip or knee arthroplasty (elective revision) [†]	Blood thinners other than aspirin postoperatively, BMI ≥35kg/m ² ; PVD; Diabetes mellitus; Current smoker; Hx of Prior Joint Infection; Current use of corticosteroids or immunomodulators; Hx or current cancer/hematological malignancy; inflammatory arthritis; Renal failure or Dialysis; Malnutrition; Liver disease; Transplant status; HIV infection	84 Days	PREVENA™ System Silver Impregnated Occlusive Dressing	80 80	≥2 7

Study/Level of Evidence	Study Design	Surgical Procedure	Subjects' Risk Factors	Study Duration	Incisional Dressings Used	No. of Subjects	Treatment Duration Days
Redfern 2017 ¹⁸ Level II	Prospective & Historical Controlled	Total hip or knee arthroplasty (elective primary)	BMI Mean Treatment: 30.5kg/m ² ; Control: 30.9kg/m ² ; Diabetes; HTN; Hx of Cancer/Tumor; Arthritis; Myocardial Infarction/Heart Disease; Tobacco Use	60 Days	PREVENA™ System Traditional Gauze Dressing	192 400	6-8 Standard
Ruhstaller 2017 ¹⁹ Level I	RCT	Unscheduled cesarean delivery [†]	Gestational Diabetes; Tobacco Use; HTN	28 Days	PREVENA™ System	67	3
Sabat 2016 ²⁰ Level I	RCT	Vascular surgery involving groin incision	NR	120 Days	Telfa bandage with gauze and surgical tape PREVENA™ System	69 30 wounds	1 5
Swift 2015 ²¹ Level II	Prospective & Historical Controlled	Cesarean section [†]	BMI ≥ 30kg/m ² ; Diabetes; Chronic Hypertension; Preeclampsia; HELLP Syndrome; Rupture of the Membranes > 4 hours; Chorioamnionitis; Anticoagulation; Multiple Gestation	42 Days	Gauze and Tegaderm™ PREVENA™ System Standard Sterile Dressing	33 wounds 110 209	NR 3 NR

*Population or Procedure identified as high-risk for wound complication

*Oxford Centre of Evidence-Based Medicine

RCT = Randomized Controlled Trial

NR= Not Reported

ciNPWT= closed incision Negative Pressure Wound Therapy

BMI= Body Mass Index

HX= History

COPD= Chronic Obstructive Pulmonary Disorder

GERD= Gastroesophageal Reflux Disease

HTN= Hypertension

AF= Atrial Fibrillation

CVD= Cardiovascular disease

CKF= Chronic kidney failure

PVD= Peripheral vascular disease

LVD= Left ventricle dysfunction

CAD= Coronary artery disease

CKD= Chronic kidney disease

LVEF= Left ventricle ejection fraction

HIV= Human immunodeficiency virus

HELLP = Hemolysis, Elevated Liver enzymes, Low Platelet counts

Together, the sixteen (16) studies contained 1,264 evaluable patients receiving the PREVENA™ Incision Management Systems therapy (treatment group) and 4,923 patients receiving conventional wound dressings (control group). The conventional wound dressings used in each study can be found in Table 3 above and range from occlusive gauze dressings to silver-impregnated dressings. The primary endpoint in the studies was the incidence of surgical site infection in the treatment group compared to the control group for at least four weeks following surgery.

The treatment effect for each study was summarized using odds ratio (OR), which was calculated using the following formula:

OR = AD/BC, where

A = the number of subjects with SSI events for the treatment group

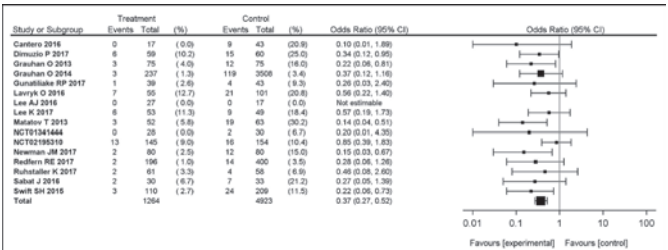
B = the number of subjects without SSI events for the treatment group

C = the number of subjects with SSI events for the control group

D = the number of subjects without SSI events for the control group

An OR of less than 1 suggests a favorable effect by the treatment in reducing SSI, whereas an OR greater than 1 suggests a favorable effect by the conventional wound dressings. The 95% confidence interval (95% CI) for the odds ratio is calculated based on the standard error of Log (OR). The individual study effects for SSI are summarized in Figure 2 below.

Figure 2. Forest plot of meta-analysis studies on surgical site infection (SSI)



Overall, there is an observable trend supporting a favorable effect by the PREVENA™ System in reducing the incidence of SSI. The SSI rates ranged from 0% to 30.2% for the control group in the individual studies, and the SSI rates in the treatment group ranged from 0% to 12.7%. However, the benefit of the PREVENA™ Systems varies considerably across different studies, possibly due to many confounding factors such as different surgical procedures and patient risk factors, which are further explored in subgroup analyses below. Additionally, there are many inherent limitations associated with meta-analyses and biases with each individual study, which are discussed in the 'Limitations of the Clinical Evidence' section below. Because of these confounding factors and limitations of the studies, statistical significance cannot be reliably inferred for the treatment effect based on the combined results from the sixteen (16) studies.

Subgroup analyses were performed to elucidate potential confounding factors contributing to the heterogeneity in the treatment effect. The subgroup analyses conducted were based on: i) Wound classification, ii) Infection depth (i.e., superficial, deep, organ space), iii) Risk factors for surgical site infection.

i. Wound classification

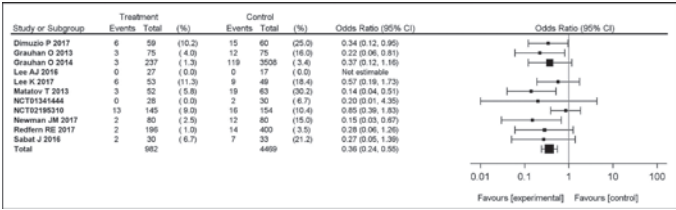
To analyze the effect of the PREVENA™ Incision Management Systems on SSI in wounds of different degrees of contamination, a wound classification designation following the Center for Disease Control and Prevention (CDC) guidelines (Table 4) was assigned to each study based on the surgical procedure performed and CDC wound classification definitions. Each study was reviewed, and a CDC wound classification was assigned by two individuals with appropriate medical and clinical trials background. All the same wound types in each study were treated the same unless the publication (e.g., Newman et. al.¹⁴) specifically gave guidance that some wounds were more severe in a particular subgroup (e.g., septic revisions). If the publication provided a CDC wound classification, the provided classification was utilized. One study (Lavryk et. al.¹⁰) was excluded as only patients with wound classifications of II, III and IV were enrolled and could not be separated into the individual wound classification groups.

Table 4. Surgical wound classifications and definitions²¹

Surgical Wound Classification	Definition
Class I/Clean	An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.
Class II/Clean-contaminated	An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.
Class III/Contaminated	Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered are included in this category.
Class IV/Dirty-infected	Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

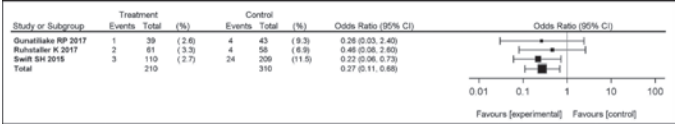
Eleven (11) of the sixteen (16) studies were determined to contain only Class I wounds, and these eleven (11) studies consist of approximately 88% of the total patient population for the overall SSI meta-analysis. The subgroup analysis results of Class I wounds (Figure 3) show a reduction in favor of the PREVENA™ Incision Management Systems therapy and are consistent with the overall reduction in SSI observed in Figure 2.

Figure 3. Forest plot of meta-analysis studies on surgical site infection in Class I wounds



Three (3) of the sixteen (16) studies were included in the subgroup analysis for Class II wounds, and these three (3) studies consist of approximately 8% of the total patient population for the overall SSI meta-analysis. The subgroup analysis results of Class II wounds (Figure 4) show a reduction in favor of the PREVENA™ Incision Management Systems therapy and are consistent with the overall reduction in SSI observed in Figure 2.

Figure 4. Forest plot of meta-analysis studies on surgical site infection in Class II wounds



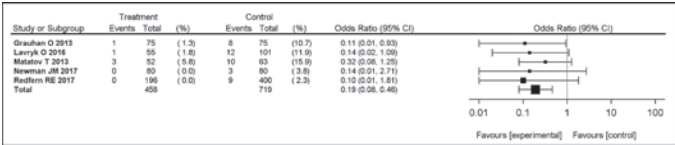
There was only one (1) study identified as having Class III wounds; therefore, a subgroup analysis for Class III wounds was not performed. In this study, no SSI events were reported for the treatment group (0 out of n=17) and nine (9) SSI events were reported for the control group (9 out of n=43). There were no studies containing Class IV wounds that could be isolated for analysis; therefore, a subgroup analysis was not performed for Class IV wounds. It should be noted that the PREVENA™ Systems are intended to be used only on closed incisions. As Class IV wounds are generally not expected to be surgically closed primarily, the PREVENA™ Systems should not be used on Class IV wounds.

ii. Infection depth

Surgical site infection (SSI) can be divided into three (3) subgroups: superficial incisional SSI, deep incisional SSI, and organ space SSI⁹. Superficial incisional SSI is infection that is limited to the skin or subcutaneous tissue of the surgical incision. Deep incisional SSI is infection that has spread to deep soft tissues such as fascial and muscle layers. Organ space SSI is deeper infection that involves any part of the anatomy that was opened or manipulated during the operation⁹.

Five (5) of the sixteen (16) studies selected for SSI meta-analyses included information to stratify patient SSI events into superficial, deep, and organ space infections. Subgroup analyses examining the effect of the PREVENA™ Systems on different SSI locations were conducted based on these five (5) studies. Among the three subgroups, the PREVENA™ Systems demonstrated the greatest benefit in reducing superficial incisional SSIs (Figure 5). The reduction in superficial SSI appears to be greater than the SSI reduction in the overall data (Figure 2). There was little to no benefit of the PREVENA™ Systems in reducing deep incisional SSIs and organ space SSIs when compared to the control group.

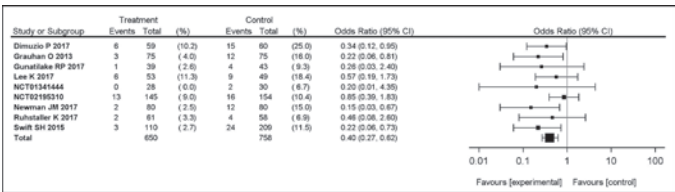
Figure 5. Forest plot of meta-analysis studies on surgical site infection in superficial incisional SSI



iii. Risk factors for surgical site infection

Patients having one or more co-morbidities are generally considered to be at higher risk for surgical site complications. High risk patients were defined in the selected studies as having one or more of the following co-morbidities: obesity (body mass index ≥ 30 kg/m²); diabetes; history of smoking; immune suppression or receiving drugs that can cause immune suppression, such as steroids, chemotherapeutic medications, and/or antimetabolites; malnutrition with a hydrated serum albumin of less than 3.0 grams/deciliter; neutropenia; preeclampsia; patients who have cardiac, pulmonary, liver or renal disease; history of previous surgery or radiation in the treatment area. Subjects' risk factors for each of the sixteen (16) studies are described in Table 3; however, some of the studies contain all comers with only a portion being high-risk patients. Upon further examination, nine (9) studies were determined to contain only high-risk patients. A subgroup analysis was performed on these nine (9) studies (Figure 6). As expected, the incidence of SSI, in both the treatment and control groups, is higher in high-risk patients (5.5% and 12.9%, respectively) compared to the overall study population (4.2% and 5.8%, respectively). Additionally, there appears to be a greater overall percentage reduction in SSI in high risk patients. Thus, while the reduction in SSI, as measured by odds ratio, in high risk patients does not appear to be significantly different than the reduction observed in the overall data (Figure 2), there is a greater clinical benefit of the PREVENA™ Systems in patients at high risk for surgical site infection based on a greater absolute percentage reduction in the incidence of SSI.

Figure 6. Forest plot of meta-analysis studies on surgical site infection in high risk patients



Together, the subgroup analyses on wound classification, infection depth, and patient risk factors for surgical site infection serve as the basis for granting the following Indications for Use:

When used with legally marketed compatible dressings, PREVENA™ 125 and PREVENA PLUS™ 125 Therapy Units are intended to aid in reducing the incidence of seroma and, in patients at high risk for post-operative infections, aid in reducing the incidence of superficial surgical site infection in Class I and Class II wounds.

Additional subgroup analyses for surgical site infection were performed based on surgical procedure risk factor, combination of surgical procedure and patient risk factors, and incision location. While the results from these subgroup analyses were reviewed, they did not serve as the basis for granting this De Novo request.

Seven (7) prospective studies were included in the meta-analysis for seroma, which are summarized in Table 5 below. Five (5) studies are randomized controlled trials, which are level I evidence. The remaining two (2) studies are considered level II evidence, which include one (1) prospective treatment and historical controls study and one (1) prospective observational study that alternated patient assignment into either the treatment or control group (i.e., not randomized).

Table 5. Characteristics of studies included in the Seroma meta-analysis

Study/Level of Evidence	Study Design	Surgical Procedure	Subjects Risk Factors	Study Duration	Incisional Dressings Used	No. of Subjects	Treatment Duration Days
Ferrando 2017 ⁵ Level II	Prospective Observational	Breast conserving surgery, oncoplastic surgery, tissue sparing, simple mastectomies ¹	BMI Mean Treatment: 27kg/m ² ; Control: 29.5kg/m ² ; Diabetes; Hx of Smoking; HTN; Use of Corticosteroids; Artery and Liver Disease; Chemotherapy; Radiation; Previous Surgery; Invasive Surgery	1 Year	PREVENA PLUS CUSTOMIZABLE™ Steri-strip skin adhesive closure	17 (25 wounds) 20 (22 wounds)	7 14
Gunatillake 2017 ⁸ Level I	RCT	Cesarean Delivery	BMI Mean Treatment: 46.3kg/m ² ; Control: 46.8kg/m ² ; Diabetes	42 +/- 10 Days	PREVENA™ System	39	5-7
NCT01341444 Level I	RCT	Renal Transplant [†]	BMA Mean Treatment: 29.05kg/m ² ; Control: 28.73kg/m ² ; Diabetes; Tobacco Use	30 Days	PREVENA™ System Steri-strips, sterile gauze, Tegaderm™	28 43	5 1-2
Pachowsky 2012 ¹⁵ Level I	RCT	Total Hip Arthroplasty	NR	10 Days	Standard Incisional Dressing PREVENA™ System Standard Wound Dressing	30 9 10	3 5 Days NR

Study/Level of Evidence	Study Design	Surgical Procedure	Subjects' Risk Factors	Study Duration	Incisional Dressings Used	No. of Subjects	Treatment Duration Days
Pauser 2016 ¹⁶ Level I	RCT	Hip Hemiarthroplasty [†]	NR	10 Days	PREVENA™ System	11	5
					Standard wound dressing consisting of dry wound coverage	10	NR
Pleger 2017 ¹⁷ Level I	RCT	Vascular procedures with access in common femoral artery [†]	BMI Mean Treatment: 26.7kg/m ² ; Control: 27.8kg/m ² ; Diabetes; Hx of Smoking; COPD; Renal Insufficiency; Malnutrition; Age >50 years; Overweight	30 Days	PREVENA™ System	43 (58 wounds)	5-7
					Conventional Adhesive Plaster	57 (71 wounds)	1
Redfern 2017 ¹⁸ Level II	Prospective & Historical Controlled	Total hip or knee arthroplasty (elective primary)	BMI Mean Treatment: 30.5kg/m ² ; Control: 30.9kg/m ² ; Diabetes; HTN; Hx of Cancer/ Tumor; Arthritis; Myocardial Infarction/ Heart Disease; Tobacco Use	60 Days	PREVENA™ System	192	6-8
					Traditional Gauze Dressing	400	Standard

[†]Population or Procedure identified as high-risk for wound complication

*Oxford Centre of Evidence-Based Medicine

NR= Not Reported

RCT = Randomized Controlled Trial

ciNPWT= closed incision Negative Pressure Wound Therapy

BMI= Body Mass Index

HX= History

COPD= Chronic Obstructive Pulmonary Disorder

GERD= Gastroesophageal Reflux Disease

HTN= Hypertension

AF= Atrial Fibrillation

CVD= Cardiovascular disease

CKF= Chronic kidney failure

PVD= Peripheral vascular disease

LVD= Left ventricle dysfunction

CAD= Coronary artery disease

CKD= Chronic kidney disease

LVEF= Left ventricle ejection fraction

HIV= Human immunodeficiency virus

Together, the seven (7) studies contained 366 evaluable patients receiving PREVENA™ Incision Management Systems therapy (treatment group) and 586 patients receiving conventional wound dressings (control group). The conventional wound dressings used in each study can be found in Table 5 above and mostly consist of gauze and occlusive dressings. The primary endpoint in the studies was the incidence of seroma in the treatment group compared to the control group for at least 10 days following surgery.

The treatment effect for each study was summarized using odds ratio (OR), which was calculated using the following formula:

OR = AD/BC, where

A = the number of subjects with seroma events for the treatment group

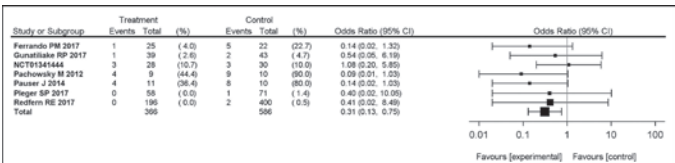
B = the number of subjects without seroma events for the treatment group

C = the number of subjects with seroma events for the control group

D = the number of subjects without seroma events for the control group

An OR of less than 1 suggests a favorable effect by the treatment in reducing seroma, whereas an OR greater than 1 suggests a favorable effect by the standard of care in reducing seroma. The 95% confidence interval (95% CI) for the odds ratio is calculated based on the standard error of Log (OR). The individual study effects are summarized in Figure 7 below.

Figure 7. Forest plot of meta-analysis studies for seroma.



Overall, there is an observable trend supporting a favorable effect by the PREVENA™ Systems in reducing the incidence of seroma formation. The seroma rates ranged from 0.5 % to 90 % for the control group in the selected studies, and the seroma rates in the treatment group ranged from

0% to 44.4%. However, the benefit of the PREVENA™ Systems in reducing the incidence of seroma formation varies broadly across different studies, possibly due to many confounding factors such as different surgical procedures and patient risk factors. Subgroup analyses for seroma were not conducted as there are only seven (7) studies total and dividing them into subgroups would not result in meaningful analyses. Additionally, there are many inherent limitations associated with meta-analyses and biases with each individual study, which are discussed in the 'Limitations of the Clinical Evidence' section below. Because of these confounding factors and limitations, statistical significance cannot be reliably inferred for the treatment effect on seroma rates based on the combined results from the seven (7) studies.

Safety

Adverse events (AEs) and Serious Adverse Events (SAEs) were reported in three (3) of the twenty (20) studies included in the meta-analyses [Gunatilake (Cesarean section) 2017⁸, NCT01341444 (Renal transplant), NCT02195310 (Sternotomy)]. There were no treatment related AEs or SAEs reported in the Cesarean section study (Gunatilake 2017⁸). In the two studies conducted by KCI (NCT01341444 (Renal transplant), NCT02195310 (Sternotomy)), there were no SAEs, and the twenty one (21) reported AEs related or possibly related to the device including pain (5), blisters (4), dehiscence (4), draining/wound secretion (2), erythema (2), skin irritation (2), ecchymosis (1), and hematoma (1), which are known adverse events that may be seen with the use of the device on surgical incisions.

No significant differences were reported in AEs or SAEs between the PREVENA™ Systems (treatment group) and conventional wound dressings (control group). No adverse device events, serious adverse device events, or device failures were reported. These results suggest that the PREVENA™ Systems have a similar safety profile as conventional wound dressing for closed surgical incisions.

Limitations of the Clinical Evidence

There are many inherent limitations to meta-analyses, such as publication bias and selection bias. In addition, surgical site infection (SSI) and seroma are complex post-operative outcomes that have many potential causes. While efforts were made in the study identification and selection process to ameliorate biases by including both published and unpublished studies and only the highest quality studies, not all aspects of each selected meta-analysis study are identical. First, even though only prospective studies were included in the meta-analyses, these studies often had many potential sources of bias. Bias assessment was conducted using the Cochrane guidelines and focused on randomization, allocation concealment, differences in baseline patient and risk characteristics, blinded assessments, loss to follow up, comparing purpose of study to outcomes reported, and when possible, comparing outcomes to those listed on ClinicalTrials.gov, when available. Fourteen (14) of the twenty (20) meta-analysis studies were identified as high-risk for bias (Cantero 2016³, DiMuzio 2017⁴, Ferrando 2017⁵, Gunatilake 2017⁸, Lavryk 2016¹⁰, Lee AJ 2016¹¹, Matatov 2013¹³, NCT013471444, Newman 2017¹⁴, Pleger 2017¹⁷, Redfern 2017¹⁸, Sabat 2016²⁰, Swift 2015²²). One (1) study was assessed as low risk for bias (Lee K 2017¹²). Risk for bias was unclear in the remaining five (5) studies due to the lack of information reported in the studies. Second, the unit of the analysis is not consistent in all studies. Some studies used the wound as the unit of analysis and others used the patient as the unit of analysis. As a result, some of the data used in these analyses were based on wounds and some patients contributed more than one (1) wound to the analyses. Third, the timing of the outcome assessments was not consistent across each of the different studies. For example, although all the SSI studies evaluated SSI events for at least four weeks post-surgery, the duration of some of the studies was much longer. Similarly, although all the seroma studies evaluated the

incidence of seroma for at least ten days after surgery, the duration of some of the studies was much longer. Fourth, the reported SSI rates in the meta-analysis studies varied broadly across different studies. It should be noted that the following SSI rates based on wound classification and types of SSI (Table 6) have recently been reported based on a retrospective review of the 2011 American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database⁹:

Table 6. Surgical Site Infection (SSI) rates based on ACS NSQIP database⁹.

30-d postoperative outcomes	Total	Wound Classification			
		Class I	Class II	Class III	Class IV
Surgical Site Infection (SSI)	3.4%	1.8%	4.8%	5.6%	8.5%
Superficial incisional SSI	1.9%	1.2%	2.6%	2.8%	2.7%
Deep incisional SSI	0.6%	0.4%	0.6%	0.8%	1.5%
Organ space SSI	1.1%	0.3%	1.6%	2.2%	4.4%

The SSI rates reported in the studies selected for the meta-analysis, even for the control groups, are generally higher than those reported in the literature. Factors contributing to this discrepancy may be surgeon-, procedure-, or patient-dependent, but nevertheless cannot be pinpointed based on the information provided in the studies. Fifth, five (5) of the seven (7) prospective studies included in the meta-analysis for SSI and one (1) prospective study included in the meta-analysis for seroma compared the PREVENA™ Systems to historical controls. There have been significant evidence-based changes in patient care to define and reduce the risk for post-operative complications, including surgical site infections. Additionally, surgical site infection reduction measures vary among surgeons, hospitals, and countries. Changes in disease definitions, interventions, and treatment effectiveness over time contribute to non-contemporaneous bias. Results of studies using historical controls should be evaluated with caution.

These limitations should be considered when examining the results from these meta-analyses.

REFERENCES

1. Ban, K. A., Minei, J. P., Laronga, C., Harbrecht, B. G., Jensen, E. H., Fry, D. E., . . . Duane, T. M. (2017). American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. *Journal of the American College of Surgeons*,224(1), 59-74. doi:10.1016/j.jamcoll-surg.2016.10.029
2. Berrios-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. *JAMA Surg.* 2017;152(8):784–791. doi:10.1001/jamasurg.2017.0904
3. Cantero R, Rubio-Perez I, Leon Metal. Negative-Pressure Therapy to Reduce the Risk of Wound Infection Following Diverting Loop Ileostomy Reversal: An Initial Study. *Adv Skin Wound Care* 2016;29:114-118. doi:10.1097/01.ASW.0000480458.60005.34.
4. DiMuzio P, Staley C, Reiter D et al. RS06: A Randomized Study Evaluating Negative-Pressure Therapy to Decrease Vascular Groin Wound Complications. *J Vasc Surg* 2017;65:133S.
5. Ferrando, P. M., Ala, A., Bussone, R., Bergamasco, L., Perinetti, F. A., & Malan, F. (2018). Closed incision negative pressure therapy in oncological breast surgery: comparison with standard care dressings. *Plastic and Reconstructive Surgery Global Open*, 6(6).
6. Grauhan O, Navasardyan A, Hofmann M, Muller P, Stein J, Hetzer R. Prevention of poststernotomy wound infections in obese patients by negative pressure wound therapy. *J Thorac Cardiovasc Surg* 2013;145:1387-1392.
7. Grauhan, O., Navasardyan, A., Tutkun, B., Hennig, F., Müller, P., Hummel, M., & Hetzer, R. (2014). Effect of surgical incision management on wound infections in a poststernotomy patient population. *International wound journal*, 11(s1), 6-9.
8. Gunatilake, R. P., Swamy, G. K., Brancazio, L. R., Smrtka, M. P., Thompson, J. L., Gilner, J. B., ... & Heine, R. P. (2017). Closed-incision negative-pressure therapy in obese patients undergoing cesarean delivery: a randomized controlled trial. *American Journal of Perinatology Reports*, 7(03), e151-e157.
9. Ju, M. H., Cohen, M. E., Bilimoria, K. Y., Latus, M. S., Scholl, L. M., Schwab, B. J., Hall, B. L. (2014). Effect of Wound Classification on Risk Adjustment in American College of Surgeons NSQIP. *Journal of the American College of Surgeons*,219(3). doi:10.1016/j.jamcollsurg.2014.04.009
10. Lavryk O, Ashburn J, Liska D et al. Incisional negative pressure wound therapy reduces surgical site infections in complex colorectal surgery patients. *Dis Colon Rectum* 2016;59:e380. doi:10.1097/01.dcr.0000482708.50838.af.
11. Lee AJ, Sheppard CE, KentWD, Mewhort H, Sikdar KC, Fedak PW. Safety and efficacy of prophylactic negative pressure wound therapy following open saphenous vein harvest in cardiac surgery: a feasibility study. *Interactive Cardiovascular and Thoracic Surgery* 2017;24:324-328. doi:10.1093/icvts/ivw400.
12. Lee, K., Murphy, P. B., Ingves, M. V., Duncan, A., DeRose, G., Dubois, L., ... & Power, A. (2017). Randomized clinical trial of negative pressure wound therapy for high-risk groin wounds in lower extremity revascularization. *Journal of vascular surgery*, 66(6), 1814-1819.
13. Matatov T, Reddy KN, Doucet LD, Zhao CX, Zhang WW. Experience with a new negative pressure incision management system in prevention of groin wound infection in vascular surgery patients. *J Vasc Surg* 2013;57:791-795.
14. Newman, J. M., Siqueira, M. B., Klika, A. K., Molloy, R. M., Barsoum, W. K., & Higuera, C. A. (2019). Use of Closed Incisional Negative Pressure Wound Therapy After Revision Total Hip and Knee Arthroplasty in Patients at High Risk for Infection: A Prospective, Randomized Clinical Trial. *The Journal of arthroplasty*, 34(3), 554-559.
15. Pachowsky, M., Gusinde, J., Klein, A., Lehl, S., Schulz-Drost, S., Schlechtweg, P., ... & Brem, M. H. (2012). Negative pressure wound therapy to prevent seromas and treat surgical incisions after total hip arthroplasty. *International orthopaedics*, 36(4), 719-722.
16. Pauser, J., Nordmeyer, M., Biber, R., Jantsch, J., Kopschina, C., Bail, H. J., & Brem, M. H. (2016). Incisional negative pressure wound therapy after hemiarthroplasty for femoral neck fractures—reduction of wound complications. *International wound journal*, 13(5), 663-667.

17. Pleger, S. P., Nink, N., Elzien, M., Kunold, A., Koshty, A., & Böning, A. (2018). Reduction of groin wound complications in vascular surgery patients using closed incision negative pressure therapy (ciNPT): a prospective, randomised, single-institution study. *International wound journal*, 15(1), 75-83.
18. Redfern RE, Cameron-Ruetz C, O'Drobinak S, Chen J, Beer KJ. Closed incision negative pressure therapy effects on postoperative infection and surgical site complication after total hip and knee arthroplasty. *J Arthroplasty* 2017;32:3333-3339.
19. Ruhstaller, K., Downes, K. L., Chandrasekaran, S., Srinivas, S., & Durnwald, C. (2017). Prophylactic wound vacuum therapy after cesarean section to prevent wound complications in the obese population: a randomized controlled trial (the ProVac study). *American journal of perinatology*, 34(11), 1125-1130.
20. Sabat J, Tyagi S, Srouji A et al. IP123- Prophylactic Negative-Pressure Therapy for Femoral Incision in Vascular Surgery: Preliminary Results of a Prospective, Randomized Trial. (Presented at the 2016 Vascular Annual Meeting, June 8-11, 2016, National Harbor, MD). [abstract]. *J Vasc Surg* 2016;63:945-955.
21. "Surgical Site Infection (SSI) Event." Surgical Site Infection (SSI) Event, 2019, www.cdc.gov/nhsn/PDFs/pscManual/9pscSSICurrent.pdf?agree=yes&next=Accept.%20Updated%20January%202019.
22. Swift SH, Zimmerman MB, Hardy-Fairbanks AJ. Effect of single-use negative pressure wound therapy on postcesarean infections and wound complications for high-risk patients. *J Reprod Med* 2015;60:21 1-218.

BIBLIOGRAPHY OF PUBLISHED STUDIES

- Atkins BZ, et al. "Does Negative Pressure Wound Therapy Have a Role in Preventing Poststernotomy Wound Complications?" Surgical Innovations. 2009 June 16(2):140-6.
- Atkins BZ, et al. "Laser Doppler flowmetry assessment of peristernal perfusion after cardiac surgery: beneficial effect of negative pressure therapy." International Wound Journal. 2011 Feb;8(1):56-62.
- Berkowitz MJ. "Use of a Negative Pressure Incisional Dressing After Surgical Treatment of Calcaneal Fractures." Techniques in Foot & Ankle Surgery. 2013 December 1;12(4):172-4.
- Blackham AU, et al. "Prevention of surgical site infections in high-risk patients with laparotomy incisions using negative-pressure therapy." American Journal of Surgery. 2013 January 30.
- Bollero D, et al. "Negative pressure surgical management after pathological scar surgical excision: a first report." International Wound Journal. 2013 Feb 19. [Epub ahead of print]
- Bonds AM, et al. "Incisional Negative Pressure Wound Therapy Significantly Reduces Surgical Site Infection in Open Colorectal Surgery." Diseases of the Colon & Rectum. 2013 December 1;56(12):1403-8
- Colli A. "First Experience With a New Negative Pressure Incision Management System on Surgical Incisions After Cardiac Surgery in High Risk Patients." Journal of Cardiothoracic Surgery. 2011 December 6;6(1):160.
- Conde-Green A, et al. "Incisional Negative-Pressure Wound Therapy versus conventional dressings following abdominal wall reconstruction. A comparative study." Annals of Plastic Surgery. 2013 Oct 71(4):394-7.
- Dutton M, Curtis K. "Well-wound therapy: use of NPWT to prevent laparotomy breakdown." Journal of Wound Care. 2012 Aug 21(8):386-8.
- Faroqi L, et al. "Use of an Incision-Line Negative Pressure Wound Therapy Technique to Protect High-Risk Diabetic Foot Wounds, Postoperatively." Journal of Diabetic Foot Complications. 2013 September 1;5(2):44-7.
- Glaser DA, et al. "Negative pressure therapy for closed spine incisions: A pilot study." Wounds. 2012 Nov 24(11):308-11
- Gomoll AH, et al. "Incisional vacuum-assisted closure therapy." Journal of Orthopaedic Trauma. 2006 Nov-Dec;20(10):705-9.
- Haghshenasskashani A, Varcoe RL. "A new negative pressure dressing (Prevena) to prevent wound complications following lower limb distal arterial bypass." The British Journal of Diabetes and Vascular Disease. 2011 Jan/Feb;11(1):21-4.
- Ingargiola MJ, Danialli LN, Lee ES. "Does the application of incisional negative pressure therapy to high-risk wounds prevent surgical site complications? A systematic review." Eplasty. 2013 September 20;13:e49.
- Karlakki S, et al. "Negative pressure wound therapy for management of the surgical incision in orthopaedic surgery: A review of evidence and mechanisms for an emerging indication." Bone and Joint Research. 2013 December 1;2(12):276-84.
- Kilpadi DV, Cunningham MR. "Evaluation of closed incision management with negative pressure wound therapy (CIM): hematoma/seroma and involvement of the lymphatic system." Wound Repair and Regeneration. 2011 Sep;19(5):588-96.
- Mark KS, et al. "Incisional Negative Pressure Therapy to Prevent Wound Complications Following Cesarean Section in Morbidly Obese Women: A Pilot Study." Surgical Innovations. 2013 September 20.
- Masden D, Goldstein J, Endara M, Xu K, Steinberg J, Attinger C. "Negative pressure wound therapy for at-risk surgical closures in patients with multiple comorbidities: a prospective randomized controlled study." Annals of Surgery. 2012 Jun;255(6):1043-7.
- Pauli EM, Krpata DM, Novitsky YW, Rosen MJ. "Negative Pressure Therapy for High-Risk Abdominal Wall Reconstruction Incisions." Surgical Infections. 2013 Jun;14(3):270-4.
- Reddix RN, et al. "The effect of incisional negative pressure therapy on wound complications after acetabular fracture surgery." Journal of Surgical Orthopaedic Advances. 2010 Jun;19(2):91-7.

- Stannard JP, et al. "Negative pressure wound therapy to treat hematomas and surgical incisions following high-energy trauma." Journal of Trauma. 2006 Jun;60(6):1301-6.
- Stannard JP, et al. "Incisional negative pressure wound therapy after high-risk lower extremity fractures." Journal of Orthopedic Trauma. 2012 Jan;26(1):37-42.
- Tauber R, et al. "Inguinal lymph node dissection: epidermal vacuum therapy for prevention of wound complications." Journal of Plastic, Reconstructive, and Aesthetic Surgery. 2013 Mar;66(3):390-6.
- Vargo D. "Negative pressure wound therapy in the prevention of wound infection in high risk abdominal wound closures." American Journal of Surgery. 2012 Dec;204(6):1021-4.
- Wilkes RP, et al. "Closed incision management with negative pressure wound therapy (CIM): biomechanics." Surgical Innovations. 2012 Mar;19(1):67-75.

SYMBOLS USED



Refer to Clinician Guide



Consult Instructions for Use

IP22

Ingress Protection



No Bathing or Showering

STERILE R

Sterile using radiation

LOT

Lot Number



Date of Manufacture



Manufacturer



Type BF applied part



Use By



Fragile

REF

Catalog Number



Keep Dry



Single Use Only



MR Unsafe



Tripping Hazard



Do Not Resterilize



Class II Device



Content Information



Temperature Limit



Do not use if package is damaged or open



Contains Phthalates
(PREVENA PLUS™ Connector Tubing)

Rx only

CAUTION: Federal (US) law restricts this device to sale by or on the order of a physician.



This product is designated for separate collection at an appropriate collection point.
Do not dispose of as household waste.

Manufactured for:
KCI USA, Inc.
12930 IH 10 West
San Antonio, TX 78249
1-800-275-4524
www.acelity.com