REF 20-2050

Read Instructions for Use Prior to Using this Product.

Instructions for Use

DESCRIPTION

The DuraSeal Dural Sealant System consists of components for preparation of a synthetic absorbable sealant, and an applicator for delivery of the sealant to the target site.

The sealant is composed of two solutions, a polyethylene glycol (PEG) ester solution and a trilysine amine solution (referred to as the 'blue' and 'clear' precursors, respectively). When mixed together, the precursors cross link to form the hydrogel sealant. The mixing of the precursors is accomplished as the materials exit the tip of the applicator.

The hydrogel implant is absorbed in approximately 4 to 8 weeks, sufficient time to allow for healing.

The DuraSeal Dural Sealant System is provided sterile and consists of the following packaged in a lidded tray:

- Powder Vial/Diluent Syringe Assembly
- Clear Precursor Syringe
  Applicator
  Spray Tips (3)
  Plunger Cap

INDICATION

The DuraSeal Dural Sealant System is intended for use as an adjunct to sutured dural repair during cranial surgery to provide watertight closure. DuraSeal should only be used with autologous duraplasty material.

CONTRAINDICATIONS

- Do not apply the DuraSeal hydrogel to confined bony structures where nerves are present since neural compression may result due to hydrogel swelling. The hydrogel may swell up to 50% of its size in any dimension.

WARNINGS

- The safety and effectiveness of the DuraSeal hydrogel has not been studied in:
  - Patients with a known allergy to FD&C Blue #1 dye.
  - Patients undergoing a contaminated cranial procedure that entails a dural incision involving penetration (other than superficial) of the air sinus or mastoid air cells.
  - Patients with severely altered renal or hepatic function.
  - Patients with a compromised immune system or autoimmune disease.

  Procedures involving petrous bone drilling
  - Patients with traumatic injuries to the head
- Do not use if an active infection is present at the surgical site.

PRECAUTIONS

- Use only with the delivery system provided with the polymer kit.
- The DuraSeal Dural Sealant System is provided sterile. Do not use if packaging or seal has been damaged or opened. Do not re-sterilize.
- The DuraSeal Dural Sealant System is intended for single patient use only. Discard opened and unused product.
- Do not use if the PEG powder is not free flowing.
- Use within 1 hour of preparation.
- Do not use in combination with other sealants or hemostatic agents.
- Do not use in patients younger than 18 years of age, or in pregnant or breast feeding females
- Prior to application of the DuraSeal hydrogel, ensure that adequate hemostasis has been achieved.
- Incidental application of DuraSeal hydrogel to tissue planes that will be subsequently approximated, such as muscle and skin, should be avoided.

ADVERSE EVENTS

The DuraSeal Dural Sealant System was evaluated in 111 investigational patients in the pivotal clinical study. The following table presents any adverse event occurring at a rate of 1% or higher in these patients. Adverse Event rates presented are based on the number of patients having at least one occurrence of a particular adverse event divided by the total number of patients treated.

The incidence and nature of adverse events observed in this patient population are consistent with the type and complexity of the surgery performed and the co-morbid state of the treated patients. There were two patient deaths (out-of-hospital). In both cases, the deaths were attributed to the patients' prior condition.

AE category Note: Patient can experience more than one AE	# of patients n (%)
Arrhythmia	6 (5.4)
Bleeding	4 (3.6)
Cerebral Edema	4 (3.6)
CSF Leak (protocol definition) Incisional Pseudomeningocele	 2 (1.8) 3 (2.7)
Dermatologic Events	11 (9.1)
Dizziness	8 (7.2)
Edema (non-systemic)	19 (17.1)
Electrolyte Imbalance	11 (9.9)
Elevated Liver Enzymes	11 (9.9)
Fever Post-op (> 38.5°C for 48 h)	6 (5.4)
Fever (< 38.5°C for < 48 h)	5 (4.5)
General Malaise	9 (8.1)
General - Other: Corneal abrasion, chemotherapy complication, hiccoughs	3 (2.7)
GI Disturbance	16 (14.4)
Headache (not responding to standard therapy)	5 (4.5)
Headache (responding to standard therapy)	9 (8.1)
Hematologic Abnormality	7 (6.3)
Hydrocephalus	4 (3.6)
Hypertension	5 (4.5)
Infection, Non-Incisional Thrush, otitis media, keratitis, catheter-related	8 (7.2)
Upper Respiratory/Bronchial Urinary Tract	4 (3.6) 11 (9.9)
Infection, Surgical Site Deep (re-operation required) Superficial	 8 (7.2) 1 (0.9)
Late (> 30 days) Wound Infection	3 (2.7)
Meningitis Aseptic Bacterial	 5 (4.5) 2 (1.8)
Musculoskeletal Events	21 (18.9)
Nausea and/or Vomiting	24 (21.6)
Neurological Symptoms Cognitive Cranial Nerve Deficit Motor Deficit Neuropsychiatric disorders Speech Difficulty Visual Disturbance	 5 (4.5) 34 (30.0) 17 (15.3) 7 (6.3) 10 (9.0) 22 (19.8)
Pain, Incisional	2 (1.8)
Peripheral edema	2 (1.8)
Pneumonia	3 (2.7)
Pseudomeningocele (responding to conservative therapy)	2 (1.8)
Respiratory Difficulties	6 (5.4)
Seizure	3 (2.7)
Stoke/CVA/Cerebral Hemorrhage	5 (4.5)
Subdural Hematoma	2 (1.8)
Ureterolithiasis	2 (1.8)
Urinary Difficulty	9 (8.1)
Urogenital - Other	2 (1.8)
Wound erythematic/inflammation	2 (1.8)

Potential, but not observed, risks and adverse events that could occur from the use of the DuraSeal Dural Sealant System include, but are not limited to, renal compromise, inflammatory reaction, neurological compromise, allergic reaction and/or delayed healing.

CLINICAL EXPERIENCE

A prospective, multi-center, non-randomized, single arm clinical investigation to evaluate the safety and effectiveness of the DuraSeal Dural Sealant System as an adjunct to sutured dural repair was conducted. The study involved 10 investigational sites within the United States and 1 site in Europe. A total of 111 patients were treated with the DuraSeal Sealant.

The primary endpoint for this study was the percent (%) success in the treatment of intraoperative CSF leakage following DuraSeal Sealant application defined as no CSF leakage from dural repair intra-operatively after up to two DuraSeal Sealant applications during Valsalva maneuver up to 20 cm H_2O for 5 to 1 seconds.

Key Inclusion/Exclusion criteria for the study included the following:

Pre-Operative Inclusion Criteria:

- Patient is scheduled for an elective cranial procedure that entails a dural incision using any of the following approaches (or combination): Frontal, Temporal, Parietal, Occipital, and/or Suboccipital
- Patient requires a procedure involving surgical wound classification Class I/Clean

Pre-Operative Exclusion Criteria:

- Patient requires a procedure involving translabyrinthine, transsphenoidal, transoral and/or any procedure that penetrates the air sinus or mastoid air cells; superficial penetration of air cells are not excluded

- Patient has had a prior intracranial procedure in the same anatomical location
- Patient has had chemotherapy treatment within 6 months prior to, or planned during the study (until completion of last follow-up evaluation)
- Patient has had prior radiation treatment to the surgical site or has planned radiation therapy within one month post procedure
- Patient has hydrocephalus (e.g. elevated intracranial pressure > 22 cm H_2O)
- Patient has a known malignancy or another condition with prognosis shorter than 6 months (patients with stable systemic disease can be included, extent of disease will be documented)
- Patient has pre-existing external ventricular drainage or lumbar CSF drain
- Patient is not able to tolerate multiple Valsalva maneuvers or an intra-operative CSF shunt does not allow for transient elevation of CSF pressure during Valsalva maneuvers
- Patient has a systemic infection (UTI, active pneumonia) or evidence of any surgical site infection (superficial, deep, or organ/space), as determined by fever > 101°F, WBC > 11,000/uL, positive blood culture, positive urine culture, and/or by a positive chest x-ray.
- Patient has been treated with chronic steroid therapy unless discontinued more than 6 weeks prior to surgery (standard acute perioperative steroids are permitted)
- Patient has a compromised immune system or autoimmune disease (WBC count less than 4000/uL or greater than 20,000/uL)
- Patient with uncontrolled diabetes, as determined by two or more incidences of elevated blood sugar levels (fasting glucose >120mg/dL) within the 6 months prior to surgery.
- Patient with creatinine levels > 2.0 mg/dL

Intra-Operative Inclusion Criteria:

- Surgical wound classification Class I/Clean (per CDC criteria)
- Linear extent of durotomy is at least 2 cm
- Dural margin from edges of bony defect is at least 3 mm throughout
- Patient must have a CSF leak after primary dural closure, either spontaneous or upon Valsalva maneuver, up to 20 cm H_2O for 5-10 seconds

tra-Operative Exclusion Criteria:

- Patient required use of synthetic or non-autologous duraplasty material
- Patient has a gap greater than 2 mm remaining after primary dural closure
- Incidental finding of any of the Pre-operative Exclusion Criteria

Of the 111 patients in this study, 67 patients (60.4%) experienced a spontaneous CSF leak intra-operatively (i.e., no need for Valsalva maneuver) prior to DuraSeal application, and 44 patients (39.6%) experienced a leak upon the Valsalva maneuver prior to DuraSeal application. One hundred five (105) patients (94.6%) were treated with one DuraSeal Sealant application, and 6 patients (5.4%) were treated with two applications.

Demographic information for patients treated in the study is shown in the table below:

Characteristic	Study Population n (%)
Duration of Surgery:	
< 2 hours	7 (6.3)
≥ 2 hours	102 (91.8)
Unknown	2 (1.8)
ASA Score:	
1	14 (12.6)
2	59 (53.2)
≥ 3	37 (33.3)
Indication for Surgery:	
AVM	7 (6.3)
Aneurysm	12 (10.8)
Chiari Malformation	6 (5.4)
Cyst	3 (2.7)
Epilepsy	10 (9.0)
Nerve Decompression	21 (18.9)
Tumor	51 (45.9)
Other	1 (0.9)

All 111 patients treated with the DuraSeal Sealant showed no leakage during the intra-operative assessment. 109 of 111 patients (98.2%) met the criteria for primary endpoint success; i.e., intraoperative sealing. Two patients were tested intra-operatively at a pressure of only 10 cm H_2O, and although no leak was seen, these patients could not technically be classified as successes. Safety was assessed based on evaluation of wound healing, the occurrence of post-operative CSF leaks, the nature and severity of other adverse events, and adverse device-related adverse events diagnosed by physical examination, protocol-specified diagnostic laboratory tests, neurological assessments (including pain and modified Rankin Scale) and CT imaging assessment performed by independent radiologists for evaluation of extradural collections and adverse findings.

The incidence of post-op CSF leaks in this study was 4.5%. Of these leaks, 1.8% were incisional and 2.7% were pseudomeningoceles. **There were 9/111 surgical wound infections (8.1%) with 7.2% identified as deep wound infections.** All deep wound infections were treated with surgical debridement. There was no concurrent control group used for comparison in the study. The clinical protocol specified only clean surgical cases and contained an intra-operative exclusion criterion for cases in which a clean case became a clean-contaminated case (e.g., sinus penetration. History of smoking and prolonged surgery were found to be independent predictors for infection.

All wounds were well healed by the 3-month post-operative visit. There was no untoward effect on hepatic or renal function associated with product use and absorption. Additionally, there were no unexpected findings based on CT imaging assessment by independent neuroradiologists.

Due to a high water content, DuraSeal appears similar to simple fluids on CT and MRI imaging following initial instillation. Thus, DuraSeal is dark on CT and T1-weighted MRI images (similar to cerebrospinal fluid). T2-weighted MRI is helpful in differentiating DuraSeal from cerebrospinal fluid. While being absorbed, vascular enhancement of the residual margins is normally seen, and the space occupied by the hydrogel collapses. Based on CT imaging of 111 patients in the study, the average reduction in extradural space at the DuraSeal application site was 74.5% at 3 months.

The hydrogel potentially may have overlapping imaging characteristics with either persistent unilocular fluid collection or with an infected surgical bed. In the event that CT or MR imaging is unable to confidently exclude infection, then an indium labeled white-blood cell nuclear medicine study may be warranted.

A post-approval study is being conducted to further characterize clinical experience with the use of DuraSeal, including infection rate.

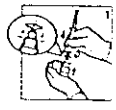
DIRECTIONS FOR USE

Polymer Kit Mixing Instructions

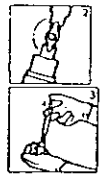
Note:

- Inspect the PEG powder vial to ensure the powder is free flowing, or can be loosened up by shaking. If the powder remains not free-flowing, discard the entire kit.

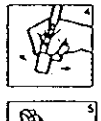
1. Open the sterile tray. Remove the contents from the tray and introduce into the sterile field.
2. Pierce the vial seal on the powder vial by pushing the syringe/stopcock into the vial cap. The vial seal is completely pierced when the vial luer neck is recessed into the vial cap and a "click" is noted; twisting is not required. Avoid pushing the syringe plunger.



3. Rotate the stopcock to the open position, and inject syringe contents into the vial.
   Note: if fluid is leaking from the vial/syringe assembly, discard the entire polymer kit.



4. Gently shake the vial/syringe assembly until the powder is completely dissolved. The solution will turn blue.



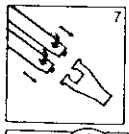
5. Invert the vial/syringe assembly, and draw the vial contents back into the syringe.

6. Unscrew the syringe from the vial/stopcock assembly and discard the vial/stopcock assembly.

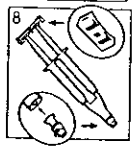
Applicator Preparation (Assembly and Priming)

Prior to attaching the syringes to the applicator, ensure syringe fluid levels are equal. If fluid levels are not equal, expel fluids out of syringes until equal.

2. Attach blue and clear precursor syringes to the applicator.



3. While holding the syringes by the plungers, carefully attach the plunger cap to the plungers of both syringes without dispensing precursors into the applicator.



Note:
Avoid touching the plunger cap before application to avoid inadvertent precursor injection and tip plugging

4. Attach a spray tip to the applicator.

Hydrogel Application

Note:

- Achieve hemostasis and minimize CSF outflow. Ensure that there are 2-3 mm margins around the durotomy edge and that the margins are clear of clots and fluids, hemostatic agents and loose connective tissue.

Position the applicator 2-4 cm from the target site. Apply firm even pressure to the center of the plunger cap to dispense the precursors. Rapid initial spraying, followed by a slower controlled rate is recommended.

2. Continue applying the hydrogel until a thin (1 – 2 mm) coating is formed.
   Note: If delivery is interrupted and the spray tip is plugged, remove the spray tip, wipe the applicator tip, attach a new spray tip and continue delivery.
   Note: The blue color of the hydrogel aids in gauging thickness. As the thickness of the DuraSeal hydrogel increases to 2 mm, the fine epidural vasculature becomes less visible.
3. Hydrogel application beyond the edges of the dural margin may be removed with scissors or mechanical disruption. Irrigation immediately after the sealant has solidified is permitted.

STORAGE
The DuraSeal Dural Sealant System should be stored at or below 77 °F (25°C).

SYMBOLS USED ON LABELING

② Do not reuse LOT Lot Number

REF Catalog Number

Use by – year and month

Latex Free

See Instructions for Use

Store below 25° C (77 °F)

STERILE R Sterile unless the package is damaged or open.
Method of sterilization – Radiation

R_x only Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

For more information, or to obtain Confluent Surgical documents or references, contact:
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DuraSeal is a trademark of Confluent Surgical, Inc.

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