DuraSeal Dural Sealant System

REF: 20 - 2050 / REF: 20 - 2010

Instructions for Use

All Instructions Should Be Read Before Use

Contraindications

- Do not use if the delivery system is 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.
- Do not 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.

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 Events 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 patient’s prior condition.

<table>
<thead>
<tr>
<th>Category</th>
<th># of patients n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound erythema</td>
<td>34 (30.0)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>11 (9.9)</td>
</tr>
<tr>
<td>Incisional weakness</td>
<td>10 (9.0)</td>
</tr>
<tr>
<td>Infection, Non-Intravascular</td>
<td>5 (4.5)</td>
</tr>
<tr>
<td>Upper Respiratory/Respiratory</td>
<td>4 (3.6)</td>
</tr>
<tr>
<td>Infection, Surgical Site</td>
<td>3 (2.7)</td>
</tr>
<tr>
<td>Lacer (&gt; 30 days)/Wound Infection</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>5 (4.5)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Mucosal drying disorders</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Nausea and/or Vomiting</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Neurological Symptoms</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Cerebral Edema</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>1 (0.9)</td>
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<td>1 (0.9)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Ulcer</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Urinary tract infection, Catheter-related</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Urinary tract infection, Non-Incisional</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Urinary tract infection, Nephrolithiasis</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Urinary tract infection, Hemorrhage</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Urinary tract infection, Infection</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Urinary tract infection, Blood loss</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Urinary tract infection, Infection</td>
<td>1 (0.9)</td>
</tr>
<tr>
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</tbody>
</table>

Precautions

- Do not use in patients who have known allergy to FD&C Blue #1 dye.
- The safety and effectiveness of the DuraSeal hydrogel has not been studied in:
  - Patients with a known allergy to FD&C Blue #1 dye.
  - The DuraSeal Dural Sealant System is intended for use as an adjunct to sutured dural repair during cranial surgery to provide watertight closure.
  - Intraoperative application of DuraSeal hydrogel to tissue planes that will be subsequently approximated, such as muscle and skin, should be avoided.

Indication

The DuraSeal Dural Sealant System is intended for use as an adjunct to sutured dural repair during cranial surgery to provide watertight closure.

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’ pre-polymer solutions, respectively. When mixed together, the pre-polymers cross-link to form the hydrogel sealant. The mixing of the pre-polymers is accomplished as the maximal exit point of the applicator.

The hydrogel implant is absorbed in approximately 4 to 6 weeks, sufficient time to allow for healing.

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

- Pre-operative Exclusion Criteria:
  - Patient has had prior radiation treatment to the surgical site or has planned radiation therapy within one month post procedure.
  - 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 intracranial procedure in the same anatomical location.
  - Patient requires a procedure involving translabyrinthine, transsphenoidal, transoral and/or any procedure that penetrates the air sinus or mastoid air cells.
  - The DuraSeal Dural Sealant System is intended for use as a surgical wound classification Class I/Engraft.

- Pre-operative Inclusion Criteria:
  - Patient has had a prior intracranial procedure in the same anatomical location.

Note:

- All Instructions Should Be Read Before Use
- Pre-operative Exclusion Criteria:
  - 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 H2O).

• 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 drain or lumbar CSF drain.

• Patient is not able to tolerate multiple Valsalva maneuvers or an intra-operative CSF leak does not allow for transient elevation of CSF pressure during Valsalva maneuvers.

• Patient has a systemic infection (e.g., active pneumonia) or evidence of any surgical site infection (superficial, deep, or organ/space), as determined by the investigator.

• Patient has undergone a previous, separate cranial or spinal operation (excluding local and limited cranial advancement flap surgery).

• Patient has a known allergy to any of the components of the DuraSeal Sealant.

• Patient has a current历史 of any systemic disease or condition that would contraindicate the use of DuraSeal Sealant.

• Patient is not able to tolerate multiple Valsalva maneuvers or an intra-operative CSF leak does not allow for transient elevation of CSF pressure during Valsalva maneuvers.

• The post-operative CSF leak rate was 7.4% and 6.0% for the Retrospective and PMA Populations respectively. Only one late surgical site infection was noted within the Retrospective Population with an associated incidence rate of 1.5% compared with an overall infection rate of 6.0% for the PMA Population. There were no device-related adverse events or unscheduled device effect-related events noted in either population.

Intra-Operative Inclusion Criteria:

• Surgical wound classification Cl/Class I (per CONC criteria).

• Gross extent of durotomy is at least 2 cm.

• Chordal margin from edge of durotomy is at least 1 mm cranial.

• Patient must have a CSF leak prior to dural closure, either spontaneous or via Valsalva maneuver, up to 20 cm H2O for 5-10 minutes.

Intra-Operative Exclusion Criteria:

• Patient required use of synthetic or non-autologous dural material.

• Patient has a giga tanner than 2 mm remaining after durotomy closure.

• Initial screening of any of the pre-operative Exclusion Criteria.

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 H2O, and although no leak was seen, these patients could not technically be classified as success. 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 device-related adverse events monitored 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 intracranial 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 111 surgical wound infections (8.1%) with 7.2% identified as deep wound infections. All deep wound infections were treated with surgical debridement.

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The mean durotomy length was slightly longer for the Retrospective Population included substantially more patients with an ASA score of 3 or more, included a small subset of Clean-contaminated procedures and degenerative changes, increased dura-brain adhesions, or impaired neodura formation.

Histologically, the application of DuraSeal over the collagen duraplasty was not associated with neurotoxicity, delayed healing, or absorption. Additionally, there were no unexpected findings based on CT imaging assessment by independent neuroradiologists.

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.

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A post-approval study is being conducted to further characterize clinical experience with the use of DuraSeal, including infection rate. Evaluation of use with non-autologous collagen duraplasty materials.

A separate evaluation, preclinical and clinical testing of DuraSeal use with non-autologous dural material has been completed. A study was performed in a canine model to evaluate the performance of DuraSeal when used in conjunction with commercially available collagen duraplasty. The results of this study demonstrated 100% improvement in intracranial seal success and at 83% reduction in postoperative CSF leaks in animals treated with DuraSeal in conjunction with collagen duroplasty compared to animals treated with collagen duroplasty alone. DuraSeal is a registered trademark of Confluent Surgical, Inc.

Storage

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A retrospective, multi-center, non randomized study was conducted to evaluate the safety of DuraSeal Sealant as an adjunct to sutured dural repair to provide watertight closure when used in conjunction with non-autologous duraplasty materials. The evaluation involved 3 sites within the United States. A total of 66 patients were treated with the DuraSeal Sealant and met the criteria for the primary endpoint success; i.e., intraoperative sealing. Two patients were tested intra-operatively at a pressure of only 10 cm H2O, and although no leak was seen, these patients could not technically be classified as success. 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 device-related adverse events monitored 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 intracranial collections and adverse findings.

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Hydrogel Application

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