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Package Insert

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Xact Sealant System

REF 20-4300
REF 20-4004

Read Instructions for Use Prior to Using this Product.

Instructions for Use

DESCRIPTION

The DuraSeal Xact Sealant System consists of components for preparation of a synthetic absorbable sealant, and applicators 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 sealant is naturally absorbed in approximately 4 to 8 weeks, sufficient time to allow for healing. The breakdown products are readily cleared from the body, primarily through the kidneys.

The DuraSeal Xact Sealant System is provided in two configurations. The 2 mL configuration consists of one 2 mL polymer kit and one MicroMyst Applicator (the MicroMyst Applicator requires the use of a compressed air source, such as the Confluent Surgical Flow Regulator or the Confluent Surgical Air Pump). The 5 mL configuration consists of one 5 mL polymer kit which includes the Dual Liquid Applicator (consisting of the Y-Applicator and three (3) Spray Tips). The polymer kits and applicators are provided sterile.

INDICATION

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

CONTRAINDICATIONS

The DuraSeal Xact Sealant System is contraindicated for use as a void filler in enclosed spaces in the spine (such as the lateral gutters and neural foramen), as post-operative hydrogel swelling may impinge on surrounding tissues.

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.
  - Procedures involving non-autologous duraplasty
  - Patients with severely altered renal or hepatic function.
  - Patients with a compromised immune system or autoimmune disease.
- Do not use if an active infection is present at the surgical site.
- Do not use the DuraSeal Xact Sealant as a hemostatic agent.

PRECAUTIONS

- Use only with the Confluent Surgical applicators.
- The polymer kits and applicators are provided sterile. Do not use if packaging or seal has been damaged or opened. Do not re-sterilize.
- The polymer kits and applicators are 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 hydrogel, ensure that adequate hemostasis has been achieved.
- Incidental application of hydrogel to tissue planes that will be subsequently approximated, such as muscle and skin, should be avoided.

ADVERSE EVENTS

The DuraSeal Xact Sealant System was evaluated in a pivotal clinical study, in which a total of 158 patients were enrolled (102 treated with DuraSeal Xact and 56 patients treated using Standard of Care methods). All Adverse Events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) and are presented based on System Organ Class.

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 no patient deaths. All Adverse Events were reviewed and adjudicated by an independent Clinical Events Committee (CEC), comprise of three independent neurosurgeons. The CEC's overall impression was that, withinin each treatment group, the observed events appeared consistent in type and severity for the study population.

Any Adverse Event	95 (93.1)	51 (91.1)
Blood And Lymphatic System Disorders	10 (9.8)	4 (7.1)
Cardiac Disorders	10 (9.8)	2 (3.6)
Eye Disorders	6 (5.9)	1 (1.8)
Gastrointestinal Disorders	21 (20.6)	9 (16.1)
General Disorders And Administration Site Conditions	33 (32.4)	18 (32.1)
Immune System Disorders	1 (1.0)	0 (0.0)
Infections And Infestations	19 (18.6)	9 (16.1)
Injury, Poisoning And Procedural Complications	44 (43.1)	7 (12.5)
Investigations	50 (49.0)	23 (41.1)
Metabolism And Nutrition Disorders	10 (9.8)	3 (5.4)
Musculoskeletal And Connective Tissue Disorders	24 (23.5)	15 (26.8)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	4 (3.9)	0 (0.0)
Nervous System Disorders	48 (47.1)	21(37.5)
Psychiatric Disorders	4 (3.9)	3 (5.4)
Renal And Urinary Disorders	20 (19.6)	4 (7.1)
Reproductive System And Breast Disorders	1 (1.0)	1(1.8)
Respiratory, Thoracic And Mediastinal Disorders	15 (14.7)	4 (7.1)
Skin And Subcutaneous Tissue Disorders	9 (8.8)	3 (5.4)
Vascular Disorders	10 (9.8)	6 (10.7)

Note: Patient can experience more than one AE

Further breakdown of the observed post-operative CSF leak and surgical site infection rates are presented in the tables below.

Presence of endpoint CSF leak within 90 days post-procedure	n (%)	8 (7.8)	3 (5.4)	0.748	13.2
CSF Fistula	n	3 (2.9)	0		2.9
Pseudomeningocele	n	5 (4.9)	3 (5.3)		10.2
Presence of SSI within 90 days post-procedure	n (%)	7 (6.9)	4 (7.1)	1.000	14

Deep Surgical Site Infection	n	5 (4.9)	1(1.7)		6.6
Superficial Surgical Site Infection	n	2 (1.9)	3 (5.3)		6.2

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

CLINICAL EXPERIENCE

A prospective, multi-center, randomized, two arm, single blind study designed to assess if the DuraSeal Xact Sealant System, when used as an adjunct to sutured dural repair, is more effective than Standard of Care methods for producing a watertight dural closure in subjects undergoing an intentional durotomy during spinal surgery was conducted. Subjects that were scheduled for spinal procedures requiring a dural incision and who met the preoperative eligibility criteria were considered for study participation. Subjects that met all of the intra-operative eligibility criteria were enrolled and randomized either to DuraSeal Xact Sealant or Control. The study involved 24 investigational sites within the United States. A total of 102 patients were treated with the DuraSeal Xact Sealant, and a total of 56 patients were treated using Standard of Care methods to obtain a watertight dural closure.

The primary endpoint for this study was the percent (%) success in obtaining a watertight closure following assigned treatment (DuraSeal Xact Sealant or Control), defined as a watertight closure of the dural repair intra-operatively confirmed by Valsalva maneuver at 20 - 25 cm H_2O for 5 to 10 seconds.

Safety was assessed based on evaluation of the occurrence of post-operative CSF leaks and surgical site infection, the nature and severity of adverse events, protocol-specified laboratory tests, neurological assessments, and wound healing.

Inclusion/Exclusion criteria for the study included the following:

Pre-Operative Inclusion Criteria:

- Subject was between 18 and 75 years of age.
- Subject was scheduled for a spinal procedure that entails a dural incision.
- Subject required a procedure involving surgical wound classification Class I/Clean (per CDC criteria).
- Subject, or authorized representative, was informed of the nature of the study, and provided written informed consent, approved by the appropriate Institutional Review Board (IRB) of the respective clinical site.

Pre-Operative Exclusion Criteria:

- Subject had active spinal and/or systemic infection.
- Subject required additional spine surgery within the study time period.
- Subject had a previous spinal surgery involving dural exposure and/or entry at the same level(s) as the study procedure.
- Subject had pre-existing external lumbar CSF drain or internal CSF shunt.
- Subject participated in a clinical trial of another investigational device or drug.
- Subject with creatinine > 2.0 mg/dL.
- Subject with total bilirubin > 2.5 mg/dL.
- Pregnant or breast-feeding females or females who wished to become pregnant during the length of study participation.
- Subject treated with chronic steroid therapy unless discontinued more than 6 weeks prior to surgery (standard peri-operative steroids are permitted). For purposes of this protocol, chronic steroid therapy is defined as greater than 4 weeks.
- Subject had documented history of significant coagulopathy with a PTT > 35 sec, PT/ INR >1.2, receiving aspirin, or NSAIDS at the time of surgery. Note: Subjects who are receiving cardiovascular prophylaxis are not excluded.
- Subject received warfarin or heparin at the time of surgery (including analogs).
- Subject diagnosed and documented compromised immune system and/or autoimmune disease.
- Subject had chemotherapy treatment within 6 months prior to, or planned during the study (until completion of last follow-up evaluation).
- Subject had prior radiation treatment to the surgical site or has planned radiation therapy within 30 days post procedure.
- Subject had a known malignancy or another condition with prognosis shorter than 6 months.
- Subjects with documented history of uncontrolled diabetes.
- The investigator determined that the subject should not be included in the study for reason(s) not already specified.

Intra-Operative Inclusion Criteria:

- Presence of non-watertight closure, either spontaneously or upon Valsalva maneuver to 20 - 25 cm H_2O for 5-10 seconds

Intra-Operative Exclusion Criteria:

- Incidental finding of any of the pre-operative exclusion criteria.
- Subject required use of a synthetic or non-autologous duraplasty material.
- Subject had a gap of greater than 2 mm remaining after primary dural closure.
- Subject had undergone laminoplasty decompression.
- Subject had undergone a syringomyelia procedure where the shunt is not placed in the subarachnoid position.
- Subject had undergone a Chiari Malformation procedure that does not entail a dural incision at or below the C1 level.
- Investigator determined that participation in the study may jeopardize the safety or welfare of the subject.

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

[redacted]	[redacted]	[redacted]
Age (years)		
Mean (SD)	47.7 (13.68)	42.3 (14.57)
Range (min, max)	(18.7 ,74.5)	(19.5 ,74.2)
Gender, n(%)		
Female	54 (52.9)	30 (53.6)
Male	48(47.1)	26 (46.4)
Height (cm)		
Mean (SD)	169.9 (11.74)	169.8 (12.52)
Range (min, max)	(132.1 ,188.0)	(132.1 ,193.0)
Weight (Kg)		
Mean (SD)	80.8 (20.62)	83.9 (24.31)
Range (min, max)	(45.7 ,147.4)	(36.0 ,180.0)
BMI (Kg/m^2)		
Mean (SD)	27.8 (6.09)	29.0 (7.74)
Range (min, max)	(17.9 ,46.2)	(16.0 ,64.0)
Smoking Status, n(%)		
Never	62 (60.8)	27 (48.2)
History	21 (20.6)	20 (35.7)
Current	19 (18.6)	9 (16.1)
ASA Score, n(%)		
I	13 (12.7)	4 (7.1)
II	66 (64.7)	40 (71.4)
III	22 (21.6)	12 (21.4)
IV	1 (1.0)	0 (0)

A-V malformation	0 (0.0)	1 (1.8)
Chiari	22 (21.6)	18 (32.1)
Cyst	8 (7.8)	0 (0.0)
Syringomyelia	4 (3.9)	1 (1.8)
Syringomyelia with arachnoid cyst	1 (1.0)	0 (0.0)
Tethered cord	3 (2.9)	1 (1.8)
Tumor removal	64 (62.7)	35 (62.5)

Of the 158 subjects randomized, all 102 subjects (100.0%) treated with the DuraSeal Xact Sealant and 36 of the 56 subjects (64.3%) treated with Standard of Care methods displayed a watertight closure after assigned treatment. Three (3) subjects randomized to Standard of Care were considered not evaluable for the per protocol analysis of the primary efficacy endpoint, as the investigator chose not to use any of the Standard of Care methods per the protocol (i.e., devices designed to provide an intra-operative watertight closure).

Following the first DuraSeal Xact Sealant application, 93 subjects (91.2%) had a watertight closure upon Valsalva, while 9 subjects expressed a non-watertight closure. A second sealant application was performed in all 9 subjects, following which all had a watertight closure upon second post-treatment Valsalva.

Within the Control group, 35 subjects (62.5%) had a watertight closure upon Valsalva following the first Standard of Care application while 21 subjects expressed with a non-watertight closure. A second attempt with Standard of Care methods was attempted in 4 of the 21 subjects, at which time only 1 subject achieved a watertight closure upon second post-treatment Valsalva.

The number and types of adverse events observed in both of the study treatment groups were anticipated, given the medical conditions of the enrolled subjects and nature of the complex neurosurgical procedures performed. There were no deaths or unanticipated adverse device effects observed in the study.

The incidence of protocol defined post-operative CSF leaks was comparable between the two treatment groups (7.8% vs. 5.4%, p= 0.748) despite that fact that the number of adjunctive therapies used in the Control subjects, following determination that subjects were a primary effectiveness endpoint failure, was greater. In fact, in **nineteen** Control subjects the primary dural repair was reinforced with buttressing materials such as synthetic duraplasty materials (i.e., dural graft matrix) or direct dural overlay of an absorbable sponge, see table below.

Further Adjunctive Therapy (ITT Population)

Number of Patients with Further Adjunctive Therapy		
Yes	n (%)	19(33.9)
No	n (%)	32(57.1)
NA	n (%)	5(8.9)
Material Used in Further Adjunctive Therapy		
Adhesive/Glue	n (%)	7(12.5)
Absorbable Gelatin Sponge	n (%)	5(8.9)
Dural Substitute	n (%)	1(1.8)
Dural Graft Matrix	n (%)	7(12.5)
Hemostatic Agent	n (%)	2 (3.6)
Other	n (%)	5(8.9)
Number of Materials Used in Further Adjunctive Therapy	n	19
	Mean	1.6
	Median	1.0
	SD	1.02
	Minimum - Maximum	1.0-4.0

Based on the CDC criteria, the incidence of post-operative SSIs was also comparable between the two groups (6.9% and 7.1% of subjects in the DuraSeal Xact and Control groups, respectively, p=1.00). Although there were a greater number of deep surgical site infections within the DuraSeal Xact group, two events occurred in subjects who were in fact ineligible for the study due to factors that put them at higher risk for infection. One of these subjects was an uncontrolled diabetic and the other had undergone revision surgery for displacement of a lumbar interbody fusion device ("cage"). Furthermore, for another subject within the DuraSeal Xact group who reportedly had a superficial SSI (described as a "crusty lesion" with no confirmation of infection), the CEC did not agree with the investigator's assessment that this was an adverse event at all, yet alone a superficial SSI. If these subjects were excluded from the analysis, the incidence of all infections in the DuraSeal Xact group becomes lower than that of the Control group (3.9% vs. 7.1% respectively) and the frequency of deep surgical site infections would be similar (2.9% vs. 1.8% respectively).
Overall, there were no clinically relevant differences in safety outcomes between the two treatment groups (DuraSeal Xact vs. Control) with respect to laboratory evaluations, neurological exams, vital signs, physical examination and wound healing. There was also **no difference between the two groups specifically with regard to CSF leak at 90 days.** In evaluation of the neurological assessment data and neurological complications, there is no indication of symptom complexes consistent with nerve root compression for subjects treated with the DuraSeal Xact Sealant, a potential concern when using hydrogel-based devices along the nerve roots. The data are consistent with the preclinical evaluation performed in a canine cauda equine discectomy model in which the DuraSeal Xact material (DuraSeal Sealant) was applied following lumbar discectomy, and exposure and abrasion of the lumbar nerve roots. In this severe model there were no significant neurological deficits noted and no adverse reactions were macroscopically observed for any of the dural sealant treated sites

DIRECTIONS FOR USE

Device Preparation – 2 mL Configuration
REF 20-4300

A. Preparing the Blue Precursor

1. Remove the polymer kit tray and the MicroMyst Applicator from their respective outer pouches and introduce into the sterile field.
2. Remove lid from polymer kit tray.
3. Remove and discard syringe cap from Diluent Syringe (blue label).
4. Attach the Diluent Syringe to the Powder Vial.
5. Without depressing the syringe plunger, pierce the vial seal until it is fully depressed (twisting is not required). The entire threaded portion of the vial cap should be depressed bellow the level of the surrounding plastic vial rim.

6. Inject syringe contents into the vial.

7. Gently shake the vial/syringe assembly until the powder is completely dissolved.
8. Invert the vial/syringe assembly, and draw the vial contents back into the syringe.
9. Unscrew the syringe from the vial and discard the vial.
10. Remove syringe cap from Clear Precursor Syringe.
11. Ensure that the precursor volume in each syringe is equal.

B. Assembling the MicroMyst Applicator

1. Remove Applicator assembly from inner pouch.
2. Remove and discard the protective sheath over the Applicator shaft and tape from the Applicator air line.
3. Connect the Applicator air line to the compressed air source (Confluent Surgical Flow Regulator or Confluent Surgical Air Pump), and turn on air source.
4. Attach the Clear and Blue precursor syringes to the Applicator.
5. Attach the Syringe Holder (A) to syringe barrels and the Plunger Cap (B) to syringe plungers.
6. Applicator metal shaft and flexible tip may be angled to improve access or

Device Preparation – 5 mL Configuration
REF 20-4004

A. Preparing the Blue Precursor

12. Remove the polymer kit tray from its outer pouch and introduce into the sterile field.
13. Remove lid from polymer kit tray.
14. Remove and discard syringe cap from Diluent Syringe (blue label).
15. Attach the Diluent Syringe to the Powder Vial.
16. Without depressing the syringe plunger, pierce the vial seal until it is fully depressed (twisting is not required). The entire threaded portion of the vial cap should be depressed bellow the level of the surrounding plastic vial rim.
17. Inject syringe contents into the vial.
18. Gently shake the vial/syringe assembly until the powder is completely dissolved.
19. Invert the vial/syringe assembly, and draw the vial contents back into the syringe.
20. Unscrew the syringe from the vial and discard the vial.
21. Remove syringe cap from Clear Precursor Syringe.
22. Ensure that the precursor volume in each syringe is equal.

B. Assembling the Dual Liquid Applicator

1. Attach the Clear and Blue precursor syringes to the Y-Applicator.
2. Attach the Syringe Holder (A) to syringe barrels and the Plunger Cap (B) to syringe plungers.

   Note:
   Avoid touching the plunger cap before application to avoid inadvertent precursor injection and tip plugging
3. Attach one Spray Tip to the Y-Applicator.

Hydrogel Application
REF 20-4300, REF 20-4004

Note:

- Achieve hemostasis and minimize fluid (CSF, blood) outflow from the target site.
- Ensure that 2-3 mm margins around the defect edge are clear of blood clots, hemostatic reagents and/or loose connective tissue.

When using the MicroMyst Applicator:
1. Prime the Applicator by dispensing a small amount of hydrogel outside the target site until both precursors flow evenly.
2. Paint the target site with a thin coating of hydrogel by gently pressing the Plunger Cap until a thin layer, approximately 1 -2 mm in thickness, is formed.

   Note: Excess gel thickness should be avoided due to hydrogel swelling. Gel thickness should be limited to 1-2 mm. [do we really want to say this?
   Note: The blue color of the hydrogel aids in gauging thickness. As the thickness of the hydrogel increases to 2 mm, the fine epidural vasculature becomes less visible.

When using the Dual Liquid Applicator
3. 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.
4. 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.
5. Hydrogel application beyond the defect edges may be removed with scissors or mechanical disruption. Irrigation immediately after the sealant has solidified is permitted.

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

SYMBOLS USED ON LABELING

	Do not reuse
	Lot Number
REF	Catalog Number
	Use by – year and month
	Latex Free
	See Instructions for Use
	Store below 25° C (77 °F)
	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 Covidien documents or references, contact:
Covidien
101A First Avenue
Waltham MA 02451 USA
1-781-839-1700

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